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Pre-exponential Factor in Hydrogen Abstraction Reactions

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The principal rules governing the variation in the pre-exponential factor in reactions involving the abstraction of hydrogen by atoms and radicals are examined using the activated complex theory. 205 references.

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I. INTRODUCTION

The homolytic removal of a hydrogen atom is one of the reactions that have been studied most fully. The great number of quantitative kinetic measurements allow this reaction to be used for verifying theories of chemical kinetics and such attempts have been made repeatedly. Stepukhovich[1] showed that the values of the pre-exponential factor for some reactions of this type can be given with an accuracy of within an order of magnitude in the framework of the simplest version of activated complex (AC) theory. Other reviews[2-13] dealing with the reactivity of individual radicals have set out from the same position.

The present review systematises the absolute values of the pre-exponential factors for reactions in which hydrogen is abstracted by radicals or atoms, studied up to 1969. These experimental results are discussed from the position of AC theory. Unlike the reviews mentioned above we have excluded trivial geometric factors, so as to investigate the role of finer effects. In particular, the effect on the reaction rate of changes in the frequencies of the deformation vibrations of the reaction centre is examined (Johnston[14] was the first to report the significant part played by this factor). The importance of steric effects is discussed.

In investigations of this type we encounter the peculiar status of the work. On the one hand, the AC theory has recently come under criticism, justified in many respects[15-17]. On the other, at present there are no other theories for explaining such complex reactions. The situation is complicated by the absence of reliable potential surfaces (except for the $H + H_2$ reaction).

The last circumstance decides the matter. Non-empirical numerical calculations of transition probabilities are quite impossible without potential surfaces. The AC theory allows rather far-reaching conclusions to be drawn,

using only the most general ideas about the structure of the transition state. After comparison with experiment these conclusions seem quite plausible. Hence there is no choice at present. In explaining the regularities in rates of reaction AC theory is still the only working tool of the chemist, who has to use it, whilst taking note of its imperfections.

2. EVALUATION OF THE PRE-EXPONENTIAL FACTOR ACCORDING TO ACTIVATED COMPLEX THEORY

The principal equation of AC theory[18]

$$\kappa = \varkappa \frac{kT}{h} \cdot \frac{F^{\neq}}{F^{AB}} \cdot \exp(-E/kT) \qquad (1)$$

expresses the reaction rate in terms of the partition functions of the transition state $F^{\neq}$ and reagents F^{AB}. For comparison with the experimental values of the Arrhenius parameters the temperature dependence must be clearly distinguished. With an accuracy of up to an order of magnitude the temperature dependence of the pre-exponential factor in Eqn. (1) can be disregarded and the factor identified with the Arrhenius pre-exponent A:

$$A = \varkappa \frac{kT}{h} \frac{F^{\neq}_{transl}}{F^{AB}_{transl}} \cdot \frac{F^{\neq}_{rot}}{F^{AB}_{rot}} \cdot \frac{F^{\neq}_{int}}{F^{AB}_{int}} \qquad (2)$$

(here the partition functions $F^{\neq}$ and F^{AB} are expanded). It is assumed that the error involved hardly exceeds the error in AC theory itself. Furthermore, the experimental values of A are usually accurate only to an order of magnitude. Further discussion is based on Eqn. (2). In this section the relative role and methods of evaluating the individual factors in this formula are briefly examined.

a. Geometrical Factor

The contribution of the translational and rotational degrees of freedom in Eqn. (2) will be termed the geometrical factor. It is determined by the geometry of the AC and is readily calculated if the position of the saddle point on the potential surface is known. A change in the geometry within rather wide limits has little effect on the value of the geometric factor. Therefore the geometry can generally be evaluated without a knowledge of the potential surface, by assuming a reasonable distance between the reagents in the AC. The values of the other geometric parameters can be obtained without serious error by interpolation between the reagents and the products or even by putting them equal to the corresponding parameters of the reagents.

b. Internal Degrees of Freedom

To calculate the contribution of the internal degrees of freedom in Eqn. (2) the form of the potential surface close to the saddle point must be known. In this region the potential is approximatelv a quadratic function of the coordinates q_i:

$$V = \frac{1}{2} \sum U_{ij} q_i q_j . \qquad (3)$$

The force constants U_{ij} are determined from the conditions for the best agreement between (3) and the calculated potential surface. Usually calculation can only give the variation of the energy with a limited number of coordinates q. For the remaining degrees of freedom the force constants are evaluated by more or less plausible extrapolation.

After this the normal vibrations and their frequencies ω_i are determined with the aid of standard procedures well known from the theory of vibrational spectra[19].

In the system of "natural" coordinates q_i (changes in bond lengths and valence angles), unlike the cartesian system, the kinetic energy is a non-diagonal quadratic of the generalised momenta p_i:

$$K = \frac{1}{2} \sum T_{ij} p_i p_j . \qquad (4)$$

The coefficients T_{ij} in Eqn. (4) and U_{ij} in Eqn. (3) form the matrices T and U. The squares of the frequencies are given to sufficient accuracy by the eigen values of the TU matrix:

$$\omega^2 = \frac{1}{4\pi^2} Q^{-1} TUQ \qquad (5)$$

where ω^2 is the diagonal matrix of the numbers ω_i^2 and Q the unit matrix, which is directly related to the matrix which determines the form of the normal vibrations.

The frequencies found by Eqn. (5) were also used to calculate the vibrational partition functions in Eqn. (2). One of the values of ω_i^2 is always negative, corresponding to an imaginary frequency. It describes the spatially-unrestricted motion along the reaction coordinate with a maximum (not a minimum) potential at the saddle point.

This procedure has been used by Johnston[20-23].

c. Transmission Factor

Strictly speaking, the quantity κ in Eqn. (2) can be found only by completely solving the problem of the motion of a system of atomic nuclei (which are present in the reactants) in the field of a multidimensional potential with subsequent averaging over the distribution of the initial conditions. When such a solution is obtained the semi-empirical AC theory is generally not needed. Therefore the inclusion of the values of κ in Eqn. (1) is formal and is significant only when this quantity is close to unity.

In several studies[24-32] the classical equations of motion for two- and three-dimensional potential surfaces were integrated numerically. These complex calculations, which require a knowledge of all the surfaces, give a set of trajectories for the motion of representative points depending on the initial conditions. They are discussed in Nikitin's book[33]. The technique of such classical calculations has been developed sufficiently well to investigate comparatively complex systems. For example, Bunker and Pattengill[34] calculated the trajectories for the reactions H + CH_4 and its isotopic analogues (using of course, an empirical potential).

Quantum calculations for empirical potential surfaces[35-38] and also more qualitative quantum estimations[39] show that the classical approximation does not introduce serious errors in those instances where the highest vibrational levels made a negligible contribution to the rate of reaction. There is evidently only one communication about the complete quantum calculation for the reaction H + H_2.[40]

In the language of AC theory such calculations imply calculation of the interaction of the reaction coordinates with the other degrees of freedom. Eqn. (1) is based on

the hypothesis of the absence of interaction. More precisely, the Hamiltonian of the AC theory is the adiabatic Hamiltonian for the vibrational degrees of freedom. The adiabatic approximation postulates the absence of vibrational transitions in motion along the reaction coordinate: the reagents in vibrational states with definite quantum numbers are converted into products in states with the same quantum numbers.

The applicability of the adiabatic approximation is determined by two factors. The sharper the change in the parameters of the potential surface (first the vibrational frequencies and the curvature of the reaction coordinate) along the reaction coordinate and the greater the rate of diffusion along it, the higher the probability of vibrational transitions. On the other hand, this probability decreases with increase in the vibrational quanta, that is, the frequency. In this respect the hydrogen abstraction reactions considered in our review occupy a favourable position. In this case the frequencies usually change little (thus in the reactions

the frequencies of the bonds being broken and being formed are almost the same, whereas the absolute values of the frequencies for the X–H bonds are high). It can be expected that the adiabatic description is applicable here, at least while the temperature is not too high, that is, the rate of relative motion is low and the highest vibrational levels are weakly populated.

There has recently been a series of papers which specially investigated range of applicability of the AC theory[41,42] and also of the calculated reaction probabilities (in particular, for H + H_2,[43-45]) in the adiabatic approximation. Their results agree with the qualitative conclusion drawn above. It must be added that when the adiabacity breaks down and vibrational transitions are observed this effect is levelled to a considerable degree by the averaging of the reaction probabilities over the vibrational states of the products in the concluding stage of the calculation of the overall rate constants. In other words, AC theory can remain a successful semiempirical method of investigating the overall rate constants even if its approximate nature is unsatisfactory for describing the elementary transition probabilities.

If it is assumed that the reaction coordinate is an adiabatically independent degree of freedom then the chief contribution to the value of κ is from a quantum correction for tunnelling through the one-dimensional potential barrier. In essence this is a correction to the classical state sum for the reaction coordinate; it is naturally included in AC theory.

In the calculation the potential barrier (that is, the section of the potential surface along the reaction coordinate around the saddle point) is approximated by an analytical expression: by a truncated parabola[46] or an Eckart potential[20,47]. The latter expression is more admissable[20,47,48]. Le Roy and coworkers[49] calculated κ by using the quantum partition function of an inverted harmonic oscillator (with imaginary virtual frequency)—this corresponds to a non-truncated parabolic model.

In any case the correction κ is determined by the effective mass μ^* for motion along the reaction coordinate, by the curvature of the potential barrier close to the saddle point, and by the energy of the reacting molecules. The characteristic parameter is

$$\lambda = \frac{hc}{kT}(\omega^*)i,$$

where ω^* is the imaginary frequency mentioned above, in cm^{-1}:

$$\omega^* = \frac{1}{2\pi}\sqrt{\frac{U^*}{\mu^*}}$$

(U^* is the negative force constant). κ increases with λ. For a hydrogen abstraction reaction, when the reaction coordinate near the saddle point is close to an antisymmetric vibration, $\mu^* \simeq \frac{1}{2}$ a.m.u. For this reaction (and probably for it alone) the tunnelling correction is rather significant at the experimental temperatures.

Table 1. Transmission coefficients for certain reactions.

T, °K	Reaction					
	H+H_2	H+D_2	H+T_2	D+D_2	CF_3+H–CD_3	CF_3+D–CHD_3
200	44.9	12.9	7.0	10.2	—	—
250	13.1	5.3	3.5	4.5	—	—
300	6.6	3.3	2.4	2.9	18.4	6.0
350	4.2	2.4	1.9	2.2	9.3	3.9
400	3.1	2.0	1.7	1.9	6.0	2.9
450	2.5	1.8	1.5	1.7	—	—
500	2.2	1.6	1.4	1.5	3.4	2.1
1000	1.3	1.2	1.1	1.1	1.5	1.3

Table 1 gives the tunnelling corrections calculated from the Eckart potential for the reaction H + H_2 and its isotopic analogues[48], and also for the reaction CF_3 + CHD_3 [21]. In the first instance the best of the potential surfaces at present available is used. The surface for the second reaction, calculated empirically, must be regarded as a rough approximation.

The figures given in Table 1 are probably too high[20,21]. Quantum calculations on a two-dimensional potential surface give somewhat smaller values of κ [35]. Generally, according to Rankin and Light's results[36], allowance for the quantum effects in hydrogen transfer reactions below 500°K is equivalent to an effective decrease in the height of the potential barrier by 1 kcal $mole^{-1}$.

Hence the existing calculated and theoretical estimates do not give reason for assuming that the errors in determining rate constants by AC theory are too high. However, this conclusion is valid only for thermal processes with relatively low reactant energies in the "chemical" temperature interval 300–500°K. At very high temperatures the assumption that the reaction coordinate is an independent degree of freedom is ineffective. At low temperatures the quantum corrections are significant.

Allowance for tunnelling within the framework of AC theory can increase the calculated value of the constant several times.

3. THE ACTIVATED COMPLEX MODEL

Johnston and coworkers have shown[20-22] that under certain conditions a considerable simplification of the real structure of the reactants and AC by replacing atomic groups by effective point masses, facilitates the calculation and has hardly any effect on the accuracy of the predicted pre-exponential factor.

For the reaction

$$M{-}H{+}R \rightarrow M \ldots H \ldots R \rightarrow M + HR$$

we have taken the AC model shown in Fig. 1. The fragments M and R are each regarded as an entity: their

internal degrees of freedom are obviously not taken into account. With each of the fragments is associated its coordinate system, positioned at its centre of gravity; the Z axis is directed along the M–H and H–R bonds respectively. Clearly there are nine internal degrees of freedom of the reaction centre to be considered:

1. The stretching vibrations of the bonds M–H (s_M) and H–R (s_R).
2. The deformation vibrations of the angles $HMX_M(\gamma_{MX})$, $HMY_M(\gamma_{MY})$, $HRX_R(\gamma_{RX})$, and $HRY_R(\gamma_{RY})$.
3. The deformation vibrations of the angle MHR in the XZ plane (γ_{HX}) and in the YZ plane (γ_{HY}).

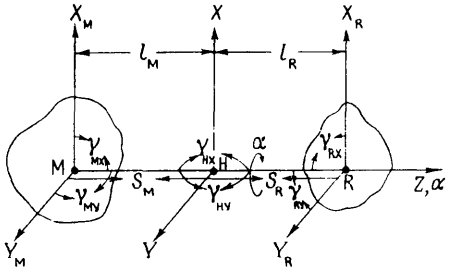


Figure 1. Model of an activated complex.

4. The internal rotation of the fragments M and R (α) relative to the axis α, coincident with the direction of the M–H and H–R bonds.

The following assumptions will be used subsequently:

I. The AC is linear—the bonds MH and HR lie in the same straight line (along axis α, common for both fragments).

II. In the calculation of the vibrational partition functions the systems of principal axes of inertia of the fragments M and R coincide with those coordinate systems introduced for these fragments in Fig. 1.

III. The above nine degrees of freedom do not interact with the internal degrees of freedom of the fragments.

IV. The stretching vibrations (s) of the reaction centre do not interact with the deformation vibrations (γ).

V. The internal rotation (α) is free and does not interact with either the stretching or the deformation vibrations.

These simplifications allow attention to be concentrated on the principal factors which determine the pre-exponential factor. Assumption (I) is almost always adopted in investigating hydrogen abstraction reactions. Assumptions (II)–(V) facilitate the assessment of the vibrational partition functions.

Refinement of the model should evidently not change the general qualitative conclusions. Quantitatively this investigation has the effect of dealing with each reaction separately only when the potential surface is known sufficiently reliably.

Since they do not depend on the form of the potential surface we tried to evaluate the rotational partition functions more accurately. Assumption (II) was not used in their calculation.

In evaluating the vibrational frequencies of the reaction centre in our model the matrix of the kinematic coefficients T_{ij} is needed (4). It has a simple form (Table 2) when assumptions (I)–(V) are used.

The following symbols are used: m_H, m_M, m_R are the masses of the hydrogen atom and the fragments M and R; I^M_X, I^M_Y, I^R_X, I^R_Y the principal moments of inertia of the fragments M or R relative to the corresponding axes; l_M and l_R the distances MH and HR;

$$\frac{1}{l_{MR}} = \frac{1}{l_M} + \frac{1}{l_R}.$$

Table 2 gives the part of the matrix to the right of the diagonal. Internal rotation is not considered, because of its separability.

4. ISOLATION OF THE GEOMETRIC FACTOR AND ITS EVALUATION

Eqn. (2) can be rewritten in the form:

$$A = A_0 A_1 \tag{6}$$

$$A_0 = \frac{kT}{h} \cdot \frac{F^{\neq}_{transl}}{F^{MH}_{transl} F^{R}_{transl}} \cdot \frac{F^{\neq}_{rot}}{F^{MH}_{rot} F^{R}_{rot}} \cdot F^{\neq}_{\alpha}, \tag{7}$$

$$A_1 = \varkappa \frac{\prod_i^7 F^{\neq}_i}{F^{M}_{\gamma MX} \cdot F^{M}_{\gamma MY} \cdot F^{M}_{sM}} \cdot \frac{F^{\neq}_{M\,int}}{F^{M}_{int}} \cdot \frac{F^{\neq}_{R\,int}}{F^{R}_{int}} \cdot \varphi_\alpha \tag{8}$$

In expression (7) $F^{\neq}_{\alpha}$ is the partition function for the free internal rotation α; the remaining symbols are obvious. In Eqn. (8), $F^{\neq}_i$ are the partition functions for the seven vibrations of the reaction centre (one stretching, six deformation); $F^{M}_{\gamma MX}$, $F^{M}_{\gamma MY}$, and F^{M}_{sM} those for the two deformation and one stretching vibrations of the C–H bond in the molecule. The remaining partition functions correspond to the internal degrees of freedom of the fragments M and R in the AC and in the reagents. The factor $\varphi_\alpha \leq 1$ is inserted into Eqn. (8) as a correction to the partition function $F^{\neq}_{\alpha}$ when the internal rotation is really restricted. When it is free, $\varphi_\alpha = 1$.

The quantity A_0 depends solely on the geometry of the AC and is independent of the form of the potential surface. It is not very sensitive to the detailed structure of the AC and therefore can be calculated reliably. The value of A_1, which is determined by the form of the potential surface, can only be estimated with a greater or lesser degree of accuracy.

Let us examine in greater detail the value of A_0 for the reaction of non-linear radicals and molecules. We obtain the first approximation by assuming that one of the reagents (the radical) is small in comparison with the other (the molecule) and the distance between the fragments M and R in the AC is not too great (<3 Å). Then

$$\frac{m_R}{m_R + m_{MH}} \ll 1; \quad \frac{I^R_X I^R_Y I^R_Z}{I^{\neq}_X I^{\neq}_Y I^{\neq}_Z} \ll 1; \quad \frac{I^R_\alpha}{I^R_\alpha + I^{MH}_\alpha} \ll 1.$$

Here m_{MH} is the mass of the molecule. The moments of inertia with subscripts X, Y, and Z are the principal moments of inertia of the radical (superscript R), molecule (superscript M), or AC (superscript ≠). The subscript α denotes calculation of the moment of inertia relative to the rotation axis α. We can assume that:

$$m^{\neq} \approx m_{MH}; \quad I^{\neq}_X I^{\neq}_Y I^{\neq}_Z \approx I^{MH}_X I^{MH}_Y I^{MH}_Z. \quad I^{\neq}_\alpha = \frac{I^R_\alpha I^{MH}_\alpha}{I^R_\alpha + I^{MH}} \approx I^R_\alpha$$

Table 2. Matrix of the kinematic coefficients for a reaction centre.

	s_M	s_R	γ_{HX}	γ_{MX}	γ_{RX}	γ_{HY}	γ_{MY}	γ_{RY}
s_M	$\frac{1}{m_H}+\frac{1}{m_H}$	$-\frac{1}{m_H}$	0	0	0	0	0	0
s_R		$\frac{1}{m_H}+\frac{1}{m_R}$	0	0	0	0	0	0
γ_{HX}			$\frac{1}{m_H l_{MR}^2}+\frac{1}{m_M l_M^2}+\frac{1}{m_R l_R^2}$	$-\frac{1}{m_H l_{MR} l_M}-\frac{1}{m_H l_M^2}$	$-\frac{1}{m_H l_{MR} l_R}-\frac{1}{m_R l_M^2}$	0	0	0
γ_{MX}				$\frac{1}{I_Y^M}+\frac{1}{m_H l_M^2}+\frac{1}{m_M l_M^2}$	$\frac{1}{m_H l_M l_R}$	0	0	0
γ_{RX}					$\frac{1}{I_Y^R}+\frac{1}{m_H l_R^2}+\frac{1}{m_R l_R^2}$	0	0	0
γ_{HY}						$\frac{1}{m_H l_{MR}^2}+\frac{1}{m_M l_M^2}+\frac{1}{m_R l_R^2}$	$-\frac{1}{m_H l_{MR} l_M}-\frac{1}{m_M l_M^2}$	$\frac{1}{m_H l_{MR} l_R}-\frac{1}{m_R l_R^2}$
γ_{MY}							$\frac{1}{I_X^M}+\frac{1}{m_H l_M^2}+\frac{1}{m_M l_M^2}$	$\frac{1}{m_H l_M l_R}$
γ_{RY}								$\frac{1}{I_X^R}+\frac{1}{m_H l_R^2}+\frac{1}{m_R l_R^2}$

where $I_\alpha^{\neq}$ is the reduced moment of inertia[50]. After these simplifications we obtain an approximate value of A_0:

$$A_0' = \text{const} \cdot \left(\frac{1}{m_R}\right)^{3/2} \left(\frac{I_\alpha^R}{I_X^R I_Y^R I_Z^R}\right)^{1/2} \frac{\sigma^R}{\sigma_\alpha^R}, \quad (9)$$

where σ^R is the complete symmetry number of the radical and σ_R^α the symmetry number for internal rotation. The temperature T is included in the constant factor.

A_0' is completely independent of the nature of the molecule MH. Since A_0 Eqn. (7), is determined by the order of magnitude of the pre-exponential factor A, Eqn. (9) gives a basis for unifying reactions for molecules with a single radical into a reaction series. In such series the pre-exponential factor should be approximately constant (excluding instances where the molecules are small). The breakdown of the constancy of A in a reaction series shows a change in the structure of the reaction centre and is associated with A_1 not being constant. Table 12 gives A_0' for various radicals.

Refinement of Eqn. (9) for small molecules, which brings it back nearer to form (7), yields the expression:

$$A_0 = A_0' \cdot \left(\frac{m_R + m_{MH}}{m_{MH}}\right)^{3/2} \cdot \left(\frac{I_X^{\neq} I_Y^{\neq} I_Z^{\neq}}{I_X^{MH} I_Y^{MH} I_Z^{MH}}\right)^{1/2} \cdot \left(\frac{I_\alpha^M}{I_\alpha^M + I_\alpha^R}\right)^{1/2} \cdot \frac{\sigma^{MH}}{\sigma^{\neq}} \quad (10)$$

where σ^{MH} and $\sigma^{\neq}$ are the symmetry numbers of the molecules in the AC. It is easy to obtain formulae, analogous to Eqns. (9) and (10), for reactions of atoms and also of linear radicals and molecules.

5. CONTRIBUTION OF THE INTERNAL DEGREES OF FREEDOM TO THE VALUE OF THE PRE-EXPONENTIAL FACTOR

We will write A_1 of Eqn. (8) in the form:

$$A_1 = \varkappa \cdot A_{11} \cdot A_{12}, \quad (11)$$

$$A_{11} = \frac{\prod_{i=1}^{Z} F_i^{\neq}}{F_{\nu_{MX}}^M F_{\nu_{MY}}^M F_{s_M}^M}, \quad (12)$$

$$A_{12} = \frac{F_{M\,int}^{\neq}}{F_{int}^M} \cdot \frac{F_{R\,int}^{\neq}}{F_{int}^R} \varphi_\alpha . \quad (13)$$

The transmission factor $\varkappa$ takes into account the quantum effects of motion along the reaction coordinate and of the interaction between this coordinate and the remaining degrees of freedom. The value of A_{11} characterises the contribution to the pre-exponential factor of the vibrations of the reaction centre. The value of A_{12} is connected with changes in the internal degrees of freedom of the fragments M and R and can be regarded as a steric effect. The relative role of the factors entering into Eqn. (11) will be examined below.

a. Dependence of the Reaction Coordinate on the Symmetry of the AC

We will write the 2×2 unit of the upper left corner of the matrix of the kinematic coefficients T (Table 2).

$$T = \begin{pmatrix} \frac{1}{m_H} + \frac{1}{m_M} & -\frac{1}{m_H} \\ -\frac{1}{m_H} & \frac{1}{m_H} + \frac{1}{m_R} \end{pmatrix}$$

In the region of the saddle point it is determined by the reaction coordinate and the stretching vibration orthogonal to it. According to Eqn. (5), the form and frequency of the normal vibrations also depend on the matrix of the force constants U:

$$U = \begin{bmatrix} U_{11} & U_{12} \\ U_{21} & U_{22} \end{bmatrix}$$

For a symmetric reaction centre we can put

$$m_R = m_M = M, \quad U_{11} = U_{22} = U, \; U_{12} = u.$$

Then the frequencies of the symmetric and antisymmetric vibrations are

$$\omega_s = \frac{1}{2\pi} \sqrt{\frac{U_s}{\mu_s}},$$

$$\omega_a = \frac{1}{2\pi} \sqrt{\frac{U_a}{\mu_a}},$$

where

$$\frac{1}{\mu_s} = \frac{1}{M}; \frac{1}{\mu_a} = \frac{2}{m_H} + \frac{1}{M}; U_s = U + u; U_a = U - u .$$

At the saddle point U_a is negative and the frequency ω_a is imaginary. The reaction coordinate is an antisymmetric vibration. Since $M \gg m_H$, the effective mass μ_α is close to $\frac{1}{2} m_H$ and, as shown above, the transmission factor can acquire a rather greater value. It also increases when the barrier thickness is reduced, that is, with increase in $|U_\alpha|$.

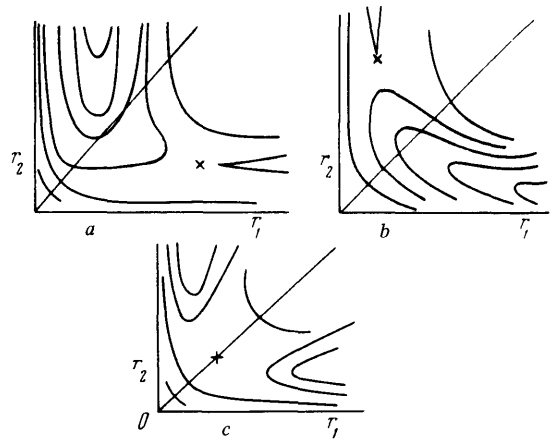


Figure 2. Types of potential surfaces for the transition states M...H...R. *a*) Attractive surface; *b*) repulsive surface; *c*) symmetric surface. $r_1 = s_{RH}$; $r_2 = s_{MH}$.

A reduction in symmetry, as is easily checked, leads to an increase in effective mass for the reaction coordinate and (at strictly the same conditions)—to a decrease in $\varkappa$ owing to the decrease in the quantum corrections. In the limiting cases the following two normal degrees of freedom are obtained:

(a) $U_{22} < 0$; $U_{11} \gg |U_{22}| \simeq |U_{12}|$: the s_{MH} vibration and the relative (counter) motion of MH and R.

(b) $U_{11} < 0$; $U_{22} \gg |U_{11}| \simeq |U_{12}|$: the s_{RH} vibration and the relative (towards opposite sides) motion of M and RH.

In considering the symmetric case in which all the force constants are essential three types of transition

states are obtained. They correspond to three types of potential surface[31,32]:
(a) "Attractive surface": the saddle point is situated on the initial linear part of the reaction coordinate; (b) "repulsive surface": the col point is situated on the final linear part of the reaction coordinate; (c) "symmetric surface": the saddle point is situated at the centre of the curvilinear part.

These surfaces are shown schematically in Fig. 2. For the first two types of AC the reaction coordinate is a relative translational motion. Only in the third "symmetric" type is it an antisymmetric vibration.

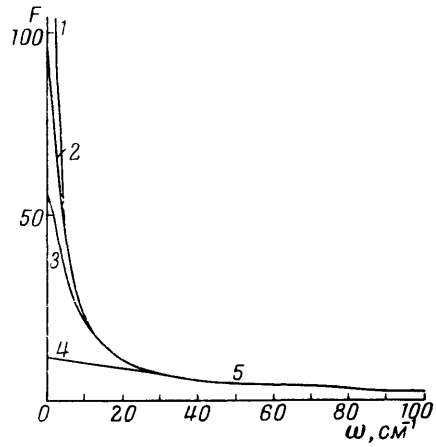


Figure 3. Variation of the vibrational partition functions with frequency (cm^{-1}). Curve *1*) calculated by Eqn. (15); curves *2*)–*4*) calculated by Eqn. (17) for specific values: *2*) for $I = 224$ (a.m.u.)Å^2 corresponds to I_X for the $(C_6H_5)_2CH$ fragment in $AK(C_6H_5)_2CH\ldots H\ldots R$; *3*) for $I = 79.4$, corresponds to the antisymmetric vibration in the XZ plane of $C_6H_5CH_2$ fragments in the activated complex $C_6H_5CH_2\ldots H\ldots CH_2C_6H_5$; *4*) for $I = 3.25$, corresponds to I_X for the CH_3 fragment in $CH_3\ldots H\ldots R$; *5*) calculated by Eqn. (14), the quantum and classical curves coincide in the range of frequencies shown.

b. Deformation Vibrations of the Reaction Centre

We have already noted that the values of the pre-exponential factor A calculated by the AC method are not very sensitive to the choice of model of the transition state. The explanation is that almost all the vibrational frequencies of the AC are high and for the corresponding degrees of freedom at the temperatures which are realised in the usual chemical experiment the higher vibrational levels are almost non-populated. Changes in these frequencies over a very wide range of values has little effect on the value of A. This very circumstance, which is quite general, means that in kinetic studies it is possible to use the AC model, which is quite unacceptable to the spectroscopist, from whose standpoint a change in any frequency by, let us say, 100 cm^{-1} already seems very great.

Fig. 3 shows the variation of the vibrational partition function with the frequency:

$$F_{vib} = \left[1 - \exp\left(-\frac{hc\omega}{kT}\right)\right]^{-1} \quad . \tag{14}$$

At frequencies of 100–300 cm^{-1} and 300–500°K this changes from the quantum kinetic inactive region to the classical:

$$F_{vib} = \frac{kT}{hc\omega} \quad . \tag{15}$$

In subsequent discussion deformation vibrations are important. For these the role of the effective mass μ is played by the effective moment of inertia I; in the one-dimension case, when U is the corresponding force constant,

$$\omega = \frac{1}{2\pi}\sqrt{\frac{U}{I}} \tag{16}$$

The classical state sum equals[51]

$$F_{vib} = \frac{kT}{hc\omega}\,\mathrm{erf}\left[\pi^2 c\omega\left(\frac{2I}{kT}\right)^{1/2}\right] \tag{17}$$

where erf is the error integral.

Eqn. (17) corresponds to a harmonic oscillator with an amplitude bounded between the limits $(-\pi, \pi)$. At very low frequencies they are converted into a one-dimensional rotational partition function $(8\pi^3 IkT)^{1/2}/h$ and at high frequencies it agrees with the classical formula (15) (Fig. 3). This model describes in the simplest manner the conversion of the vibrational degree of freedom into rotational. It was used for estimating the pre-exponential factor in recombinations, where the AC are assumed to be very loose[52].

The kinetically active frequencies are found to lie in the classical region. Frequencies in the quantum region are generally not of interest.

It is evident that the lowest values of the frequencies must be sought among the deformation vibrations. In our model (Fig. 1 and Table 2) the matrix T for six deformation vibrations is broken down into two three-dimensional blocks: vibrations in the XZ and YZ planes.

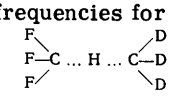
Let us consider the symmetric example (M = R) for motion in the XZ planes. We will introduce the symbols: $m_M = m_R = M$, $l_M = l_R = l$, $I_X^M = I_X^R = I_X$. The vibrations γ_{MX} and γ_{RX}, on mixing, form symmetric $\frac{1}{\sqrt{2}}(\gamma_{MX} + \gamma_{RX})$ and antisymmetric $\frac{1}{\sqrt{2}}(\gamma_{MX} - \gamma_{RX})$ vibrations with kinematic coefficients:

$$\frac{1}{I_s} = \frac{1}{I_X} + \frac{1}{l^2 M} + \frac{2}{l^2 m_H} \text{ and } \frac{1}{I_a} = \frac{1}{I_X} + \frac{1}{l^2 M} \, . \tag{18}$$

The antisymmetric vibration does not mix with the γ_{HX} vibration. It has the most effective moment of inertia, since the term which contains the small quantity m_H in the denominator is lost. According to Eqn. (16), when the force constants are approximately the same the antisymmetric frequency ω_α should be least. These qualitative discussions are still valid when the fragments M and R are different but their mass is sufficiently great and the reaction centre is symmetric or almost symmetric, that is, the M–H and H–R bonds are almost the same.

The closest vibrations of normal molecules to γ_{MX} and γ_{RX} are the in-plane deformation vibrations of the C–H bonds in aromatic molecules. Their frequencies are 400–1000 cm^{-1} [53,54]. These quantities should be reduced by approximately 50% since in comparison with the bonds in the normal molecules the CH bonds in the AC are longer, and their force constants are reduced (in some studies[20-22] it has been assumed that the force constants are reduced by 50%). The frequency ω_α of the antisymmetric vibration is further reduced as a result of

the interaction of γ_{MX} and γ_{HX}. Hence we estimate ω_α to be 100–400 cm^{-1}, lying at the boundary between the classical and quantum regions. We note that allowance for the interactions which we neglected in our model can only decrease the value of the least frequency, that is, the figure obtained can be regarded as the upper bound of the frequency ω_α. The frequencies for the AC



have been calculated[21].

An empirical potential surface was used and the estimates of the force constants were doubly approximate. Nevertheless it is helpful to compare the results of this calculation with our estimates obtained without any calculation. The values found for the vibrational frequencies of the reaction centre are 304 cm^{-1} for the symmetric stretching vibration, 1026 and 470 cm^{-1} for the two doubly degenerate, almost symmetric, deformation vibrations in the XZ and YZ planes, and $\omega_\alpha = 147$ cm^{-1} for the doubly degenerate, (almost) antisymmetric vibrations. The two antisymmetric vibrations contribute a factor of 4.3 to the vibrational partition function (the full value of this sum is ~10). In the calculation mentioned allowance was made for all interactions of the normal coordinates, including interaction with the vibrations within the fragments CF_3 and CD_3. Strictly speaking, these frequencies belong not to the above vibrations of the reaction centre but to the normal vibrations which contain these vibrations as one of their components (probably the main one). Consequently, these results confirm numerically that our model is suitable for approximate evaluations.

If the force constant U in Eqn. (16) is approximately the same for different AC then the upper bound of the deformation frequency ω_α corresponds to small values of the moment of inertia I_X in expression (18). This happens, for example, when the fragments M and R (or even one of them) are CH_3 groups, that is, only the hydrogen atoms contribute to the moment of inertia I_X. Then the effective moment of inertia I_α is also small. As an example, we give the calculated[22] least values of the frequencies for the reactions Cl + HM. For M = CH_3, CH_2Cl, $CHCl_2$, and CCl_3 they are 457, 233, 187, and 159 cm^{-1} respectively.

When the fragments M and R, or one of them, are atoms, the corresponding deformation vibrations generally disappear. Therefore the lowest frequencies for the reactions of radicals with the same molecules should be less.

Hence for a symmetric reaction complex (surface of type *c* in Fig. 2)the contribution of the deformation vibrations (mainly due to two antisymmetric vibrations) can, according to Eqn. (12), lead to values of $A_{11} \simeq 10-100$.

Considerably greater effects must be expected for potential surfaces of types *a* and *b* (Fig. 2). For these the value of one of the force constants U in formula (16) can be expected to be very small. The frequency is reduced accordingly. At the limit this corresponds to the change of the (almost) antisymmetric deformation vibrations into rotation of the fragment M or R according to Eqn. (17). Since there are thus two degrees of freedom (in the planes XZ and YZ) values of $A_{11} \simeq 10^3-10^4$ can be obtained.

We must remember that, as shown above (Section 2c), the adiabatic resolution of the variables is of little effect for low frequencies. Although the change in frequency along the reaction coordinate is also smaller in this instance, the problem of whether AC theory can describe the contribution of kinetically active low-frequency vibrations is unresolved. The conclusion about the increase in the pre-exponential factor remains in force but the estimates given of the magnitude of this effect could be greatly changed on making allowance for the exchange of energy between the reaction coordinate and the rotational degrees of freedom.

c. Internal Degrees of Freedom of the Reactants

The value of A_{12} in expression (13) is usually close to unity. This is because even if any frequencies of the fragments M and R are altered in the AC as compared with the isolated reactants, all the same these frequencies are kinetically inactive. There are exceptions when the structure of the fragments is rather complex:- there are bulky substituents. Then internal rotations which are restricted in the reactants can be freed in the formation of the AC, or on the other hand rotations which are free in the reactants can become restricted. An example of this is the restriction of the free rotation around the M...H...R bond in the AC. Such steric effects can make significant contributions to the pre-exponential factor.

6. SUMMARY OF THE EXPERIMENTAL VALUES OF THE PRE-EXPONENTIAL FACTOR

Tables 3–10 give the experimental values of the pre-exponential factors recalculated per single active (in bold type in the tables) hydrogen atom (A, litre $mole^{-1}$ s^{-1}). Reactions in the gas phase and liquid phase are considered (in the latter instance, in non-polar media). Results from existing reviews on hydrogen abstraction reactions[55-59] and from the individual papers listed in the references are used.

The absolute values of A for the reactions of a fluorine atom were obtained from results on competing fluorination and the reference value of $A = 10^{10}$ litre $mole^{-1}$ s^{-1} for the reaction F + C_2H_6. This value was calculated by assuming that the fluorine atoms react with C_2H_6 at every collision[2].

Absolute values of A in the reactions of Cl atoms were obtained from results on competitive chlorination; in the reactions of Cl with various isotopic modifications of H_2 and CH_4 the standard adopted was the value of $A = 4.1 \times 10^{10}$ litre $mole^{-1}$ s^{-1} for the reaction Cl + H_2 [2], in other instances the reference quantity was $A = 0.6 \times 10^{10}$ litre $mole^{-1}$ s^{-1} for the reaction Cl + CH_4 [2].

For the reactions of Br atoms the absolute values of the pre-exponential factor were obtained from results on competitive bromination and the absolute value of $A = 1.67 \times 10^7$ litre $mole^{-1}$ s^{-1} for the reaction Br + CH_3Br [2].

In determining the absolute values of A for the reactions of alkyl and halogenoalkyl radicals the reference quantities used were A for their recombinations. For the reaction CH_3 + CH_3 A was taken as 2.2×10^{10} litre $mole^{-1}$ s^{-1} [60], and for CF_3 + CF_3 $A = 2.3 \times 10^{10}$ litre $mole^{-1}$ s^{-1} [61]. For the recombination of other alkyl and halogenoalkyl radicals we took $A = 10^{11}$ litre $mole^{-1}$ s^{-1} [59].

The absolute values of A for the reactions of 2-cyano-2-methylethyl radical were calculated from our results[62]. $A = 2 \times 10^9$ litre $mole^{-1}$ s^{-1} was used as the reference quantity for the recombination of $C(CH_3)_2CN$ radicals[63].

7. CALCULATION OF MOMENTS OF INERTIA

The principal moments of inertia I_X, I_Y, and I_Z are determined as the eigenvalues of the I matrix of the inertia tensor. The direction cosines of the principal axes

Table 3. Pre-exponential factor of reactions involving the abstraction of hydrogen by atoms.

Atom	Molecule	T, °K	$10^{-10}A$, litre mole^{-1} s^{-1}	Reference
1	2	3	4	5
H	H_2	400	6.0	64
	HD	400	1.3	64
	DH	400	1.2	64
	D_2	400	2.1	64
	D_2	368—468	0.2	65
D	D_2	300—750	2.5	66
	H_2	400	2.3	64
	H_2	250—750	2.2	66
	HD	400	1.0	64
	DH	400	0.9	64
	D_2	400	3.1	64
	CH_4	1220—1790	5.0	67
	CH_4	372—436	0.0003	68
H	CH_4	500—803	0.02	69
	CH_4	673—753	1.4	70
D	CH_4	620—738	0.3	71
H	CH_3CH_3	323—523	0.2	72
	$CH_3CH_2CH_3$	330—793*	3.3	73
	$CH_3CH_2CH_3$	330—490	0.3	74
	$CH_3(CH_2)_2CH_3$	323—523	0.01	72
	$CH_3(CH_2)_2CH_3$	753—793*	0.8	72
	$(CH_3)_3CH$	753—793*	1.0	72
	$(CH_3)_3CH$	323—523	0.04	75
O	H_2	409—928	2.0	76
	CH_4	300—900	0.4	76
	C_2H_6	320—590	0.3	76
F	H_2	178—373	5.9	77, 78
	CH_4	178—373	3.1	78
	CH_3CH_3	178—373	1.3	9
	$CH_3CH_2CH_3$	178—373	0.6	9
	$CH_3CH_2CH_3$	178—373	0.6	9
	$CH_3(CH_2)CH_3$	178—373	0.5	9
	$CH_3(CH_2)_2CH_3$	178—459	0.6	9, 78
	$(CH_3)_3CH$	178—373	0.5	9
	$(CH_3)_3CH$	178—459	0.7	9, 78
	$(CH_3)_4C$	178—373	0.5	9
	cyclo-C_6H_{12}	178—373	0.5	9
Cl	H_2	—	4.1	2
	HD	243—350	3.3	79
	HT	234—345	3.0	80
	D_2	273—305	3.0	81
	CH_4	200—600	0.6	8, 82
	CH_3CH_3	273—588	1.5	2
	$CH_3CH_2CH_3$	200—600	1.7	8
	$CH_3CH_2CH_3$	200—600	3.6	8
	$CH_3(CH_2)_2CH_3$	200—600	1.4	8
	$CH_3(CH_2)_2CH_3$	200—600	2.4	8, 78
	$(CH_3)_3CH$	200—600	1.3	8
	$(CH_3)CH$	200—600	2.1	8, 78
	$(CH_3)_4C$	200—600	1.4	8
	cyclo-C_3H_6	200—600	0.9	8
	cyclo-C_4H_8	200—600	3.2	8
	cyclo-C_6H_{10}	200—600	2.3	8, 82
	CH_3Cl	273—573	1.1	82, 83
	CH_2Cl_2	273—573	1.3	83
	$CHCl_3$	273—573	0.7	83
	$CDCl_3$	253—573	0.5	83, 84
	C_2H_5Cl	200—600	0.7	82, 8
Cl	C_6HCl_5	273—573	0.5	83, 85
	$ClCH_2(CH_2)_2CH_3$	308—419	1.2	86
	$FCH_2(CH_2)_2CH_3$	273—419	1.3	86
	$ClCH_2CH_2CH_2CH_3$	308—419	1.1	86
	$ClCH_2CH_2CH_2CH_3$	308—419	2.4	86
	$FCH_2CH_2CH_2CH_3$	273—419	1.9	86
	$FH_2CCH_2CH_2CH_3$	273—419	2.6	86
	H_2	273—1071	14.0	2
Br	D_2	—	10.0	2
	CH_4	210—503	1.5	87
	CH_4	311—421	5.0	10
	CH_3Cl	477—614	1.3	10
	CH_3Br	210—503	1.7	87
	CH_3CH_3	332—573	1.2	10
	$(CH_3)_4C$	330—573	1.5	10
	$CH_3CH_2CH_3$	286—418	2.5	10
	$CH_3(CH_2)_2CH_3$	267—371	4.1	10
	$(CH_3)_3CH$	311—421	2.0	10
	$CHCl_3$	420—455	1.5	88
I	H_2	667—800	5.0	11
	D_2	667—800	5.0	12
	$CH_3CH_2CH_3$	580—613	5.0	89
	$(CH_3)_3CH$	525—583	7.6	90
	$CH_3—CH_2—CH=CH_2$	465—572	0.1	91
	CH_3CHO	495—541	2.0	92

* The reaction is not selective at high temperature. The corresponding values of A are obtained by dividing the experimental value by the total number of hydrogen atoms.

Table 4. Pre-exponential factors for the reactions: $CH_3 + CH_3-X$.

Molecule	T, °K	$10^{-7}A$, litre mole^{-1} s^{-1}	Reference
1	2	3	4
CH_4	473—623	17	93
	623—793	16	94
CH_3F	—	9.3	55
CH_3Cl	—	16	55
CH_3Br	—	70	55
CH_3OH	406—473	2.0	95
	413—523	6.7	96
	403—523	0.8	97
CH_3OD	403—523	6.6	96, 98
CD_3OH	403—523	6.7	96, 98
	406—473	6.0	95
	403—523	0.5	97
CH_3NH_2	393—448	3.3	99
CD_3NH_2	393—448	2.6	99
CH_3ND_2	393—448	4.7	99
$CH_3N_2CH_3$	383—453	1.3	99
	383—458	1.3	100
	383—453	1.2	101
$CH_3N_2D_2$	383—453	1.7	100
CH_3CN	373—573	6.7	102
CH_3SH	403—473	2.5	103
$CH_3—CH_3$	433—493	27	104, 105
	578—689	18	106, 107
$CH_3CH_2CH_3$	433—423	12	107
	568—792	1.1	108
$(CH_3)_4C$	458—581	16	109
	423—573	1.3	110, 111
$(CH_3)_3CC(CH_3)_3$	343—613	0.7	112
$(CH_3)_3C(CH_3)_2CC(CH_3)_3$	343—617	0.7	112
$(CH_3)_3CD$	568—729	0.1	113
$CH_3CH=CH_2$	343—613	1.4	112
$CH_3—CH=CH—CH_3$	343—613	1.1	112
$(CH_3)_2C=CH_2$	343—613	1.8	112
$(CH_3)_2C=C(CH_3)_2$	343—613	2.5	112
$CH_3C\equiv CCH_3$	343—613	5.4	112
CH_3OCH_3	343—613	3.3	112
	413—523	6.7	96
CH_3OOCH_3	393—523	6.1	114
CH_3COCH_3	413—523	4.8	96
	403—473	3.8	103
	343—613	5.0	112
	386—573	4.7	115
		4.5	116
	393—523	5.7	117
	373—573	6.7	118
CD_3COCD_3	413—523	7.0	96
	393—523	3.7	114
$CH_3COCOCH_3$		0.9	55
CH_3OCOCH_3	450—489	3.7	114
$(CH_3)_3COOC(CH_3)_3$	450—489	4.3	119
$N(CH_3)_3$	400—440	25.0	120
	343—613	5.8	112
$(CH_3)_2NCOCH_3$	396—433	2.8	121
CH_3CONH_2	398—430	2.6	122
$CH_3C_6H_5$	395—532	4.5	122
$CH_3C_6H_5$	343—613	3.3	112
$CH_3COC_6H_5$	33—533	1.0	123
o-$CH_3C_6H_4CH_3$	557—687	1.7	124
	373—473	2.3	125
m-$CH_3C_6H_4CH_3$	273—368	0.8	126
	373—473	4.8	125
	273—368	0.8	126
p-$CH_3C_6H_4CH_3$	373—473	1.1	125
	273—368	0.8	126
p-$FC_6H_4CH_3$	606—733	0.4	127
o-$FC_6H_4CH_3$	604—734	0.6	127
m-$FC_6H_4CH_3$	602—753	0.5	127
$C_6H_5(CCH_3)_3$	273—368	0.5	126

(I_i, m_i, n_i) form a matrix of eigenvectors **I**. The matrix elements I_{ik} were calculated by the formula

$$I_{ik} = \Sigma m_n(x_n^2\delta_{ik} - x_{ni}x_{nk}) - m(a^2\delta_{ik} - a_ia_k), \qquad (19)$$

where x_n is the radius vector of the atom n, a the radius vector of the centre of inertia, m_n the mass of atom n, and $m = \Sigma m_n$ the mass of the entire system.

This standard procedure was used to calculate the moments of inertia of the molecules and radicals. Tables 11 and 12 give the results. Fig. 4 shows the geometric characteristics employed in the calculation and the choice of coordinate axes.

Since the geometry of the AC is not known precisely, it is desirable to use a simple approximate method for calculating its moments of inertia. Assuming that the radical is small in comparison with the molecule and the

distance between the fragments M and R is not too great we will model the fragment R by the point mass $m_R = \Sigma m_n$ equal to it in mass and located at its centre of inertia R with radius vector r. We choose as coordinate system the principal axes of the molecule with the direction cosines from Table 12. Then Eqn. (19) takes the form:

$$I_{ik}^{\neq} = I_i^M \delta_{ik} + m_R (r^2 \delta_{ik} - r_i r_k) - (m_{MH} + m_R) \cdot (a^2 \delta_{ik} - a_i a_k) .$$

In the system of coordinates used

$$a_i = \frac{m_R}{m_R + m_{MH}} r_i ,$$

whence

$$I_{ik}^{\neq} = I_i^M \delta_{ik} + \mu (r^2 - r_i r_k); \ \mu = \frac{m_{MH} \cdot m_R}{m_{MH} + m_R} .$$

By using perturbation theory, we obtain to the first order:

$$I_i^{\neq} = I_i^{MH} + \mu (r^2 - r_i^2) \qquad (20)$$

Table 5. Pre-exponential factors for the reactions $CH_3 + CH_2X^1X^2$ and $CH_3 + H-C\swarrow$.

Molecule	T, °K	$10^{-7}A$, litre mole^{-1} s^{-1}	Reference
1	2	3	4
$CH_3CH_2CH_3$	578—723	36	107, 113
$CH_3CD_2CH_3$	629—723	7.0	104
$CH_3(CH_2)_2CH_3$	523—723	13	104
	668—744	19	110
$CH_3(CH_2)_3CH_3$	668—744	12	110
$CH_3(CH_2)_4CH_3$	668—744	15	110
CH_3CH_2OH	403—523	20	98
	463—613	20	128
cyclo- C_3H_6	668—744	12	110
	427—713	17	129
cyclo- C_4H_8	427—713	6.3	129
cyclo- C_5H_{10}	427—713	6.6	129
cyclo- C_6H_{12}	427—713	6.6	129
cyclo- C_7H_{14}	427—713	6.3	129
CH_3=CH·CH_2CH_3	343—613	5.5	112
CH_2=CH—$CH_2CH_2CH_3$	343—613	5.8	112
CH≡C—CH_2CH_3	343—613	27	112
$(CH_3)_2NH$	383—448	6.9	101
$CH_3CH_2NH_2$	393—453	8.0	121
$CH_3CH_2NH_2$	283—453	8.0	130
$(CH_3CH_2)_2NH$	396—533	15	121
$(CH_3CH_2)_3N$	396—533	3.3	121
$NH_2(CH_2)_2NH_2$	363—448	2.0	131
$(CH_3CH_2)_2O$	318—353	25	132
$(CH_3CH_2)_2CO$		2.5	132
CH_3CH_2CN	373—573	1.0	102
$C_6H_5CH_2CH_3$	273—368	1.5	126
$(C_6H_5)_2CH_2$	273—368	3.2	126
$(C_6H_5)_2(CH_2)_2$	273—368	1.3	126
CH_2Cl_2		10	133
$(CH_3)_3CH$	578—732	30	107, 113
	343—613	6.3	112
$(CH_3)_2CH$-$CH(CH_3)_2$	343—613	6.5	112
$(CH_3)_2CH(CH_3)CHCH(CH_3)_2$	343—613	4.3	112
$(CH_3)_2CH$—OH	297—613	6.3	112
$(CH_3)_2CH$—OH	408—523	1.5	96, 98
$(CH_3)_2CH$—O—$CH(CH_3)_2$	408—523	1.6	96
	453—513	8.0	112
$(CH_3)_2CHOOCH(CH_3)_2$	394—432	1.6	134
$C_6H_5C(CH_3)_2H$	273—368	2.7	126
n-$C_4H_9C_6H_4C(CH_3)_2H$	273—368	2.1	126
$(C_6H_5)_2CH$	273—368	3.9	126
C_6H_5—CHC_5H_{10}	273—368	3.0	126
$CHCl_3$		6.0	133
CF_3H		2.3	135
CF_3CF_2H		14	135
n-C_3F_7H		91	135

Formula (20) allows the moments of inertia of the AC to be found easily from the data of Tables 11 and 12. When there is a large radical and a small molecule, the moment of inertia of the molecule is replaced by the moment of inertia of the radical and the radius vector of the radical by that of the molecule.

When the moments of inertia I_i^{MH} in formula (20) are the same or very similar to one another, the error in the individual values of $I_i^{\neq}$ can be rather high (then perturbation theory with allowance for degeneracy leads to the full task of diagonalisation of the I matrix) but the product $\Pi I_i^{\neq}$ is also determined with acceptable accuracy in this instance (cf. the calculation for methane). Table 13 compares the calculations by Eqn. (20) with the full calculations.

In the complete calculation the geometry of the fragments M and R is unchanged in the AC. The distance between the carbon atoms of the reaction centre C—H—C was assumed equal to 2.4 Å. For a reaction centre X—H—Y, where although one of the atoms X and Y is not a carbon atom, the lengths of the bonds X—H and Y—H in the AC were evaluated by the Pauling formula[23,199],

Table 6. Pre-exponential factors for the reactions: $CH_3 + H-COX$.

Molecule	T, °K	$10^{-8}A$, litre mole^{-1} s^{-1}	Refs.	Molecule	T, °K	$10^{-8}A$, litre mole^{-1} s^{-1}	Refs.
HCOH	392—448	0.8	120	C_2F_5COH	673—717	79	136
H—$OCCH_3$	392—448	7.9	120	C_3F_7COH	673—717	160	136
H—COC_2H_5	392—448	10	120		393—523	1.8	117
HCO n-C_3H_7	392—448	6.3	120	$HCOOCH_3$	348—443	0.5	137
HCO iso- C_3H_7	392—448	40	120	$HCOOC_2H_5$	350—450	0.3	138, 139
HCO n-C_4H_9	392—448	13	120	HCOO n C_3H_7	392—448	0.1	120
HCO s-C_4H_9	392—448	200	120	HCOO i-C_3H_7	350—450	0.8	120, 139
HCO i-C_4H_9	392—448	20	120	HCOO n C_4H_9	393—453	0.4	120
HCO t-C_4H_9	392—448	100	120	$HCONH_2$	443—520	0.3	140
CH_3CH-$CHCOH$	392—448	200	120	$HCON(CH_3)H$	434—560	0.8	140
CF_3COH	673—717	13	136	$HCON(CH_3)_2$	393—571	0.3	140

Table 7. Pre-exponential factors for the reactions $CH_3 + H-N\swarrow$, $CH_3 + H-O-$, and $CH_3 + H-S-$.

Molecule	T, °K	$10^{-7}A$, litre mole^{-1} s^{-1}	Refs.	Molecule	T, °K	$10^{-7}A$, litre mole^{-1} s^{-1}	Refs.
NH_3	383—453	2.3	141	$(C_2H_5)_2NH$	398—430	60	142
ND_3	383—453	3.3	141	$(C_3H_7)_2NH$	398—430	100	142
H_2NNH_2	383—453	2.5	100, 141	$(CH_3)_2NH$	383—448	1.5	101
CH_3NH_2	363—448	0.2	99	CH_3OH	403—523	3.0	96
CD_3NH_2	368—448	0.3	99		403—523	2.9	97
$(CH_3)_2NNH_2$	383—448	10	100	C_2H_5OH	403—523	8.0	96
$C_2H_5NH_2$	383—453	0.5	130	iso-C_3H_7OH	403—523	0.1	96
CH_3ONH_2	383—448	2.5	99	iso-C_3H_7OD	403—523	0.1	96
$H_2NCH_2CH_2NH_2$	363—448	0.5	131	CD_3SH	403—523	10	103
$(CH_3)_2NN(CH_3)H$	383—448	0.5	100	H_2S	323—473	13	143
$(CH_3)_2NH$	398—430	52	142				

$l_{H-X}^{\neq} = l_{H-X} - 0.6 \ln n$, where l_{H-X} is the length of the H—X bond in the ordinary molecule and n the bond order (assumed to be 0.5).

8. ANALYSIS OF THE VALUES OF A_i FOUND FROM EXPERIMENT

Having determined the value of A_0 from formulae of the type of Eqn. (10) with moments of inertia calculated by the method described in the previous section, "experimental" values of A_i can be obtained. According to Eqn. (6) the experimental values of the pre-exponential factor must be separated from A_0. Table 14 gives the values of A_i thus found. The values of A_0 were calculated for 373 °K.

In discussing the values of A_1 caution is necessary because both the experimental results and the AC theory itself, which form the basis of the discussion, are imprecise. We will examine the effects which seem to be unquestioned: either they are of the order of 10^2-10^3, or (for effects of the order of 10^1) they are repeated with sufficient regularity in several reaction media.

According to Eqn. (11), A_1 is the product of three factors. The transmission factor κ can be either greater or less than unity owing to the competition of two effects: tunnelling and the interaction between the reaction coordinate and the remaining degrees of freedom (strictly,

Table 8. Pre-exponential factors for hydrogen abstraction by trifluoromethyl radicals.

Molecule	T, °K	$10^{-7}A$, litre mole^{-1} s^{-1}	Refs.	Molecule	T, °K	$10^{-7}A$, litre mole^{-1} s^{-1}	Refs.
CH_4	391—673	14	144	$CH_3CH_2CH_3$	540—570	23	149
	426—568	23	145		300—392	28	158
	357—534	24	146	$CH_3(CH_2)_2CH_3$	300—392	3.5	159
CD_4	379—560	3.8	146		540—570	7.0	149
CHD_3	601—900	11	21		357—435	5.0	155
CH_3Cl	417—673	46	145	cyclo-C_5H_{10}	540—570	3.5	149
CH_3Br*	423—533	14	142	cyclo-C_6H_{12}	292—364	4.7	151
CH_3Br**	423—533	48	142	$(CH_2)_2NH$	433—503	2.0	158
CH_3I	327—583	1.4	142	$(CH_3)_2CHCH(CH_3)_2$	540—570	3.5	149
CH_2Cl_2	358—722	8.4	147	$(CH_3)_3CH$	350—392	14	159
$CHCl_3$	367—999	14	147		291—673	15	144
	390—524	97	146		338—537	300	146
$CDCl_3$	338—537	60	146	CH_3OCOH	393—523	26	117
CH_3CH_3	601—900	7.0	11	CH_3OCOD	393—523	20	117
	668—797	21	148	CH_3COH	291—673	6.9	144
$C(CH_3)_4$	540—570	4.8	149	CF_3COH	291—673	54	144
CH_3CH_3	668—797	8.0	148		300—434	90	160
$CH_3C_6H_5$	300—383	4.3	150	C_2F_5COH	300—434	13	160
$CH_3C_6H_5$	300—400	1.3	151	C_3F_7COH	300—580	47	161
	571—627	7.0	149		300—434	12	160
$CH_3C_6F_5$	300—383	1.9	150	CD_3OH	357—435	0.3	155
o-$CH_3C_6H_4CH_3$	310—341	8.0	152	CH_3OD	650—798	400	156
CH_3COCF_3	298—623	0.7	153	CH_3NH_2	303—433	0.4	157
CH_3COCH_3	302—442	1.0	154	$(CH_3)_2NH$	300—434	3.2	158
	540—570	5.0	149	$(CH_3)_2ND$	300—434	7.5	158
CH_3OH	357—435	0.3	155	$(CH_3)_2NH$	300—434	2.0	158
CD_3OH	357—435	0.5	155	H_2S	368—434	8.0	162
CH_3OD	680—798	11	156		330—370	20	163
CH_3CO_2H	393—523	3.3	117		333—384	33	164
CH_3NH_2	303—433	1.7	157	D_2S	353—484	40	165
CH_3ND_2	303—433	4.0	157	NH_3	286—513	1.2	165
$(CH_3)_2ND$	300—434	7.3	158	ND_3	286—513	0.9	165
$(CH_3)_3N$	300—434	11	158	SiF_3H	383—563	135	166

* High value.
** Low value.

the transmission factor). The vibrational factor A_{11} is greater than or equal to unity. The steric factor A_{12} can be either greater or less than unity.

The last two factors are not present in reactions of atoms with diatomic molecules. On the basis of the data in Table 14 in this instance $A_1 \simeq \kappa \leqslant 1$. Consequently, the opposing effects which contribute to κ are either insignificant or compensated. When a factor of 2 – 5 is taken for the tunnelling, the transmission factor proper is 0.1 – 0.5. Thus or otherwise, κ is of the order of unity ($\kappa \simeq 0.3-1$), that is, the simple AC theory does not contradict experiment in any instance. Subsequently we will take $\kappa = 1$.

For the remaining reactions it is possible with sufficient confidence to distinguish those instances in which the steric effect is absent ($A_{12} \simeq 1$). These are reactions with molecules of simple structure. From Table 14 we find $A_1 \simeq A_{11} \geqslant 1$ for them. Table 15 gives values of A_1 for typical pairs of reactants.

From the results of Table 15: (1) In the reactions of one molecule with a series of radicals A_{11} is least for the radical CH_3; (2) in the reactions of one radical with a series of molecules it is least for the CH_4 molecule.

Table 9. Pre-exponential factors for hydrogen abstraction reactions of alkyl, halogenoalkyl, phenyl, and alkoxy radicals.

Radical	Molecule	T, °K	$10^{-7}A$, litre mole^{-1} s^{-1}	Reference
1	2	3	4	5
C_2H_5	CH_4		16	58
	C_2H_6		11	58
	$C(CH_3)_4$	323—573	3.0	167
	$N(CH_3)_3$	363—431	0.3	168
	$CH_3(CH_2)_2CH_3$	323—573	5.0	167
	$CH_3(CH_2)_4CH_3$	360—525	3.4	169
	$CH_3(CH_2)_5CH_3$	400—476	10	170
	$CH_2{=}CH{-}CH_2(CH_2)_3CH_3$	357—473	16	170
	$CH_2{=}CH{-}CH_2(CH_2)_4CH_3$	298—456	13	170
	$CH_3CH_2CH_2CH{=}CHCH_2CH_2CH_3$	359—439	16	170
	$CH{\equiv}C{-}CH_2(CH_2)_3CH_3$	298—454	8.0	170
	cyclo-C_6H_{10}	300—526	31	170
	$CH_3COCH_2CH_3$		10	56
	$(CH_3CH_2)_2CO$		6.2	56
	$(CH_3CH_2)_2CO$	363—433	6.2	168
	$(CH_3CD_2)_2CO$		20	56
	$(CH_3CD_2)_2CO$		8.3	56
	$(CD_3CD_2)_2CO$	298—587	10	171
	$(CH_3CH_2)_2N_2$		4.0	56
		301—425	13	172
	$(CH_3CH_2)_2Hg$		1.0	56
	cyclo-C_6H_{12}	371—564	4.4	169
	$(CH_3)_3CH$	323—573	8.3	167
	CH_3CH_2COH	323—778	18	173
	C_3H_7OCOH	340—440	8.0	120
	H_2NNH_2	363—430	1.3	124
	CH_3COCH_3	403—503	1.9	117
	$(CH_3CH_2CH_2)_2CO$	328—530	0.6	174
n-C_3H_7	n-C_3H_7COH	371—634	20	175
	$CH_3CH_2CH_2COH$	464—573	5.0	175
iso-C_3H_7	n-C_3H_7OCOH	347—451	16	176
	$(CH_3)_2CHCOH$	556—650	2.5	177
	$(CH_3)_2CDCOCD(CH_3)_2$		0.4	59
	$(CH_3)_2CDCOCD(CH_3)_2$		33	59
	iso-C_3H_7COH	390—627	16	177
	iso-C_3H_7OCOH	367—454	2.5	176
	$(CH_3)_2CHNNCH(CH_3)_2$		1.3	59
n-C_4H_9	n-C_4H_9COH	334—503	7.9	178
s-C_4H_9	s-C_4H_9COH	297—621	5.0	179
iso-C_4H_9	n-C_4H_9OCOH	348—459	1.6	180
	iso-C_4H_9COH	451—580	50	181
	$(CH_3)_2CHNNCH(CH_3)_2$	298—441	1.6	182
t-C_4H_9	t-C_4H_9COH	392—448	3.2	120
C_6H_5	CH_4	561—697	20	124
		453—623	3.6	183
	cyclo-C_3H_6	561—657	6.3	124
	$(CH_3)_3CH$	561—697	63	124
	$CH_3COC_6H_5$	561—697	13	124
		453—623	1.3	183
CH_3O	CH_4	403—523	16	97
	$CH_3C_6H_5$	463—536	4.0	184
	$(CH_3)_4C$	463—536	4.0	184
	$CH_3(CH_2)_2CH_3$	463—536	0.6	184
	cyclo-C_3H_6	463—536	21	184
	$(CH_3)_3CH$	463—536	8.0	184
	$CH_3CH_2CH_3$	463—536	8.0	184
	CH_3COOCH_3	450—483	1.3	119
	CH_3OCOH	450—489	160	114
C_2H_5O	$C_2H_5COOCH_2CH_3$		2.5	58
CH_2F	$(CH_2F)_2CO$	294—585	1.25	185
C_2F_5	CH_4	423—544	10	186
	C_2F_5CHO	300—588	19	161
C_3F_7	CH_4	370—455	2.4	187
	CH_3CH_3	379—455	29	187
	cyclo-C_6H_{12}	296—566	1.2	188
	$(CH_3)_2CO$	300—579	11	189
	C_3F_7CHO	300—588	1.8	161
CCl_3	$CH_3(CH_2)_3CH_3$	423—630	0.3	190
	$CH_3(CH_2)_3CH_3$	423—630	0.2	190
	$FCH_2(CH_2)_2CH_3$	423—630	0.8	190
	$FCH_2CH_2CH_2CH_3$	423—630	0.5	190
	$CF_3CH_2(CH_2)_2CH_3$	423—630	0.1	190
	$CF_3CH_2CH_2CH_2CH_3$	423—630	0.8	190
	$CF_3CH_2CH_2CH_2CH_3$	423—630	0.5	190
	$CF_3(CH_2)_3CH_3$	423—630	0.8	190
$C(CH_3)_2CN$	$(CH_3)_3C_6H_3$	353—383	0.1	62
	$(CH_3)_2NC_6H_5$	353—383	0.5	62
	$(CH_3CH_2)_3N$	353—383	0.1	62
	$(C_6H_5)_2CH_2$	353—383	4.4	62
	$(C_6H_5CH_2)_2O$	353—383	54	62
	$(C_6H_5CH_2)_3N$	353—383	10	62

The quantity A_{11} is a minimum for the reaction CH_3 + CH_4, where it is ~1. As the hydrogen atoms in the radical and molecule are replaced it gradually increases, reaching values of 10^2-10^3 for complete replacement. This is a qualitative conclusion, following from an analysis of a large number of reactions, which we think reliable. It can be explained with the aid of the arguments given in sections 5 and 6.

Considering the reaction complex to be approximately symmetric, we assume that the value of A_{11} is determined by the contribution of two antisymmetric deformation vibrations. By using Fig. 3 we estimate their frequencies ω_α:

A_{11}	1	10	100	1000
ω_a	200	50—100	20—30	5—10 cm^{-1}

Table 10. Pre-exponential factors for reactions involving abstraction of hydrogen by radicals from H–X molecules.

Radical	Molecule	T, °K	$10^{-8}A$, litre $mole^{-1}$ s^{-1}	Reference
CH_3	H—H	403—663	0.5	191
	H—D	403—663	1.1	192
	H—**D**	403—663	2.3	192
	D—D	403—663	1.4	191
CD_3	H—H	403—663	1.6	191
		403—663	4.7	192
	H—D	403—663	2.5	192
	H—**D**	403—663	1.4	192
	D—D	403—663	0.4	191
CH_3	H—Cl		2.5	117
CF_3	H—H	375—447	3.6	193
		—	2.4	194
	D—D	375—447	1.4	193
	H—D	375—447	6.0	193
CF_3	H—D	375—447	2.2	193
	H—Cl	313—578	2.4	194
	D—Cl	313—578	2.4	194
	H—Br	328—607	7.1	164, 195
	H—I		8.0	164
		343—562	5.4	194
C_2H_5	H—H	323—573	3.2	167
		327—560	10	196
C_2F_5	H—H	410—610	23	289
		419—586	79	197
	D—D	430—592	14	197
C_3F_7	H—H	430—592	36	198
			22	58
	D—D	438—570	48	197
C_6H_5	H—H	453—623	30	183

For the reaction of $CH_3 + CH_4$ calculations[20-22] give $\omega_\alpha \simeq 200$ cm^{-1}. For a tenfold decrease in ω_α the moment of inertia I_a must be increased a hundredfold. The last quantity is mainly determined by the value of I_X for the corresponding radical or molecule, Eqn. (18). According to Table 11 the values of I_X for the radicals CH_3, CF_3, CCl_3, and Ph are respectively 2, 50, 170, and 170. Hence an observable effect within the framework of our model is naturally explained by a change in the kinematic coefficients for corresponding AC.

A natural exception is the radical $C(CH_3)_2CN$ for which the value A_{11} is anomalously low. We will assume that the AC for the reaction of this radical (for example, with toluene) is more "rigid" than the typical AC for the reactions considered above, that is, one or both C–H bonds of the reaction centre are shorter for it. Most probably there is a shortening of the newly formed bond in accordance with the Hammond rule, since the $(CH_3)_2CCN$ radical is much less active than other radicals considered—for example, the activation energies for the reactions of CH_3, CF_3, and $(CH_3)_2CCN$ with toluene are 8, 6, and 11 kcal $mole^{-1}$ respectively. Then an increase in the moment of inertia I_X seems to be compensated by an increase in the force constant for the R–H bond being formed. This assumption agrees with the more detailed discussion given below.

Now let us examine the effect which is evidently due to the steric factor A_{12}. In the reaction for hydrogen abstraction from the carbonyl group of the aldehydes the value of A_1 is in many instances anomalously high (Tables 14 and 15). This can be explained as follows. During the course of the reaction the hybridisation of the carbonyl carbon atom changes from trigonal to digonal. The angle between the R–C and C=O bonds in R–C(=O)–H alters from 120° to 180°. Here the internal rotation of the substituent R or its fragments, restricted in the initial aldehyde by steric interaction with the oxygen atom, is freed. In the AC such an "aldehydic" effect should appear, even if only partly. In addition the effect of the moment of inertia, considered above, must be considered. From Table 14, clearly when the substituent R has a simple structure and a steric effect cannot be expected, the value of A_1 for RCHO and for molecules with a tertiary hydrogen atom are approximately the same. An anomalous increase in the pre-exponential factor is observed for aldehydes having a substituent of complex structure.

Table 11. Calculated values of the principal moments of inertia (a.m.u.).Å² and of $Å_0$ for radicals and molecules.

Compound	I_X	I_Y	I_Z	A_0'
CH_3	1.8	1.8	3.6	$4.5 \cdot 10^6$
CH_2CH_3	22.3	5.0	34.1	$1.9 \cdot 10^5$
$CH_3CH_2CH_2$	54.4	13.3	61.2	$4.5 \cdot 10^4$
$(CH_3)_2CH$	13.8	60.5	67.8	$3.1 \cdot 10^4$
$CH_3CH_2CH_2CH_2$	221	23.9	210	$7.6 \cdot 10^3$
$CH_3CHCH_2CH_3$	125	35.1	117	$1.5 \cdot 10^4$
$(CH_3)_2CHCH_2$	105	62.5	60.5	$1.2 \cdot 10^4$
$(CH_3)_3C$	63.7	63.7	118	$1.7 \cdot 10^4$
$C(CH_3)_2CN$	132	60.5	126	$4.9 \cdot 10^3$
C_6H_5	172	83	38.8	$1.0 \cdot 10^3$
CCl_3	173	172	307	$8.8 \cdot 10^3$
CF_3	48.2	48.2	94.1	$8.4 \cdot 10^3$
C_2F_5	213	138	263	$1.2 \cdot 10^3$
C_3F_7	429	270	508	$3.9 \cdot 10^2$
CH_4	3.25	3.25	3.25	$4.4 \cdot 10^6$
CH_2CH_3	24.9	6.5	24.9	$4.4 \cdot 10^5$
$(CH_3)_2CH_2$	17.8	57.6	65.7	$8.2 \cdot 10^3$
$(CH_3)_3CH$	63.8	63.8	169	$8.3 \cdot 10^3$
$(CH_3)_4C$	107	108	111	$8.4 \cdot 10^3$
$(CH_3)_3N$	56.1	59.5	100	$1.3 \cdot 10^4$
$(CH_3)_2NH$	15.2	54.0	61.4	$2.8 \cdot 10^4$
CH_3COCH_3	102	60.4	48.4	$1.2 \cdot 10^4$
$C_6H_5CH_3$	199	92.6	288	
$BrCH_3$	53.1	3.25	53.1	
$C_6H_5CH_2CH_3$	415	114	334	
$C_6H_5COCH_3$	547	411	139	
$(C_2H_5)_3N$	269	120	338	
$CH_3(CH_2)_2CH_3$	142	133	22.2	
CH_3OH	55.0	9.75	48.4	$3.4 \cdot 10^4$
C_2H_5OH	104	32.2	78.2	
n-C_3H_7OH	203	35.2	177	
iso-C_3H_7OH	134	60.1	171	
s-C_4H_9OH	250	23.9	191	
iso-C_4H_9OH	217	168	79.7	
t-C_4H_9OH	180	106	175	
CF_3CH_2OH	169	97.7	175	
$C_2F_5CH_2OH$	353	280	250	
$C_3F_7CH_2OH$	635	341	659	
$(C_6H_5)_2CH_2$	225	1430	1300	
$(C_6H_5CH_2)_2O$	193	344	1760	
$(C_6H_5CH_2)_3N$	2760	749	3150	

Let us discuss yet another effect. As shown above, the value of A_1 for the radical $C(CH_3)_2CN$ in reactions with small molecules is anomalously low. However, it becomes rather and possibly even too great ($\sim 10^3$) in reactions with complex molecules: diphenylmethane, dibenzyl ether, tribenzylamine (Table 14). This result can be interpreted in two ways. On the one hand, it could be supposed that in the latter instance, steric interactions in the AC make its structure looser than the structure of the AC for reactions with simple molecules, where there is no such interaction[62]. Then the pre-exponential factor is increased owing to a decrease in the force constants for the C–H bonds in the reaction complex, which involves a decrease in the antisymmetric frequencies ω_a. Hence a relative increase in the activation energy is to be expected.

Table 12. Calculated values of the coordinates of the centre of mass a_i, Å, and of the direction cosines of the principal axes for radicals and molecules.

Compound	a_X	l_1	l_2	l_3	a_Y	m_1	m_2	m_3	a_Z	n_1	n_2	n_3
CH_3	0.00	0.728	−0.686	0.000	0.00	0.686	0.728	0.000	0.00	0.000	0.000	1.000
CH_3CH_2	0.00	1.000	0.000	0.000	0.78	0.000	1.000	0.000	0.35	0.000	0.000	1.000
$CH_3CH_2CH_2$	0.55	0.815	−0.580	0.000	1.19	0.580	0.815	0.000	0.00	0.000	0.000	1.000
$(CH_3)_2CH$	0.00	1.000	0.000	0.000	−0.52	0.000	1.000	0.000	0.00	0.000	0.000	1.000
$CH_3CH_2CH_2CH_2$	0.00	1.000	0.000	0.000	2.11	0.000	0.950	−0.311	−0.73	0.000	0.311	0.950
$CH_3CHCH_2CH_3$	0.34	0.897	0.427	0.113	0.70	−0.366	0.863	−0.349	−0.31	−0.247	0.271	0.930
$CH_3CH(CH_3)CH_2$	−0.33	0.805	0.339	0.486	1.40	−0.207	0.929	−0.306	−0.19	−0.556	0.146	0.819
$(CH)_3C_3$	0.00	0.729	−0.684	0.000	0.00	0.685	0.729	0.000	0.00	0.000	0.000	1.000
$(CH_3)_2C(CN)$	0.00	1.000	0 000	0.000	0.45	0.000	1.000	0.000	0.00	0.000	0.000	1.000
C_6H_5	0.00	1.000	0.000	0.000	0.00	0.000	1.000	0.000	1.44	0.000	0.000	1.000
CCl_3	0.00	0.729	−0.685	0.000	0.00	0.685	0.729	0.000	0.41	0.000	0.000	1.000
CF_3	0.00	0.729	−0.685	0.000	0.00	0.685	0.729	0.000	0.28	0.000	0.000	1.000
C_2F_5	0.00	1.000	0.000	0.000	0.87	0.000	1.000	0.000	0.00	0.000	0.000	1.000
C_3F_7	0.24	0.095	−0.292	−0.337	1.21	0.160	0.916	−0.367	−0.43	0.416	0.247	0.807
CH_4	0.00	0.730	−0.683	0.0	0.00	0.683	0.730	0.000	0.00	0.000	0.0	1.000
CH_3CH_3	0.00	1.000	0.000	0.0	0.72	0.000	0.943	−0.333	−0.25	0.000	0.333	0.943
$(CH_3)_2CH_2$	0.00	1.000	0.000	0.0	0.00	0.000	0.817	0.577	0.00	0.000	−0.577	0.817
$(CH_3)_3CH$	0.00	0.842	−0.540	0.0	0.00	0.540	0.842	0.000	−0.39	0.000	0.0	1.000
$(CH_3)_4C$	0.00	1.000	0.000	0.0	1.44	0.000	1.000	0.000	−0.49	0.000	0.0	1.000
$(CH_3)_3N$	0.00	0.979	−0.197	−0.047	1.36	0.198	0.980	0.013	−0.06	0.043	−0.022	0.999
$(CH_3)_2NH$	0.00	1.000	0.000	0.0	−0.49	0.000	0.749	0.662	−0.29	0.000	−0.662	0.749
CH_3COCH_3	0.00	1.000	0.000	0.0	1.36	0.000	0.760	0.650	−0.55	0.000	−0.650	0.760
$C_6H_5CH_3$	0.00	1.000	0.000	0.0	2.30	0.000	0.943	−0.333	−0.81	0.000	+0.333	0.943
$BrCH_3$	0.00	1.000	0.000	0.0	1.53	0.000	0.943	−0.333	−0.54	0.000	+0.333	0.943
$C_6H_5CH_2CH_3$	−0.18	0.984	−0.174	−0.032	1.90	0.165	0.966	−0.201	−0.78	0.066	0.192	0.979
$C_6H_5COCH_3$	0.00	1.000	0.000	0.000	1.66	0.000	0.975	0.223	−2.16	0.000	0.223	0.975
$(C_2H_5)_3N$	−0.19	0.949	−0.306	0.070	1.68	0.308	0.951	−0.012	−0.26	−0.063	0.327	0.997
$CH_3(CH_2)_2CH_3$	0.00	1.000	0.000	0.000	1.44	0.000	0.714	0.700	−1.27	0.000	−0.700	0.714
CH_3COH	0.00	1.000	0.000	0.000	0.08	0.000	0.996	0.091	−0.46	0.000	−0.091	0.996
C_2H_5COH	0.00	1.000	0.000	0.000	0.30	0.000	0.782	−0.623	−0.93	0.000	0.623	0.782
C_3H_7COH	0.00	1.000	0.000	0.000	0.74	0.000	0.773	−0.634	−1.29	0.000	0.634	0.773
s-C_4H_9COH	0.20	0.910	0.276	0.309	0.97	−0.062	0.827	−0.558	−1.14	−0.41	0.489	0.770
iso-C_4H_9COH	−0.20	0.971	0.171	−0.170	0.41	−0.027	0.775	0.630	−1.53	0.240	−0.607	0.757
t-C_4H_9COH	0.01	0.984	−0.023	−0.176	0.91	0.016	0.999	−0.041	−0.74	0.177	0.037	0.984
iso-C_4H_7COH	0.02	1.000	0.000	0.000	0.89	0.000	1.000	0.000	−0.42	0.000	0.000	1.000
CF_3COH	0.03	0.972	−0.025	0.233	0.98	0.045	0.996	−0.077	−0.76	0.230	0.085	0.969
C_2F_5COH	0.00	1.000	0.000	0.000	0.95	0.000	0.940	0.341	−1.47	0.000	−0.341	0.940
C_3F_7COH	0.00	1.000	0.000	0.000	1.48	0.000	0.748	−0.664	−1.84	0.000	0.664	0.748
$(C_6H_5)_2CH_2$	0.00	1.000	0.000	0.000	−0.75	0.000	0.933	0.358	−0.77	0.000	−0.358	0.933
$(C_6H_5CH_2)_2O$	0.93	0.815	−0.476	−0.330	1.25	0.370	0.866	−0.336	−1.67	0.445	0.152	0.882
$(C_6H_5CH_2)_3N$	0.64	0.906	−0.391	0.164	2.46	0.400	0.916	−0.025	−0.79	−0.140	0.085	0.986

Table 13. Values of $(\pi I_i^{\neq})^{1/2}$ for certain activated complexes.

Activated complex	$(\pi I_i^{\neq})^{1/2}$, (a.u.)$^{3/2}$Å^3 complete calculation geom. activated complex	Calculation by Eqn.(20)
CH_3+H—CH_3	$1.3\cdot10^2$	$0.87\cdot10^2$
CH_3+H—$CH_2C_6H_5$	$4.9\cdot10^3$	$3.1\cdot10^3$
CH_3+H—$CH(C_6H_5)_2$	$2.9\cdot10^4$	$2.8\cdot10^4$
$C(CH_3)_2CN$+H—CH_3	$2.6\cdot10^3$	$2.1\cdot10^3$
$C(CH_3)_2CN$+H—$CH_2C_6H_5$	$1.6\cdot10^4$	$1.4\cdot10^4$
$C(CH_3)_2CN$+H—$CH(C_6H_5)_2$	$5.7\cdot10^4$	$4.7\cdot10^4$

Actually in these reactions show a clearly expressed compensation effect.

On the other hand, a change in the hybridisation of the carbon atom of the molecule from tetrahedral to trigonal can lead to the freeing of internal vibrations: similar to what is observed in aldehydes.

In the first instance A_{11} increases, in the second, A_{12}. In each specific reaction either the first or the second can predominate; they can also act simultaneously. In the next section we will investigate the reaction with diphenylmethane as an illustration.

9. STERIC EFFECTS IN THE REACTIONS OF THE 2-CYANO-2-METHYLETHYL RADICAL WITH DIPHENYLMETHANE

The model calculation given below clearly shows the complex picture of steric interactions in the reaction

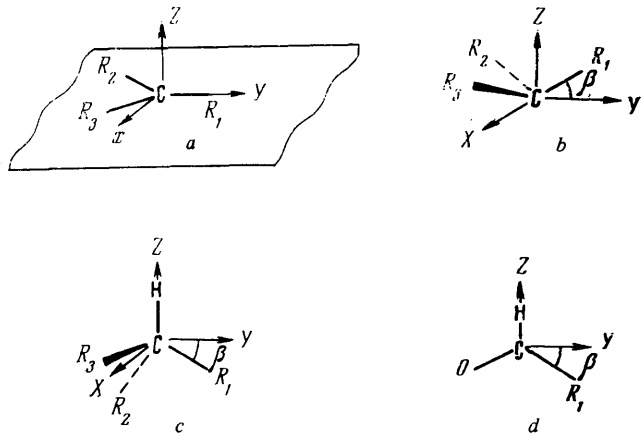


Figure 4. Configurations of molecules and radicals. The Z axis coincides with the direction of the molecule's CH bond that is being broken; one of the bonds of the central carbon atom (in the molecule or radical) lies in the YZ plane. All the angles β for the exit of C−R bonds from the XY plane for a given system are the same. *a*) $\beta = 0°$, alkyl radicals; *b*) $\beta = 15°$, CF_3 or CCl_3 radicals, *c*) $\beta = 19°\ 28'$, removal of H from a tetrahedral carbon atom; *d*) $\beta = 30°$, removal of H from a trigonal carbon atom (aldehydes). Standard values were adopted for the bond lengths and angles in the molecules and radicals.

Table 14. Experimental values of A_1, the contribution of the internal degrees of freedom to the pre-exponential factor.

Radical or atom	Molecule	A_0, litre mole^{-1} s^{-1}	A_1
1	2	3	4
H	H_2	$7.8\cdot10^{10}$	0.8
	HD	$4.4\cdot10^{10}$	0.3
	HD	$3.4\cdot10^{10}$	0.4
	D_2	$3.9\cdot10^{10}$	0.5
D	H_2	$6.0\cdot10^{10}$	0.4
	D_2	$2.8\cdot10^{10}$	1.1
	HD	$2.5\cdot10^{10}$	0.4
	HD	$1.9\cdot10^{10}$	0.5
H	CH_4*	$3.7\cdot10^{10}$	0.9
	$CH_3CH_2CH_3$	$4.3\cdot10^{9}$	4.2
	$(CH_3)_3CH$	$3.9\cdot10^{9}$	2.5
O	H_2	$8.2\cdot10^{10}$	0.2
	CH_4	$9.3\cdot10^{9}$	0.4
	CH_3CH_3	$6.5\cdot10^{8}$	4.6
F	H_2	$5.5\cdot10^{10}$	0.9
	CH_4	$9.0\cdot10^{9}$	3.4
	$C(CH_3)_4$	$1.4\cdot10^{8}$	36
	$CH_3CH_2CH_3$	$3.2\cdot10^{8}$	19
	$(CH_3)_2CH$	2.0	35
CH_3	H_2	$2.1\cdot10^{9}$	0.8
	HCl	$2.9\cdot10^{8}$	0.9
	CH_4	$1.9\cdot10^{8}$	0.9
	CH_3Br	$2.4\cdot10^{8}$	3.0
	CH_3CH_3	$6.7\cdot10^{7}$	3.4
	$CH_3C_6H_5$	$1.37\cdot10^{7}$	0.8
	$(CH_3)_4C$	$1.5\cdot10^{7}$	0.9
	CH_3COCH_3	$4.9\cdot10^{7}$	1.1
	$CH_3COC_6H_5$	$1.6\cdot10^{7}$	1.1
	$(CH_3)_3N$	$1.7\cdot10^{7}$	2.5
	$CH_3CH_2CH_3$	$2.9\cdot10^{7}$	13
	$CH_3CH_2C_6H_5$	$8.8\cdot10^{6}$	1.7
	$C_6H_5CH_2C_6H_5$	$7.0\cdot10^{6}$	4.6
	$(CH_3CH_2)_3N$	$9.0\cdot10^{6}$	3.7
	$(CH_3)_3CH$	$1.6\cdot10^{7}$	10
	$(CH_3)_2NH$	$2.1\cdot10^{7}$	25
	CH_3COH	$3.6\cdot10^{7}$	22
	C_2H_5COH	$2.2\cdot10^{7}$	46
	n-C_3H_7COH	$1.8\cdot10^{7}$	35
	iso-C_3H_7COH	$1.5\cdot10^{7}$	270
	s-C_4H_9COH	$1.8\cdot10^{7}$	1100
	iso-C_4H_9COH	$1.4\cdot10^{7}$	150
	t-C_4H_9COH	$1.1\cdot10^{7}$	930
	CF_3COH	$1.2\cdot10^{7}$	110
	C_2F_5COH	$8.9\cdot10^{6}$	900
	C_3F_7COH	$7.8\cdot10^{6}$	2100
CF_3	H_2	$2.7\cdot10^{8}$	1.2
	HD	$1.7\cdot10^{8}$	3.6
	HD	$1.6\cdot10^{8}$	1.3
	HCl	$2.6\cdot10^{6}$	65
	HBr	$3.4\cdot10^{6}$	29
	HI	$3.0\cdot10^{6}$	23
C_3F_7	H_2	$6.7\cdot10^{8}$	4.3
	D_2	$1.2\cdot10^{8}$	32
	CH_4	$1.6\cdot10^{6}$	15
	CH_3CH_3	$7.7\cdot10^{5}$	380
	CH_3COCH_3	$3.2\cdot10^{4}$	3600
	C_3F_7COH	$4.1\cdot10^{3}$	4500
Cl	H_2	$7.5\cdot10^{10}$	0.6
	D_2	$2.7\cdot10^{10}$	1.1
	HD	$2.7\cdot10^{10}$	1.2
	CH_4	$9.4\cdot10^{9}$	0.7
	CH_3CH_3	$6.0\cdot10^{8}$	2.5
	$C(CH_3)_4$	$1.0\cdot10^{8}$	140
	$CH_3CH_2CH_3$	$2.0\cdot10^{8}$	180
	$(CH_3)_3CH$	$1.5\cdot10^{8}$	140
Br	H_2	$8.4\cdot10^{10}$	1.7
	CH_4	$9.5\cdot10^{9}$	3.5
	CH_3CH_3	$5.5\cdot10^{8}$	22
	$(CH_3)_4C$	$9.5\cdot10^{8}$	16
	$CH_3CH_2CH_3$	$2.0\cdot10^{8}$	130
	$(CH_3)_3CH$	$1.2\cdot10^{8}$	170
I	H_2	$11\cdot10^{10}$	0.5
	D_2	$4.7\cdot10^{10}$	1.1
	$CH_3-CH_2CH_3$	$1.8\cdot10^{8}$	276
	$(CH_3)_3CH$	$1.1\cdot10^{9}$	690
	CH_3COH	$3.5\cdot10^{8}$	57
CF_3	CH_4	$1.8\cdot10^{7}$	7.5
	CH_3CH_3	$2.6\cdot10^{6}$	3.1
	CH_3COCH_3	$2.0\cdot10^{5}$	51
	$C(CH_3)_4$	$1.2\cdot10^{5}$	410
	$CH_3C_6H_5$	$1.1\cdot10^{5}$	710
	$(CH_3)_3N$	$1.5\cdot10^{5}$	480
	CF_3COH	$9.5\cdot10^{4}$	5700
	C_2F_5COH	$6.1\cdot10^{4}$	4900
	C_3F_7COH	$4.7\cdot10^{4}$	4200
	$(CH_3)_3CH$	$1.0\cdot10^{5}$	1400
	$(CH_3)_2NH$	$2.9\cdot10^{5}$	110
C_2H_5	H_2	$4.0\cdot10^{8}$	0.8
	D_2	$2.4\cdot10^{8}$	4.2
	CH_4	$3.7\cdot10^{7}$	4.3
	CH_3CH_3	$3.5\cdot10^{6}$	30
	$C(CH_3)_4$	$8.1\cdot10^{5}$	37
	$(CH_3)_3N$	$1.1\cdot10^{6}$	79
	C_2H_5COH	$1.5\cdot10^{6}$	82
n-C_3H_7	CH_3COOH_3	$4.4\cdot10^{5}$	44
	n-C_3H_7COH	$4.2\cdot10^{5}$	480
iso-C_3H_7	iso-C_3H_7COH	$2.1\cdot10^{5}$	760
s-C_4H_9	s-C_4H_9COH	$8.2\cdot10^{4}$	620
iso-C_4H_9	iso-C_4H_9COH	$1.0\cdot10^{5}$	5000
t-C_4H_9	t-C_4H_9COH	$1.1\cdot10^{5}$	350
C_6H_5	CH_4	$1.6\cdot10^{7}$	13
C_6H_5	$(CH_3)_3CH$	$7.7\cdot10^{4}$	8300
	$C_6H_5COCH_3$	$8.4\cdot10^{4}$	1600
CCl_3	$CH_3(CH_2)_2CH_3$	$9.1\cdot10^{4}$	29**
C_2F_5	H_2	$4.9\cdot10^{8}$	10
	D_2	$1.1\cdot10^{8}$	12.7
	CH_4	$9.8\cdot10^{6}$	11
	C_2F_5COH	10^{4}	18000
$C(CH_3)_2CN$	$C(CH_3)_2CNCH_3C_6H_5$***	$5.3\cdot10^{4}$	23
	$(CH_3CH_2)_3N$	$2.5\cdot10^{4}$	57
	$C_6H_5CH_2C_6H_5$	$1.8\cdot10^{4}$	2400
	$(C_6H_5CH_2)_2O$	$1.7\cdot10^{4}$	3100
	$(C_6H_5CH_2)_3N$	$9.4\cdot10^{3}$	10000

* In calculating A_1, the value $A = 3.2\times10^{10}$ litre mole^{-1} s^{-1}, obtained[200] as the mean of the available[58-60,200] values of A, was used.

** In calculating A_1, the value $A = 0.3\times10^{7}$ litre mole^{-1} s^{-1}, corresponding to the loss of H from a methyl group in the n-C_5H_{10} molecule, was used.

*** The experimental value of A for mesitylene[62] was used.

$(CH_3)_2CCN + H_2CPh_2$. The energy of the steric interactions between the reagents in the linear AC is investigated as a function of their relative orientation and the positions of the individual groups. Our results give information about the contribution of the internal rotations to the pre-exponential factor.

Table 15. Values of A_1 for some typical reactions.

Radical	Molecule										
	CH_4	C_2H_6	CH_3COCH_3	$(CH_3)_4C$	CH_3Ph	CH_3COPh	$(CH_3)_3N$	$-CH_3$	$-CH_2-$	$>CH-$	aldehydes
CH_3	0.9	3.4	1.1	0.9	0.8	1.1	2.5	1—3	~5	~10	100—1000
C_2H_5	4.3	30	—	37	—	—	3	3—30	~25	~80	~80
n-C_3H_7	—	—	43	—	—	—	—	~40	—	—	~500
iso-C_3H_7	—	—	—	—	—	—	—	—	—	—	~800
CF_3	7.5	—	50	400	710	—	475	50—500	~1000	1400	100—5000
CCl_3	—	—	—	—	—	—	—	~30	—	—	—
$C(CH_3)_2CN$	—	—	—	—	23	—	—	~20	~60	—	—
C_2F_5	11	—	—	—	—	—	—	~10	—	—	20000
C_3F_7	15	380	3600	—	—	—	—	15	—	—	~5000
Ph	13	—	—	—	—	1600	—	—	—	8300	—

Fig. 5 shows the geometry of the AC and the reactants. For the radical all the angles are assumed to be tetrahedral. The rotations of the methyl groups are characterised by the angles Ψ_1 and Ψ_2. The rotation of the phenyl rings in the molecule were described by angles ρ_1 and ρ_2 between the plane of the corresponding ring and the plane of the angle ω between the C – Ph bonds. The angles between the C – H bond being broken and the CH and C – PH σ-bonds were assumed to be the same for all three bonds (~107°). The rotation around the C... H... bond was characterised by the angle α (Fig. 5*a*). The relative position of the methyl and phenyl groups at $\alpha = 0$ for various values of the remaining angles are shown schematically in Fig. 6.

The interaction energy U was regarded as the sum of the pairwise intermolecular interactions $U_{rr'}$ between the atoms (not bound by valence) r of the radical and r' of the molecule. The interaction due to changes during the reaction with the hydrogen atom were not taken into account. The generally accepted approximation

$$U_{rr'} = A\exp(-al) - Bl^{-6},$$

where $l \equiv l_{rr'}$, the distance between the atoms, was used. The empirical coefficients A, a, and B were evaluated for various pairs of atoms from published data[201-205]. The steric interaction energy is

$$U = \Sigma U_{rr'}$$

First let us examine the effect of the angle ω in the isolated diphenylmethane molecule. Fig. 7 shows the interaction energy between the phenyl rings as a function of the angles of their rotation ρ_1 and ρ_2. Rotation of the rings is impossible, and only torsional vibrations about the equilibrium position at $\rho_1 = \rho_2 = 90°$ are admissible. As ω is varied from 109° to 120° the energy at the minimum changes from 8 to 3 kcal mole^{-1} and the potential well as a whole becomes much more shallow. The absolute value of the energy does not affect the pre-exponential factor (it makes a contribution solely to the activation energy). The decrease in the curvature of the potential surface $U(\rho_1, \rho_2)$ corresponds to a decrease in the force constants for the torsional vibrations, that is, to some freeing of the internal motions which was postulated above. For aldehydes, when the angle between the bonds is changed by 60, not 11, degrees, this effect is probably more significant.

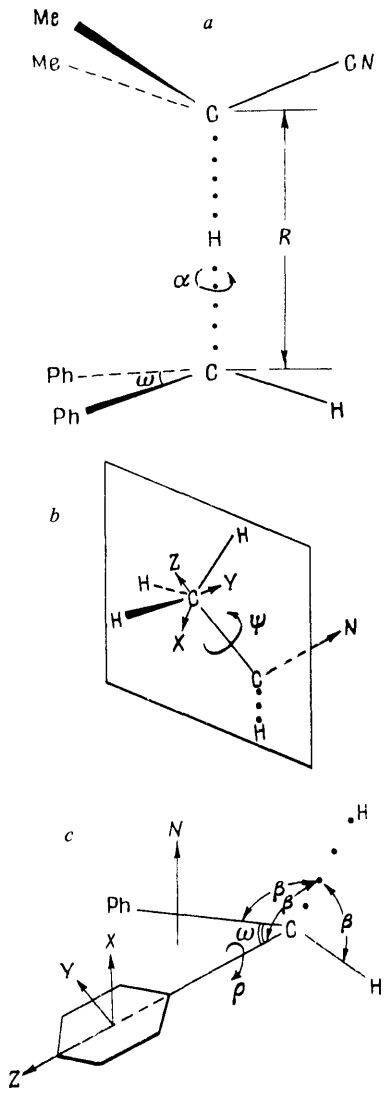


Figure 5. Geometric parameters of activated complexes for the reactions. *a*) Model of an activated complex: the C – CN bond of the radical and the C – H bond of the molecule lie in the plane of the diagram. The rotation angle α is reckoned from this plane; for the configuration shown $\alpha = 0$; *b*) rotation of methyl groups in the radical. The coordinate system is rigidly attached to the methyl group: the Z axis is directed along the C – C bond, the Y axis lies in the plane passing through one of the C – H bonds and the rotation axis; Ψ is the angle between the X axis and the normal N to the plane represented on the diagram (in the Figure, $\Psi = \pi/2$); *c*) rotation of the phenyl rings in the molecule. The coordinate system is rigidly attached to the ring, which lies in the YZ plane; the rotation angle ρ is the angle between the X axis and the normal to the plane of the PhCPh angle (in the Figure, $\rho = 0$), the angles β equal 106° 47′.

Subsequently it was assumed that in the AC a more favourable (and in energetic and in statistical respects) configuration with $\omega = 120°$ is realised. All the values of ρ_1 and ρ_2 were taken from the region situated close to the minimum.

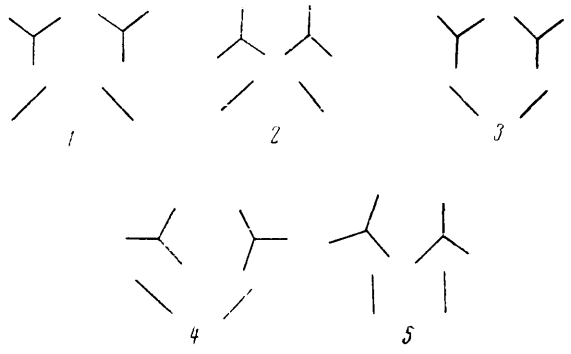


Figure 6. Schematic representation of the various configurations of the activated complex at $\alpha = 0$; ⟩⟨ denotes a methyl group, / the plane of the phenyl ring. *1*) $\Psi_1 = \Psi_2 = 0$, $\rho_1 = 120$, $\rho_2 = 60$; *2*) $\Psi_1 = 60°$, $\Psi_2 = 300°$, $\rho_1 = 120°$, $\rho_2 = 60°$; *3*) $\Psi_1 = \Psi_2 = 0°$, $\rho_1 = 60°$, $\rho_2 = 120°$; *4*) $\Psi_1 = 30°$, $\Psi_2 = 330°$, $\rho_1 = 60°$, $\rho_2 = 120°$; *5*) $\Psi_1 = 30°$, $\Psi_2 = 60°$, $\rho_1 = \rho_2 = 90°$.

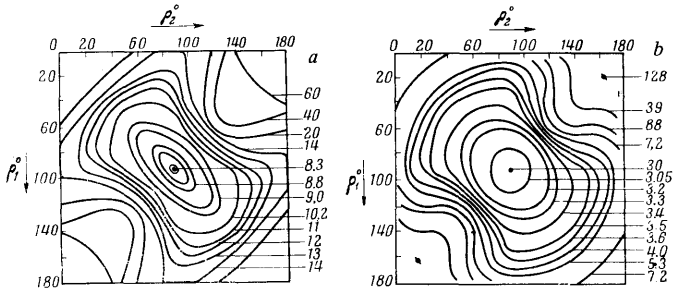


Figure 7. Potential surfaces for the interaction of the rings in diphenylmethane; energy in kcal mole^{-1}. *a*) $\omega = 109° 28'$; *b*) $\omega = 120°$.

Fig. 8 gives the relation between the intermolecular steric interaction in the AC from angle α in the fixed position of the methyl groups ($\Psi_1 = 60°$, $\Psi_2 = 300°$) and a distance of $R = 2.2$ Å between the carbon atoms of the reaction centre. Curves 1–5 correspond to different pairs $\rho_1 - \rho_2$. Of the five conformations considered rotation around the C–H–C bond seems possible for only one: $\rho_1 = 120°$, $\rho_2 = 60°$. For all the other instances steep and deep potential wells are characteristic.

The conformation with $\rho_1 = 120°$, $\rho_2 = 60°$ was investigated more thoroughly. Potential curves $U(\alpha)$ at various orientations of the methyl groups were constructed for these values of ρ. From Fig. 9, clearly for most of the conformations considered the rotation is strongly restricted or quite impossible. Hence the internal rotation α is practically free only for the conformations rigidly held about the values $\rho_1 = 120°$, $\rho_2 = 60°$, $\Psi_1 = 60°$, $\Psi_2 = 300°$. In other words, the rotation of the methyl groups is restricted, and the region of admissible values of ρ is greatly restricted. These motions might be made freer—with the same reagents at certain fixed values of angle α, that is, at the price of restricting the internal rotation around the C–H–C bond. The internal rotation as a whole in such an AC is greatly restricted.

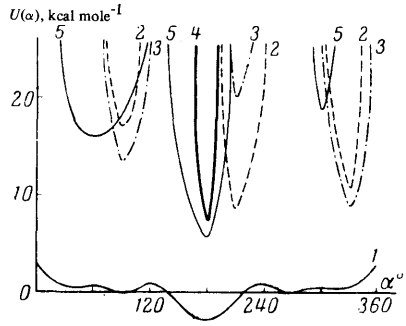


Figure 8. Variation of the energy of the intermolecular steric interaction in an activated complex with the angle α in a fixed arrangement of the methyl groups ($\Psi_1 = 60°$, $\Psi_2 = 300°$). *1*) $\rho_1 = 120°$, $\rho_2 = 60°$, *2*) $\rho_1 = \rho_2 = 40°$; *3*) $\rho_1 = 20°$, $\rho_2 = 80°$; *4*) $\rho_1 = \rho_2 = 90°$; *5*) $\rho_1 = 160°$, $\rho_2 = 100°$.

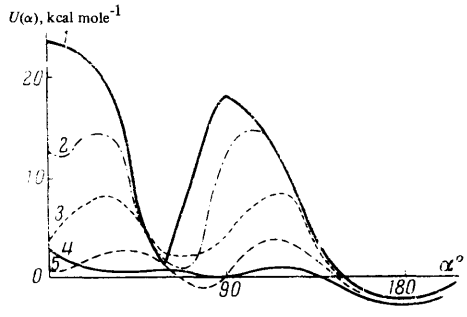


Figure 9. Variation of the potential curves $U(\alpha)$ with the orientation of the methyl groups for the conformations $\rho_1 = 120°$, $\rho_2 = 60°$. *1*) $\Psi_1 = \Psi_2 = 0$; *2*) $\Psi_1 = 15°$, $\Psi_2 = 345°$; *3*) $\Psi_1 = 30°$, $\Psi_2 = 330°$; *4*) $\Psi_1 = 60°$, $\Psi_2 = 300°$; *5*) $\Psi_1 = 45°$, $\Psi_2 = 315°$.

The calculations quoted relate to a rigid AC with the distance $R = 2.2$ Å. The variation with R of the potential curves $U(\alpha)$ is illustrated in Fig. 10. The deep minima characteristic for small R are gradually smoothed out. At $R = 2.5$ Å, the "poorest" of the curves given in Fig. 9 already permits restricted rotation; for $R = 2.7-2.8$ Å the rotation is free.

Of course, this result is obtained for optimal values of $\rho_1 = 120°$, $\rho_2 = 60°$. For other pairs ρ_1, ρ_2 free internal rotations occur at $R \geq 3$ Å. It can be considered

that in the range 2.6–3.0 Å the rotations Ψ and α are already sufficiently free, but the motion of the phenyl rings is still restricted in comparison with the isolated diphenylmethane molecule.

Now we can discuss more specifically the values of A_1 found for the $(CH_3)_2CCN$ radical. $A_1 \simeq 20$ for reactions with toluene†, for example. This is a low value: for the reaction $CF_3 + CH_3-Ph$, $A_1 \simeq 700$. In the previous section we assumed that the AC for the first reaction is more rigid, owing to the shortening of the R–H bond. Then an increase in the force constants explains the decrease in A_1. The value $R \simeq 2.6$ Å was taken[20-22] for reactions of CH_3 and CF_3 radicals. Consequently, we can take $R \simeq 2.4-2.5$ Å for the AC in the reaction $(CH_3)_2CCN + H_3C-Ph$. Calculations analogous to those given above show that in this system there is no steric interaction even at $R = 2.2-2.3$ Å.

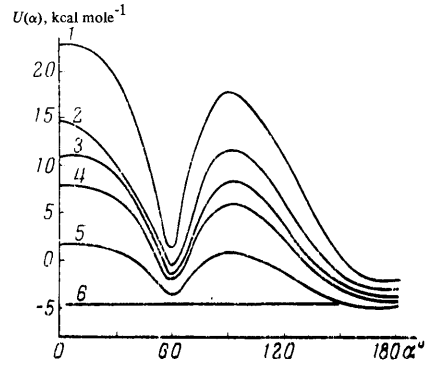


Figure 10. Variation of the potential curves $U(\alpha)$ with R at fixed positions of the methyl groups in the radical ($\Psi_1 = 0°$, $\Psi_2 = 0°$) and of the phenyl rings in the molecule ($\rho_1 = 120°$, $\rho_2 = 60°$). R, Å: *1*) 2.2; *2*) 2.25; *3*) 2.3; *4*) 2.35; *5*) 2.5; *6*) 2.8.

However, for AC of reactions with diphenylamine at $R < 2.5$ Å the steric effects are considerable. We therefore assume that in the AC represented in Fig. 5 R is increased to the value $R \leqslant 2.6$ Å, at which the change in internal motions compared with those of the reagents can be neglected. Such a system has a reaction centre close to the reaction centres of active radicals, for example, CF_3. Correspondingly (owing to the decrease in the force constants) the value of A_1 has increased to $A_1 = 2400$.

It is most probable that the increase in R takes place owing to the stretching of the C–H bond in diphenylmethane in accordance with the Hammond rule. A change to the favourable trigonal hybridisation with $\omega = 120°$ is facilitated thereby. The high values of A in the reactions of the isobutyronitrile radical with dibenzyl ether ($A_1 \simeq 3000$) and tribenzylamine ($A_1 \simeq 10\,000$) can probably be explained in approximately the same way but the details of the action of the "steric factors" should, of course, change.

It is impossible to maintain that this explanation is absolutely true, although it seems plausible. Information about the true values of R for various AC is not available and empirical calculations of the interaction energies are very approximate. The figures obtained (distances and angles) have an illustrative nature in every instance. But steric factors undoubtedly play an important part in the reactions of rather complex molecules.

Our calculations show certain specific mechanisms by means of which the internal degrees of freedom can affect the value of the pre-exponential factor.

† More precisely, the value of A_1 given in Table 14, relates to mesitylene, not toluene.

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Photoemission of Electrons from Metals into Electrolyte Solutions

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Photoemission of electrons from a metal into an electrolyte solution occurs when the metal is irradiated with sufficiently energetic light quanta through a layer of the solution. The emitted electrons become solvated and take part in various chemical and electrochemical reactions. Hence, photoemission studies in electrochemical systems can form the basis of a method for investigating the kinetics of various reactions, the structure of the electrical double layer at the metal-electrolyte interface, and the behaviour of electrons in liquids.
The theory of photoelectron emission, the relevant experimental techniques, and the most important results obtained in this new branch of electrochemistry are discussed. 117 references.

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I. INTRODUCTION. HISTORICAL REVIEW OF THE PHOTOEFFECT IN ELECTROCHEMICAL SYSTEMS

The phenomena which have been termed photovoltaic (and photogalvanic) at the boundary between a metal and an electrolyte solution have been studied for over 130 years. In 1839 Becquerel found[1] that the potential of metal electrodes immersed in salt solutions or in solutions of acids or alkalies is affected by illumination. This effect, known as the "Becquerel effect", has been the object of detailed studies†. It is clear, from the multiplicity of systems which have been examined and of explanations which have been put forward, that the "Becquerel effect" is a complex combination of different phenomena. Only recent progress in photoelectrochemical research has made it possible to separate the effect into its "component elements".

The revival of interest in photoelectrochemistry in the early 1960's was due to the efforts of three workers, each of whom put forward his own explanation of the origin of the photocurrent (or of the photopotential)‡.

Berg studied the effect of light[11-20] on the dropping mercury electrode by the standard techniques of polarographic analysis ("photopolarography"). He ascribed the appearance of a photocurrent to the increase in the energy of an electron within a metal resulting from the absorption of light by the metal. The probability of electron transfer from the metal to ions or molecules is enhanced on such a "hot" electrode, and hence the rate of electrochemical reactions becomes greater.

According to Heyrovský[21-26], the photo-effect is associated with the decomposition (under the influence of light) of a surface charge-transfer complex formed by the metal electrode with molecules of the solvent (water, ethanol, etc.) or of the solute. The polarisation of the chemical bond in a complex of this type can be of either sign, depending on the electron donor or acceptor properties of the adsorbate. Absorption of a light quantum can break this bond: the bonding electrons are transferred either to the electrode (anodic photocurrent) or to the absorbed molecule, which then migrates away from the electrode surface (cathodic photocurrent). It should be noted that the idea of photodesorption or photodecomposition of a surface compound as the elementary act in photogalvanic processes is implicit in the earlier work of Veselovskii[27].

Lastly, Barker showed[28,29] that over some ranges of light frequency and electrode potential the primary process consists in electron transfer from the metal to the solution (the external photoeffect).

Strictly speaking, the concept of photoemission of electrons in the metal–electrolyte system is not new: it was first put forward in the 1920's to account for the photopotential of a number of metals[30] and for the effect of light on the rate of decomposition of alkali metal amalgams[31,32]. The same concept is found in the work of Berg[33,34]. However, only Barker was able to prove (albeit by indirect but reliable methods) the reality of photoemission into solutions and to delineate the actual limitations of the concept. Barker's work stimulated further experimental and theoretical developments in the study of photoemission into solutions, and in particular it led to the formulation of a quantum-mechanical theory of the effect (Brodskii, Gurevich, Levich[35-41]).

These three hypotheses have been considered to be mutually incompatible. However, we now have grounds to believe that each can be applied over a particular range of experimental conditions.

† The early work has been reviewed by Copeland and coworkers[2]. The work of Bowden[3], and of Hillson and Rideal[4], on the influence of light on the rate of cathodic hydrogen evolution deserves a special mention.

‡ We shall not be concerned with phenomena associated with the absorption of light by the solution, which give rise to homogeneous photochemical reactions. In this case the change in potential (or current) at the electrode is simply due to the photolysis products, excited molecules, etc. (see, for example, Refs. 5 and 6). The following photoelectrochemical processes are also beyond the scope of the present review: processes on semiconductor electrodes[7,8], on metals covered with semiconducting oxide films[9], and on "insulator" electrodes[10].

This review is concerned with the present state of the theory of photoemission into solutions§. A few photoelectrochemical phenomena not involving photoemission but frequently associated with it are briefly considered in Section VI.

II. THEORY OF THE EXTERNAL PHOTOEFFECT AT THE METAL–ELECTROLYTE INTERFACE

1. Photoemission of Electrons into Electrolyte Solutions

Photoemission at the metal–electrolyte interface differs in a number of important respects from the photoemission of electrons from a metal into a vacuum. Processes involving photoelectrons can be divided[29,35] into the following consecutive steps (Fig. 1): 1) intrinsic photoemission, i.e. the transfer of an electron through the interface following the absorption of a light quantum by the metal; 2) thermalisation and solvation of the electron, which lowers the energy of the emitted electron to thermal values and results in the formation (in times of the order of 10^{-11} s[44,45]) of a solvated electron¶; 3) chemical reaction between the solvated electron and species with electron-capturing properties present in solution (electron acceptors). The commonest acceptors are the ions H_3O^+ and NO_3^-, the molecules O_2 and N_2O, etc.

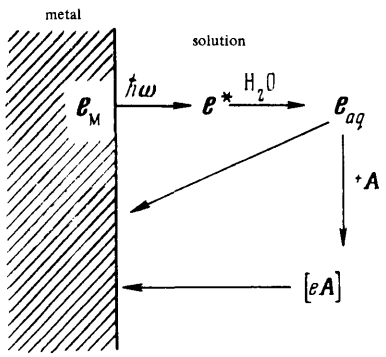

Figure 1. Processes occurring in photoemission.

In the absence of acceptors, the solvated electrons are quickly recaptured by the electrode, and the net photocurrent is approximately zero†. Thus, photocurrents in solutions (unlike photocurrents in the metal–vacuum system) can be observed experimentally only in the presence of electron acceptors.

Because there is an electrical double layer at the metal–electrolyte interface, where practically the whole of the externally applied potential difference appears, a new photoemission parameter has to be considered: the electrode potential. (This parameter is not relevant to the metal–vacuum interface.) The emission properties of the electrode can be drastically altered by varying the electrode potential‡.

Lastly, the work function of an electron is lower for the metal–electrolyte than for the metal–vacuum transition, because the electron gains interaction energy when it is emitted into a condensed medium. The motion of the electron in solution during the period preceding thermalisation and solvation is also different from the motion of an electron in a vacuum.

The photoemission of electrons from a metal into an electrolyte solution shows features similar to those of electrochemical reactions: both types of electron transfer reaction at the metal–electrolyte interface are described by essentially similar fundamental laws.

2. Quantum-mechanical Theory of Photoemission

The general theory of photoemission phenomena, including emission into electrolyte solutions, was developed by Brodskii and Gurevich[35–41]. Previous theories had a limited, phenomenological approach (Fowler's theory, for example[55,56]), and included a number of artificial assumptions or relied on models of doubtful generality[57,58]. Measurements of photoemission into a vacuum at frequencies close to the threshold value ω_0 agree very well with Fowler's parabolic law[56] $I \sim (\omega - \omega_0)^2$. However, attempts to apply Fowler's theory to photoemission into an electrolyte have been unsuccessful[29,59].

The modern quantum-mechanical theory of photoemission phenomena at the metal–electrolyte interface has been discussed in detail by Brodskii and Gurevich[41], and in this review the discussion will be confined to the underlying physical concepts.

Let a semi-infinite metal sample ($x < 0$) be irradiated with light of frequency ω (Fig. 2). Energies will be measured relative to that of an electron in solution, and the thickness of the layer affected by surface forces at the interface will be denoted by δ. In the present case, the thickness δ is that of the electrical double layer. The work function for the transfer of an electron from the metal to the solution is equal (but opposite in sign) to the energy of an electron at the Fermi level.

The current density of the emission from a microscopically uniform metal surface can be expressed in the form[41]

$$I = \int J(E, p_\parallel, A) \frac{1}{e^{\frac{E-\mu}{kT}} + 1} \rho(E, p_\parallel) dE dp_\parallel. \qquad (1)$$

§ A simplified treatment of the problem can be found in the semi-technical literature[42,43].

¶ The formation of a hydrated electron in aqueous solutions, first suggested by Platzman[46] in 1953, can now be taken as established. In particular, the hydrated electron appears as an intermediate in radiation-chemical and photolytic reactions. Many publications and monographs[45,47–51] have dealt with the methods of preparation of solvated electrons, their physicochemical properties, and their reactivity.

† The hydrated electron can undergo further reaction with a water molecule: $e^-_{aq} + H_2O \rightarrow H + OH^-$. However, the rate of this reaction is very slow, and in practice the electron can reach the electrode before interaction with H_2O can occur.

‡ At very negative potentials (for example, on mercury in alkaline solutions) thermal emission of electrons from the metal into the solution cannot be excluded[52,53]. The resulting hydrated electrons can be treated as intermediates in cathodic electrochemical reactions. However, a more recent analysis[54] has shown that the probability of thermo-electron emission into aqueous solutions is very low.

In this expression, E and $p_{\parallel} = \{p_y, p_z\}$ are the energy and the momentum (in a direction parallel to the surface) of the emitted electrons; A is an arbitrary term which allows for interactions with any external electromagnetic field; $J(E, p_{\parallel}, A)$ is the asymptotic value (i.e. at a point far removed from the metal surface) of the partial current density; $\rho(E, p_{\parallel})$ is the function which describes the distribution of the density of states for the electrons in the metal; μ is the chemical potential of the electrons.

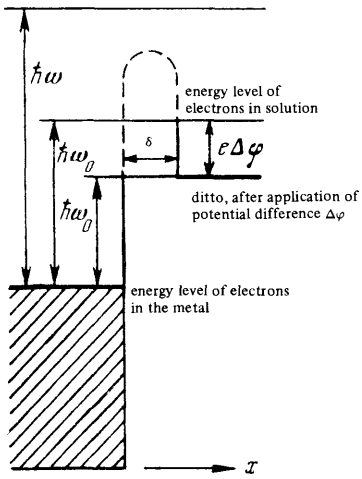

Figure 2. Electronic energy level diagram for photoemission from a metal into an electrolyte.

The limits of integration with respect to E and $p_{\parallel}^2$ are obtained from the law of conservation of energy:

$$p = \sqrt{2m(E + \hbar\omega) - p_{\parallel}^2}, \tag{2}$$

where p and m denote the x-component of the momentum and the mass, respectively, of the emitted electron. Since the partial photocurrent J differs from zero only for real values of p, the integration must extend over all values of E and $p_{\parallel}$ which satisfy the condition

$$\begin{gathered} 2m(E + \hbar\omega) \geqslant p_{\parallel}^2 \text{ or} \\ 0 \leqslant p_{\parallel}^2 \leqslant 2m(E + \hbar\omega), -\hbar\omega < E < \infty. \end{gathered} \tag{3}$$

Essentially, the quantum-mechanical problem consists in calculating the partial photocurrent $J(E, p_{\parallel})$. The motion of the electrons with an energy higher than kT can be treated as the motion of free particles with an effective mass m; in this case the wave function of the electron far from the metal surface has the form $\psi_f = A(p)\exp(ip_x/\hbar)$. It follows from the general expression for the quantum-mechanical current density operator [60] that our expression for J must be of the form

$$J = e(p/m)|\psi_f|^2. \tag{4}$$

The function $|\psi_f|^2$ can be treated as independent of the momentum of the emitted electron as long as its kinetic energy is less than $\hbar^2/2m\delta^2$. In other words, the de Broglie wavelength of the emitted electron must be greater than the thickness of the double layer,

$$\lambda > \delta. \tag{5}$$

Another condition for constant $|\psi_f|^2$ is given by the inequality

$$\hbar(\omega - \omega_0) < E_F, \tag{6}$$

where E_F is the energy of the Fermi level, measured from the bottom of the conduction band. The significance of inequality (6) is the following: the frequency of the light is so close to the threshold frequency that only those electrons within $\hbar(\omega - \omega_0)$ of the Fermi surface can take part in the photoemission process.

Eqns. (5) and (6) are the conditions for the threshold approximation, which allows the problem to be solved without reference to any specific model of the metal or of the interface. This approach has been used to discuss quantum-mechanical threshold phenomena [61].

Image forces, which operate at long range, play an important role in electron emission into a vacuum. At sufficiently low energies, $|\psi_f|^2 \sim p^{-1}$ and $J = \text{const}$ [35,37]; this justifies Fowler's approach, which involves substituting into Eqn. (1) some constant (for $p > 0$) or zero (for $p < 0$) instead of Eqn. (4).

However, when the electrons are emitted into an electrolyte, and conditions (5) and (6) apply, $J = \text{const} \cdot p/m$, and the electron density in the metal can be treated as constant to a first approximation and equal to the electron density at the Fermi surface.

Inserting the value of J into Eqn. (1), and simplifying, gives the following expression for the density of the emission current:

$$I = A_0\left(\frac{kT}{\hbar\omega}\right)^{1/2} T^2 \chi \int_0^{\infty} \frac{u^{3/2}}{e^{u-\beta} + 1} du. \tag{7}$$

where A_0 is Sommerfeld's constant, equal to 120 A cm^{-2} deg^{-1}, χ is a dimensionless function depending on the properties of the metal and the interface, and $\beta = \hbar(\omega - \omega_0)/kT$. At $T = 0$,

$$I = 0 \qquad \text{for } \omega < \omega_0, \tag{8a}$$

$$I = A_0\chi \frac{2\hbar^2}{5k^2\omega^{1/2}}(\omega - \omega_0)^{5/2} \qquad \text{for } \omega > \omega_0. \tag{8b}$$

Eqn. (8) shows that Fowler's parabolic law for the photocurrent as a function of frequency close to the threshold value is replaced by a "five-over-two" law. Formula (8b) applies also at ordinary temperatures if $\hbar(\omega - \omega_0)/kT \gg 1$.

The current–voltage characteristic for the photocurrent can be obtained by allowing for the effect of the electrode potential on the electron energy in the metal. A negative shift of the potential by φ raises the Fermi level of the metal by $e\varphi$. Thus, the electronic work function from the metal into the solution varies linearly with potential: $\hbar\omega_0(\varphi) = \hbar\omega_0(\varphi{=}0) + e\varphi$. Hence, the current–voltage characteristic takes the form

$$I \simeq A(\hbar\omega - \hbar\omega_0 - e\varphi)^{5/2}. \tag{9}$$

The work function $\hbar\omega_0$ applies for $\varphi = 0$, and is (of course) a function of the chosen reference electrode.

It follows from the inequality (5) that the "five-over-two law" should hold only in concentrated solutions of electrolytes ($\geqslant$ 0.1 M). In dilute solutions the thickness of the double layer is greater than the wavelength of the electron, and condition (5) is not satisfied. If the thickness of the diffuse part of the double layer is much greater than the de Broglie wavelength, the final state of the emitted electron in solution will be altered by an amount

$-e\psi_1$, where ψ_1 is the potential at the outer Helmholtz plane. Therefore we must re-write Eqn. (9) in the form

$$I \simeq A\,[\hbar\omega - \hbar\omega_0 - e(\varphi - \psi_1)]^{4/3} \qquad (10)$$

(which in any case is correct for $\psi_1 > 0$). In dilute solutions, therefore, we expect a linear relationship between $I^{0.4}$ and $(\varphi - \psi_1)$. Thus, the "five-over-two law" applies also to dilute solutions, but the electrode potential in this case must be "corrected" by subtracting the ψ_1 potential. An analogous correction of the ψ_1 potential appears also in the electrochemical kinetic equations[62]. In both cases (photoemission and discharge at the electrode) the rate of the electron transfer process is controlled by $\varphi - \psi_1$ rather than by φ.

A quantitative analysis of photoemission, allowing for the finite thickness of the fixed part of the double layer[63], has yielded an expression for the photocurrent which differs from the five-over-two law only in having an additional factor depending on the potential and on the energy of the light quantum. The deviation of the photocurrent from the five-over-two law at high potentials can be used to calculate the thickness of the fixed part of the double layer.

Lastly, Brodskii and Gurevich[41,64] have developed a multiphoton theory of the external photoeffect.

3. Theory of Photodiffusion Currents[29,65,66]

As stated above, the photoemission of electrons from a metal into an electrolyte is accompanied by successive steps leading to the formation of solvated electrons in solution. The products of the reaction between the electrons and acceptor species in solution can take part in electrode reactions. This process gives rise to "photodiffusion" currents in solution, resulting from discharge of the solvated electrons and their reaction products. The observed photocurrent, corrected for the backward migration (towards the electrode) of the solvated electrons and their reaction products, is described (at steady state) by the equation§

$$j = \nu \int_0^\infty f(x)\{1 - \exp[-(kc/D_e)^{1/2}x]\}dx. \qquad (11)$$

The function $f(x)$ of the electron source describes the rate of formation of solvated electrons as a function of distance from the electrode; k is the rate constant for the reaction between electrons and acceptors (present in solution at concentration c); D_e is the diffusion coefficient of the solvated electron; the stoichiometric number ν characterises the reactions, at the electrode and in solution, of the products formed by the capture of solvated electrons. For example, $\nu = 0$ corresponds to oxidation of free radicals formed by electron capture, and $\nu = 2$ corresponds to reduction of these radicals with emission of one additional electron from the electrode for each particle undergoing reduction.

At low acceptor concentrations, and noting that the source function differs from zero only in a narrow region close to the electrode, the expression for the current can be simplified by a series expansion of the exponential in Eqn. (11) to give

$$j = \nu\sqrt{kc/D_e}\,\langle x\rangle\, I, \qquad (12)$$

where $\langle x\rangle$ characterises the average distance from the electrode at which solvation occurs. It follows from formula (12) that the potential dependence of the photocurrent is the same as that of the photoemission current to the precision of the factors ν and $\langle x\rangle$. The variation of ν and $\langle x\rangle$ with potential will be discussed below by considering real examples.

If the electrode is illuminated with light of variable intensity, or polarised with a fluctuating potential, a significant difference is found experimentally between the time dependence of the photocurrent and that of the emission current. In particular, j and I show a phase shift whose magnitude and sign are determined by the diffusion rate of electrons and free radicals in solution and by the rate constants of the chemical reactions in the solution and at the electrode surface. The phase angles for some specific cases have been calculated[29,66].

Rotenberg and coworkers[67] have calculated the photoimpedance Z_φ of electrochemical systems, measured at an illuminated electrode polarised with a fluctuating potential of amplitude φ_0, and defined by the expression $\varphi_0 = Z_\varphi I_0$ (where I_0 is the amplitude of the fluctuating photocurrent). The equivalent circuits of a cell undergoing various photodiffusion processes have been discussed by Barker and coworkers[29].

III. EXPERIMENTAL TECHNIQUES USED IN PHOTOEMISSION STUDIES

Photoemission studies in metal–electrolyte systems are usually made by illuminating the electrode with light of 250–450 nm wavelength (quantum energy 2.5–5 eV). The most popular light sources are high-pressure mercury and xenon lamps, giving a continuous spectrum or line spectra. The required part of the spectrum is isolated with a high-intensity monochromator or with interference filters. The latter can produce a spectral band 5–10 nm wide. The cell and its associated optics are made of quartz.

Experimental assemblies for photoemission studies can be arbitrarily divided into three types (direct current, alternating current, and pulsed) according to the mode of illumination used and therefore also to the design of the measuring circuit. In assemblies of the first type the light intensity is kept constant and d.c. measuring circuits are used. For the light intensities most commonly used, the measured photocurrent densities are of the order of 10^{-6}–10^{-7} A cm^{-2}.

Time-modulation of the light intensity offers (in principle) a solution to two problems: the scientific problem of identifying processes in the electrochemical cell which may result in slow relaxation of the photocurrent (for example, the diffusion of reactants or of intermediates), and the experimental problem of exploiting the more convenient measuring systems based on a.c. amplifiers. In the first case, frequencies above 10 kHz are required, but in the second case it is sufficient to modulate the intensity of the light at a frequency of the order of 100 Hz, either mechanically (by inserting a rotating, perforated disk in the path of the light beam), or by modulating the power supplied to the lamp. The photocurrent (or photopotential) is measured with a selective amplifier tuned to the chosen modulation frequency. The most sophisticated

§ Eqn. (11) was obtained making the following assumptions: the emitted electron reacts with an acceptor only after being solvated; the concentration of solvated electrons is so low that interaction between these species can be ignored; no electric field exists in the solution.

apparatus of this type was described by de Levie and coworkers[68-70]. It uses a dropping mercury photocathode, with a constantly renewed surface, and the photocurrent is measured at a predetermined stage in the life of the drop. The state of the surface is monitored by measuring the components of the electrode impedance as well as the photocurrent.

The technique developed for flash photolysis[71] is used in pulsed measurements. The light source is a flash lamp, fired by discharging a condenser. The normal duration of a flash is 10^{-4}–10^{-3} s, the energy of the flash can be as high as 100 J.

We have shown, in Section II. 2, that the photoemission current density is a fundamental characteristic of the photoemission process which readily lends itself to experimental determination. For accurate measurements, the potential of the electrode must be kept constant and independent of the intensity of illumination. Under steady light, or with low-frequency modulation of the light beam, this condition is easily satisfied by practically any design of potentiostatic current source. On the other hand, a potentiostat for high-frequency or pulsed measurements is much more difficult to construct, because the low impedance of the electrode (determined by the capacity of the interfacial double layer) requires a circuit with a very low source resistance. Under these conditions, measurements are usually made in the galvanostatic rather than the potentiostatic regime (i.e. with a constant current flowing through the electrochemical cell¶), and the measured quantity is the photopotential instead of the photocurrent. Provided that the differential capacitance of the electrode is known, no difficulty arises in converting one measured quantity into the other. Delahay and coworkers[59,72] used a pulsed coulostatic apparatus to study the photoemission from stationary and dropping mercury electrodes.

Comparing the merits of the three methods, we note that steady illumination offers the simplest and most accurate measurement of photocurrent, but the method is not applicable in the presence of significant dark currents, and it cannot give any information on the relaxation processes involved. The pulse method has a low precision, and it requires correct measurements of the electrode capacity, which introduces additional uncertainty. The most universally applicable method is undoubtedly the modulated beam method.

Most of the work on photoemission published so far has been done with a dropping, or stationary, mercury electrode in aqueous solution. The most widely used electron acceptors are hydrogen ions and nitrous oxide.

IV. EXPERIMENTAL STUDIES ON THE BASIC LAWS OF PHOTOEMISSION

1. Dependence of Photocurrent on Electrode Potential and Quantum Energy of the Light

As shown in Section II. 2, existing theories of the photoeffect predict different variations of the photocurrent with electrode potential and with the energy of the light quanta. According to Fowler's modified theory, used to explain some of the early experimental measurements of photoemission in solutions[29,59,72], the photocurrent is a quadratic function of the quantity $(\hbar\omega - \hbar\omega_0 - e\varphi)$. The theory of Brodskii and Gurevich leads to the "five-over-two" law. Lastly, Heyrovský's model (photodissociation of surface charge-transfer complexes) predicts an exponential dependence of the photocurrent on potential or quantum energy.

The inadequacy of the quadratic law when applied to photoemission in solutions was demonstrated by Gurevich and coworkers[35]. The first experimental test of the "five-over-two" law was reported by Korshunov and coworkers[73], but these workers used a pulse method without allowing for the potential dependence of the electrode capacity.

In order to provide the data for a rational choice between the "five-over-two" law and Fowler's law, measurements of photocurrent have been made[74,75] as a function of potential under steady illumination, i.e. under conditions likely to yield the required precision and uncomplicated by considerations of double layer capacitance. The experimentally measured photocurrents were plotted in both $j^{0.5}$–φ and $j^{0.4}$–φ coordinates. Straight lines were drawn through the experimental points, using a computer for the least-square calculations. The intercept of the straight line on the potential axis (termed the threshold potential φ_a) was noted in each case, and used to calculate the work function of electrons in water and also the dispersion of the results (standard deviation of the experimental points from the best straight line).

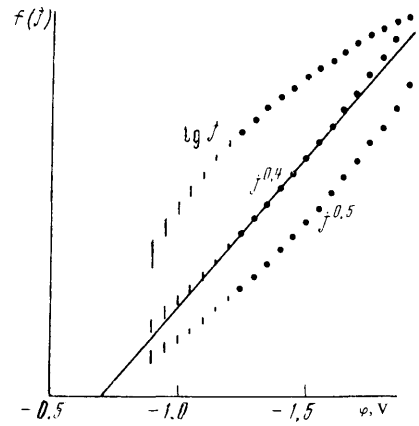

Figure 3. Graphical treatment of the experimental photocurrent–potential curve according to the theoretical formulae of Fowler ($j^{0.5}$), Heyrovský (lg$j$), and Brodskii and Gurevich ($j^{0.4}$). 0.1 N KF solution saturated with N_2O; light of 436 nm wavelength[70].

The dispersion was found to be much lower for the $j^{0.4}$–φ plot than for Fowler's $j^{0.5}$–φ plot. On this evidence, therefore, we must conclude that the "five-over-two" law is the more satisfactory.

These results were later confirmed by other workers. Fig. 3 shows the results of photocurrent measurements[70] on a dropping mercury electrode with modulated illumination, plotted as $j^{0.4}$–φ (according to Brodskii and Gurevich),

¶ The coulostatic method (zero current through the cell, constant charge on the electrode) is a special case of this regime.

$j^{0.5}-\varphi$ (according to Fowler), and $\lg j-\varphi$ (according to Heyrovský). It is evident from the Figure that a good straight line can be drawn only in the first plot†.

Although the reliability of the above results is lessened by occasional failure to comply with the condition of high acceptor concentration (see Section IV. 5), we may nevertheless conclude that photoemission in electrolyte solutions (in contrast to emission into a vacuum) is more accurately described by the "five-over-two" law than by Fowler's law.

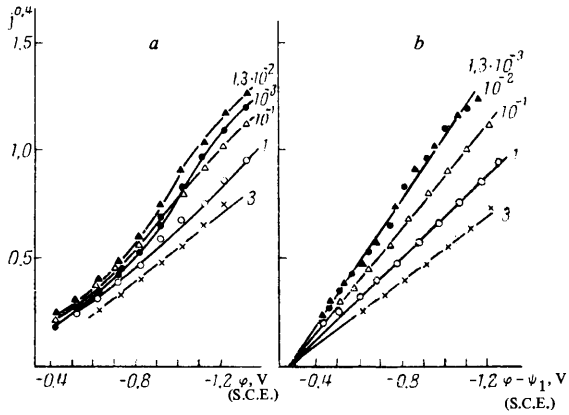

Figure 4. Plots of $j^{0.4}$ against (*a*) φ, and (*b*) $\varphi - \psi_1$ for KF solutions of different concentrations, saturated with N_2O.[76] In Figs. 4, 6, 7, 9, 10, and 13 the wavelength of light is 365 nm and the potential is referred to the saturated calomel electrode.

2. Photoemission into Dilute Electrolyte Solutions

The diffuse potential barrier found in dilute electrolyte solutions leads to a potential dependence of the photocurrent different from that observed in concentrated solutions (the "modified five-over-two law", Eqn. (10))‡.

Fig. 4 shows plots of the photoemission current in KF solutions at different concentrations, with N_2O as the electron acceptor[76]. Straight lines in $j^{0.4}-\varphi$ coordinates are obtained only in concentrated solutions (1 M and 3 M, see Fig. 4*a*).

In Fig. 4*b* the same experimental data are re-plotted as $j^{0.4}-(\varphi - \psi_1)$. The plots now show linear portions over a wide potential region for all concentrations of indifferent electrolyte. Furthermore, all the curves can be extrapolated to the same point on the potential axis, showing that the threshold potential is the same for all concentrations. The linearity of these plots, and the fact that they can be extrapolated to the same threshold potential, are convincing evidence that Eqn. (10) can be confidently applied to dilute solutions of electrolytes§.

Similar results were reported by Korshunov and coworkers[77]. However, de Levie and Kreuser[70] found that the potential dependence of the photocurrent was satisfactorily described by Eqn. (9) in dilute as well as in concentrated solutions: the reason for this discrepancy is not clear.

An attempt has been made[78] to allow quantitatively for the drift of solvated electrons in the field of the electrical double layer in dilute solutions.

3. Lack of Dependence of Photoemission Threshold on the Electrode Metal and on Adsorption

When photoemission proceeds in a vacuum the "red edge" of the photoeffect depends on the electronic work function of the metal: the standard method of measuring work functions is based on this effect. By analogy, we could expect the threshold potential at the metal–electrolyte interface to be a function of the metal: in other words, the intercept at $j = 0$ of the $j^{0.4}-\varphi$ straight lines obtained for different metals should be shifted by an amount equal to the difference in work function (or in the point of zero charge) of the metals[59].

However, there is one very important difference between the metal–electrolyte and the metal–vacuum interface: the former is the seat of an additional variable—the electrode potential. Changes in electrode potential are reflected in the work function, and therefore the latter must always be referred to some defined potential. However, if we assign a potential to the electrode we simultaneously fix the initial energy level of the electron. In practice, different metals at the same electrode potential have the same Fermi level. On the other hand, the final energy level of the electron in solution is independent of the nature of the metal. The specific properties of the metal influence only the height and the shape of the potential barrier at the interface (i.e. the region of thickness δ, as shown in Fig. 5). But under the conditions of the threshold approximation ($\lambda > \delta$) the properties of the barrier are irrelevant to the energetics of the photoemission process, which are determined only by the difference between the initial and the final state of the electron. Hence, the photoemission threshold in an electrolyte should be independent of the electrode metal.

This conclusion is fully consistent with the general laws of electrochemical kinetics. Indeed, the electronic work function of a metal in a vacuum does not appear explicitly in the kinetic equations if potentials are measured with respect to that of some arbitrary but constant reference electrode[79–81]. Photoemission, like any other type of electron transfer process at the metal–solution interface, must obey this law. Yet, photoemission offers a new insight into the role of the electronic structure of metals in electrochemical kinetics, because (unlike the majority of "classical" electrochemical reactions) it does not involve

† The deviations from linearity at voltages close to threshold are discussed more fully in Section IV. 5.

‡ If the measured photocurrent is lower than its limiting value, secondary effects of the ψ_1 potential on the photocurrent are also possible: changes in the concentration of charged acceptors near the electrode, and also drift of solvated electrons in the electric field of the diffuse part of the double layer.

§ It would be incorrect to conclude, however, that the emission of electrons proceeds only as far as the Helmholtz plane. The potential continues to vary (albeit slowly) beyond this plane. Hence, even if the point which describes the final state of the emitted electron is further from the electrode surface than the Helmholtz plane, the barrier presented by the diffuse part of the double layer remains practically impermeable to electrons, and the applicability of Eqn. (10) is unaffected.

the formation and breaking of chemical bonds, which complicate the interpretation of experimental results.

The lack of dependence of the photoemission threshold upon the nature of the metal was discovered experimentally in an investigation of mercury and of thallium and indium amalgams [74,82] (Fig. 6), and subsequently confirmed for various other metals [83]. In spite of the large difference between the points of zero charge of the metals examined (up to 0.4 V), the photoemission threshold potentials are indistinguishable within experimental error (±0.03 V).

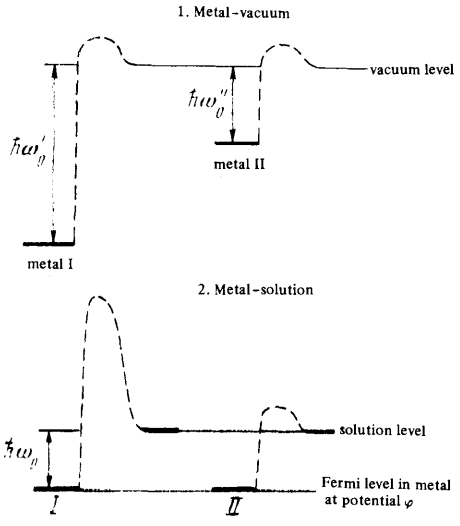

Figure 5. Energy diagram for photoemission into electrolytes from metals with different work functions.

Specific adsorption of surface-active ions or molecules is also not expected to shift the photoemission threshold provided that the condition $\lambda > \delta$ is not violated, i.e. as long as the thickness of the adsorption layer remains smaller than the wavelength λ of the emitted electron. (This wavelength is ~ 10 Å for an electron energy of ~ 1 eV.) For example, with the relatively small halide ions the conditions are satisfied and the photoemission threshold of a mercury electrode is practically unaffected by adsorption (Fig. 7) in spite of significant changes in the point of zero charge¶. Similar results were obtained for the adsorption of small organic molecules [70,84]. Adsorption of organic molecules with long carbon chains invalidates the condition $\lambda > \delta$ and (as expected) influences the potential dependence of the photocurrent. Thus, photoemission experiments can provide information on the extent of adsorption and on the characteristics of the adsorbed layer [85,86].

¶ The reported [72] shift in threshold following adsorption of halide ions on mercury is due to a misunderstanding. The shift was observed in the so-called "rational" potential scales for the adsorption of halide ions, and was effectively equal to the difference between the origins of these scales. When the results are recalculated for a common reference electrode the shift in photoemission threshold for different ions almost completely disappears.

4. Influence of Polarisation of the Light on the Photoemission Current

A characteristic feature of photoemission, which distinguishes it from other photoelectrochemical phenomena (such as photodissociation of surface charge-transfer complexes), is its sensitivity to polarisation of the light.

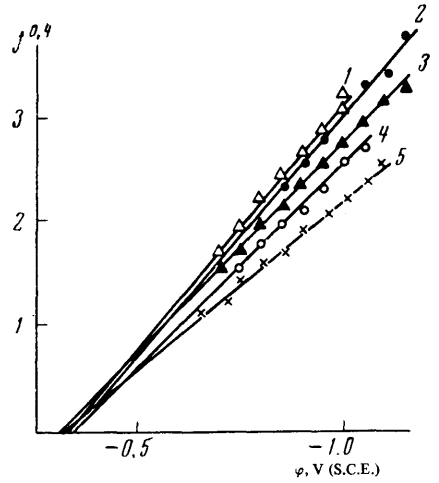

Figure 6. $j^{0.4}$–φ curves for different metals: *1*) mercury, *2*) thallium amalgam (3%), *3*) indium amalgam (18%), *4*) indium amalgam (50%), *5*) lead [74].

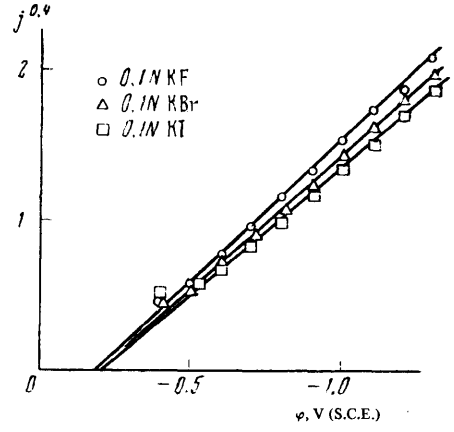

Figure 7. $j^{0.4}$–φ curves for a mercury electrode in 0.1 N solutions of KF, KBr, and KI saturated with N_2O. [84]

An electron cannot emerge from the metal after absorption of a light quantum unless its momentum in a direction perpendicular to the interface is greater than zero. It follows from the law of conservation of momentum that the transition can be induced only by the x-component of the electric vector. The absorption of a wave which is polarised in the plane of the surface cannot generate a

significant amount of photocurrent. Hence, we expect the photocurrent to increase with the projection of the electric vector on the normal to the metal surface ($j \sim \sin^2\theta \cdot \cos^2\psi$, where θ is the angle of incidence of the light and ψ is the polarisation angle in the plane of incidence, see Fig. 8).

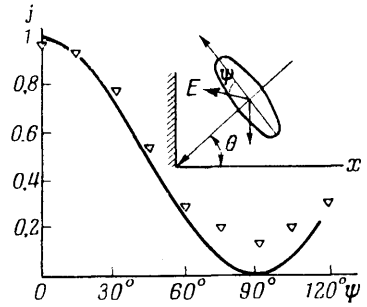

Figure 8. Effect of polarisation of the light on photoemission. Mercury electrode in 0.1 N K_2SO_4 solution (open triangles). The full curve is a plot of $\cos^2\psi$.[88]

The variation of photoemission current with polarisation of the light, which had been previously observed experimentally at the metal–vacuum interface[87], has been reported also in electrochemical systems[31,32,70,88]. Fig. 8, reproduced from the paper by Korshunov and coworkers[88], shows the photocurrent at a mercury electrode in K_2SO_4 solution saturated with N_2O (electron acceptor) as a function of the polarisation angle ψ of the light (for a fixed value of θ). The relatively small discrepancy between the experimental points (triangles) and the expected $\cos^2\psi$ law (solid line) is obviously due to incomplete polarisation of the incident light.

Experiments with polarised light allow us to separate photoemission from other concomitant photoelectrochemical processes which do not show polarisation selectivity (photoeffect in the bulk electrolyte, photodissociation of charge-transfer complexes, etc.).

5. Photoemission into Solutions with Low Concentrations of Electron Acceptors

If the concentration of acceptors is insufficient, some of the emitted electrons will be recaptured by the electrode and the measured photocurrent will be smaller than the true emission current. The expected proportionality (at low acceptor concentrations) between the photocurrent and the square root of acceptor concentration (Eqn. (12)) has been observed experimentally[29,89,78,89-91]. The proportionality coefficient can be used to assess the mean distance $\langle x \rangle$ from the electrode surface at which hydrated electrons are formed in solution. In concentrated electrolyte solutions (0.1–1 M) this distance is found[89,90] to be ~ 20 Å, but as the ionic strength of the solution decreases $\langle x \rangle$ appears to increase to ~ 100 Å.[89]

The calculated value of $\langle x \rangle$ is a mean over the whole energy spectrum of the emitted electrons for given values of φ and $\hbar\omega$. The function $f(x)$, i.e. the distribution of velocities of the solvated electrons along the coordinate x, can be evaluated in principle from the dependence of the photocurrent on the concentration of acceptors (at intermediate concentrations), or alternatively from relaxation experiments[92]. The calculation has not yet been attempted, because of the inadequate precision and reproducibility of photocurrent measurements[78], but it may already be stated that $\langle x \rangle$ increases with the electron energy E, since $\langle x \rangle$ increases when the potential is shifted towards more negative values (for $\hbar\omega$ = const.)[29,89]. It should be noted that Korshunov and coworkers[90] arrived at the opposite conclusion from their measurements of photocurrent as a function of electrode potential and acceptor concentration. But we must stress that the precision of measurements on concentration dependence is often suspect. A more reliable argument for the dependence of $\langle x \rangle$ on electron energy is the experimentally observed shift[93] of the threshold potential (found by extrapolating the $j^{0.4}$–φ straight lines) on increasing the concentration of acceptors in solution (Fig. 9).

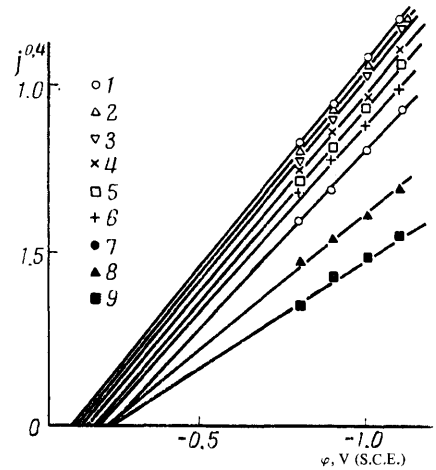

Figure 9. Effect of acceptor concentration (H_3O^+) on the apparent photoemission threshold: *1*) 0.42, *2*) 0.25, *3*) 0.11, *4*) 0.063, *5*) 0.044, *6*) 0.03, *7*) 0.018, *8*) 0, *9*) 0.0012 mole litre^{-1}.[89]

This shift does not imply a change in the "true" work function of the electrode metal with respect to the electrolyte; it is merely the result of a change in the dependence of the photocurrent on potential as the concentration of acceptors is varied but the method of graphical interpretation of the results is kept unchanged. By assuming an explicit form of the function $\langle x \rangle$ (E) we can calculate a j–φ curve which is not described by the "five-over-two" law. The positive deviations from this law (see Fig. 3) have been explained qualitatively by these arguments.

As already stated, the precision of present-day experiments is insufficient to calculate the functions $f(x)$ and $\langle x \rangle$ (E). The greatest accuracy is obtained in measurements of photoemission at high acceptor concentrations, when diffusion processes play only a minor role[78,93].

The true photoemission threshold has been determined[93] by correcting the apparent shift due to diffusion of hydrated electrons, and used to calculate the work function for electron emission from mercury into water at the zero-charge potential (3 eV). (This value is lower by 0.2–0.3 eV than the previously accepted value[73,74], which did not

include a diffusion correction.) The lower work function of mercury in water as compared with the vacuum value (4.5 eV) is due, as we have already pointed out, to the interaction of a super-thermal electron with the polar solvent medium. The lowering (1.5 eV) is less than the hydration energy of the electron (1.7 eV[45]). Hence, the final state of the photoemission process is a quasi-free electron rather than a fully thermalised and hydrated electron.

The electronic work function in other solvents, measured by the photoemission method, has also been found to be lower than the work function in a vacuum. The lowering is close to the energy of the electronic polaron in these solvents, and is evidently due to the electronic polarisation of the medium by the emitted electron[82].

6. The Multi-photon Effect

The experiments discussed above relate to the one-photon photoeffect, in which the energy of a single light quantum is sufficient to cause photoemission. Korshunov and coworkers[94] discovered two- and three-photon external photoeffects at the mercury–solution interface. A laser was used as the light source: a ruby laser in the first case (quantum energy $\hbar\omega = 1.78$ eV), and a neodymium laser in the second ($\hbar\omega = 1.18$ eV). As in the one-photon effect, the photocurrent varies with potential according to the "five-over-two" law. The relationship between the photocurrent and the light intensity is, as expected from the theory, an exponential function with an exponent approximately equal to the number of photons absorbed for every emitted electron.

V. PHOTOEMISSION AS A METHOD OF STUDYING THE KINETICS OF CHEMICAL AND ELECTROCHEMICAL REACTIONS

When electrons are emitted into a solution as a result of irradiation, many processes in which the solvated electrons are involved in further transformations can occur in the layer of solution adjacent to the electrode. The most interesting of these are homogeneous and heterogeneous reactions involving free radicals. The kinetics of these reactions are reflected in the magnitude of the experimentally measured photocurrent, and therefore we may think of photoemission as a convenient method of monitoring such processes. We shall limit the discussion to the simplest systems, for which quantitative experimental data are available.

1. Kinetics of the Electrochemical Conversion of Atomic Hydrogen at a Mercury Electrode

Atomic hydrogen is formed in solution by the capture of a hydrated electron by a hydrogen ion:

$$e_{aq}^- + H_3O^+ = H + H_2O. \qquad (A)$$

The hydrogen atom undergoes reduction over a wide range of potentials (from −0.7 to −1.5 V against the saturated calomel electrode)

$$H + HS + e^- = H_2 + S. \qquad (B)$$

In the above equation the symbol HS denotes a source of protons, which could be H_3O^+ or H_2O. At more positive potentials the ionisation of atomic hydrogen becomes increasingly important

$$H + H_2O = H_3O^+ + e^-, \qquad (C)$$

leading to a drop in the measured cathodic photocurrent (first observed by Barker[29]).

We shall outline the results of some kinetic studies of the conversion of atomic hydrogen, obtained from photoelectrochemical measurements[95,96]. Photoemission is used as a source of atomic hydrogen in the region of the electrode surface: the procedure is more convenient than others used so far[97–99].

The photocurrent experimentally measured in the electrochemical system is defined by the expression $j = j_0 + \vec{j} - \overleftarrow{j}$, where j_0 is the emission current (not including the current of electrons recaptured by the electrode without having reacted), $\vec{j}$ is the cathodic current of reaction (B), $\overleftarrow{j}$ is the ionisation current of atomic hydrogen. The variation of j_0 with potential, as already stated, has approximately the form $j_0 \sim (\varphi - \varphi_a)^{5/2}$, where φ_a is the threshold potential for light quanta of a given energy.

A hydrogen atom can take part in reactions (B) and (C) either in an adsorbed state at the surface of the metal or in the layer of solution adjacent to the electrode.

At negative potentials, when the rate of oxidation of the H atom can be ignored, $j = 2j_0$, and the experimental dependence of the photocurrent on potential is (to a first approximation) the same as that of the emission current. In the more general case, when reaction (C) cannot be neglected, the photocurrent j is given by the expression[96]

$$\varphi = \frac{2.3RT}{(\alpha+\beta)F}\left[lg\left(\frac{2j_0}{j} - 1\right) + lg\frac{\kappa_1}{\kappa_2}\right], \qquad (13)$$

where α and β are the transfer coefficients of reactions (B) and (C) respectively, and κ_1 and κ_2 are the rate constants of these reactions at $\varphi = 0$†.

Eqn. (13) predicts a linear relationship between φ and $\lg(2j_0/j - 1)$, with a slope determined by the transfer coefficient of the appropriate reaction. The current $2j_0$ (in the absence of oxidation of the atomic hydrogen) can be found either by extrapolating the linear portion of the $j^{0.4}$–φ plot to the potentials where non-linearity sets in owing to the oxidation of hydrogen (see Fig. 10), or by measuring the photocurrent with a different acceptor, reacting with the hydrated electron to give products which are not oxidised at the electrode. One such acceptor is nitrous oxide, which forms the $OH^\cdot$ radical after capturing an electron. This radical is reduced at the electrode to the hydroxyl ion over the whole of the accessible range of potential.

Fig. 10 shows some plots of the photocurrent ($j^{0.4}$) against potential in KCl, KBr, and KI solutions containing 0.01 g-equiv. litre^{-1} of HCl. The relationship is linear at negative potentials, and the deviations from linearity (i.e. decrease in photocurrent) set in at increasingly negative potentials on going from Cl^- to I^-. It is evident from Fig. 10 that specific adsorption of the iodide ion has a strong positive effect on the anodic current $\overleftarrow{j}$ (as compared with the cathodic current $\vec{j}$). The experimental data for all solutions give linear plots in φ–$\lg(2j_0/j - 1)$ coordinates, thus confirming the correctness of Eqn. (13). The slopes of these straight lines (100–120 mV) indicate that $\alpha + \beta = 1/2$, i.e. the transfer coefficient of one of the

† The logarithmic term $2j_0/j - 1$ is identically equal to $\overleftarrow{j}/\vec{j}$.

conjugated reactions is zero and hence its rate is independent of potential. Additional information on the mechanism by which atomic hydrogen is removed from solution can be obtained from the effect of pH in decreasing of photocurrent.

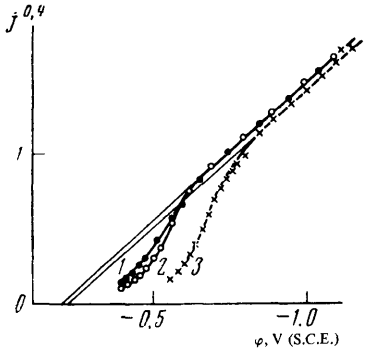

Figure 10. Effect of oxidation of H on the photocurrent. Mercury electrode in 0.1 *N* solution of: *1*) KCl, *2*) KBr, and *3*) KI containing 0.01 *N* HCl.[96]

Fig. 11 shows the variation of the potential φ^*, at which $\vec{j} = -\vec{j}$‡, with the concentration of hydrogen ions, over the $c_{H_3O^+}$ range between 10^{-3} and 1 *N* in solutions containing a total concentration of electrolyte of 1 *N*. As the Figure shows, φ^* increases monotonically with acidity, the increase being most marked in the most strongly acid solutions. At low acid concentrations (10^{-2}–10^{-3} *N*) φ^* is practically independent of pH.

From these results it was concluded[96] that two mechanisms of hydrogen removal are possible: the two conjugated reactions proceed without an adsorption step, or both reactions involve adsorbed hydrogen, in which case one of the reactions is non-activated§. Further experimental data are needed to identify the potential-independent reaction: in particular, we need information from other metals, having a hydrogen adsorption energy different from that of mercury.

The variation of the φ^* potential with pH suggests a new type of electrochemical desorption, involving hydrogen ions and water molecules simultaneously¶. The removal of adsorbed hydrogen by an electrochemical mechanism involving water molecules in acid solutions was first considered by Krishtalik[102].

Specific adsorption of anions accelerates the ionisation of hydrogen (if activated) by producing a more positive potential difference across the fixed part of the double layer. At the same time, anion adsorption should accelerate the electrochemical desorption involving hydrogen ions. As Fig. 10 shows, adsorption of iodide influences ionisation more markedly than electrochemical desorption (particularly, since water takes part in the latter)†.

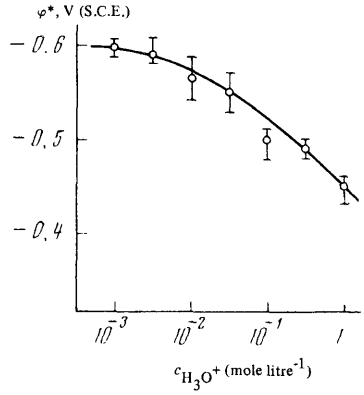

Figure 11. Variation of φ^* potential with concentration of H_3O^+.[96]

The concept of a non-activated electrochemical reaction was first put forward in 1936[103,104], but it has not been possible so far to observe limiting currents due to non-activated discharge in direct experiments. Krishtalik's barrierless processes[100] may be quoted as an indirect experimental proof of the reality of non-activated reactions.

2. Homogeneous Chemical Reactions Involving Free Radicals

The most detailed studies of homogeneous chemical reactions involving the radicals H, OH[105], and NO_3^{2-} [106-108] have been made by the photoemission method.

Barker[105] studied the reaction between methanol and ethanol, on the one hand, and H and OH radicals formed by the photoemission of electrons into acid solutions and into solutions containing N_2O, on the other hand. We know, from radiation-chemical experiments, that the H and OH radicals attack the α-hydrogen in alcohols. The resulting RĊHOH radicals are easily oxidised at the electrode to the corresponding aldehydes. For the case of the oxidation of RĊHOH radicals, the coefficient ν which appears in the kinetic equations (11) and (12) takes the form

$$\nu = \left(1 + \frac{\sqrt{k_R \cdot c_R / D_R}}{\sqrt{k \cdot c / D_e}}\right)^{-1}, \qquad (14)$$

‡ It follows from Eqn. 13 that

$$\varphi^* = \frac{2.3\,RT}{(\alpha + \beta)\,F} \lg \frac{\varkappa_1}{\varkappa_2}. \qquad (D')$$

§ The hydrogen removal mechanism through the adsorbed state seems the more probable, since both reactions (ionisation and reduction in solution) should be non-activated at these potentials[100], and hence the experimentally observed loss of photocurrent cannot be ascribed to them.

¶ The observed variation of φ^* with pH can be formally explained by assuming the formation (in acid solutions) of the H_2^+ radical, which is subsequently reduced at the electrode. However, the rate constant for the reaction between H and H_3O^+ is very small (10^4 litre mole^{-1} s^{-1})[101], and therefore the contribution of this reaction to the photocurrent cannot be substantial.

† The effect of iodide adsorption can be explained in a similar way by assuming that the ionisation of hydrogen is non-activated.

where c_R is the concentration of alcohol present in solution, k_R is the rate constant for the capture of a radical by the alcohol, and D_R is the diffusion coefficient of the H or OH radical.

Eqn. (14) predicts a decrease in photocurrent in the presence of alcohol. The decrease is observed experimentally at $\varphi > -1.4$ V. At more negative potentials the photocurrent is the same as in the absence of alcohol ($\nu \to 2$). The linear relationship predicted by Eqn. (14) between the reciprocal of the current and the square root of the alcohol concentration has been satisfactorily demonstrated (Fig. 12) for the case of OH radicals. The rate constants for the reaction of OH with methanol and ethanol, calculated from the experimental results by means of Eqn. (14), are both equal to 2×10^9 litre mole^{-1} s^{-1}. For the reaction involving H the result is $k_R = 8 \times 10^6$ litre mole^{-1} s^{-1}.

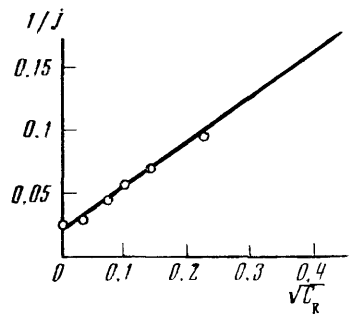

Figure 12. Reciprocal of the photocurrent in 0.2 N KCl solution containing N_2O against square root of ethanol concentration[105].

In the presence of alcohol, the variation of the photocurrent with the concentration c of electron acceptors (N_2O and H_3O^+) is also altered. When the products of the capture of H and OH by the alcohol are not oxidised at the electrode, and at low concentration of acceptors, we have $j \sim \sqrt{c}$ [Eqn. (12)]. If the RĊHOH radicals are oxidised, and the second term in Eqn. (14) is large compared with unity, we have $j \sim c$. This dependence has been observed experimentally.

Barker, using pulsed illumination, was able to monitor the kinetics of the electrochemical oxidation of RĊHOH radicals on mercury by studying the anodic photocurrent which persists after the period of illumination‡. The observed exponential decay of the anodic photocurrent was taken as evidence that the oxidation of RĊHOH radicals is preceded by an adsorption step. The rate constant of the oxidation was $\sim 10^{-3}$ cm s^{-1} at −1.4 V (S.C.E.).

The rate constants for the reaction of H and OH with alcohols found by the photoemission method are in good agreement with experimental results obtained by pulse radiolysis of the same solutions[105].

‡ Levin and Delahay[109] observed anodic currents during the pulse irradiation of acid solutions in the absence of added materials. Their results have not yet been explained satisfactorily.

The chemical reactions of the ion-radical NO_3^{2-} have been studied by two photoelectrochemical methods, using pulsed[106,108] and steady[95,107] illumination. This radical is formed when electrons are photo-emitted into solutions containing NO_3^-. The following chemical reactions take place at the electrode and in its immediate vicinity

$$\left.\begin{aligned} NO_3^- + e_{aq}^- &= NO_3^{2-} \\ NO_3^{2-} &= NO_2^- + O^- \end{aligned}\right\} \text{in solution}, \quad \begin{matrix}(D)\\(E)\end{matrix}$$

$$NO_3^{2-} = NO_3^- + e^- \quad \text{at the electrode}, \quad (F)$$

$$O^- + H_2O = OH + OH^- \text{ in solution}, \quad (G)$$

$$OH + e^- = OH^- \text{ at the electrode}. \quad (H)$$

The NO_3^{2-} ion-radical is oxidised at the electrode at potentials more positive than −1.2 V leading to a decrease in the measured photocurrent[29].

A quantitative study of this reaction by Eletskii and coworkers[107] showed that two "limiting" portions appear on the photocurrent curve (at negative and positive potentials respectively). Both portions obey the "five-over-two" law, and extrapolate to the same threshold potential. Fig. 13 shows the $j^{0.4}$–φ plot for a concentrated solution of $NaNO_3$.

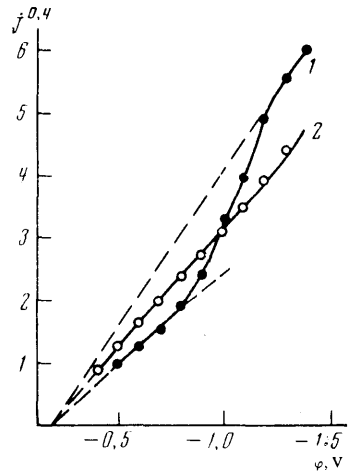

Figure 13. $j^{0.4}$–φ curves in: *1*) 1 N solution of $NaNO_3$ and *2*) the same solution containing 10^{-4} N tetrabutylammonium salt[95].

The experimental results are in good agreement with the theory. Two linear portions (for high and low potentials respectively) are separated by a curvilinear portion extending from −0.7 to −1.2 V relative to the saturated calomel electrode. Small additions of tetrabutylammonium salt (10^{-4} mole litre^{-1}) produce a marked change in the shape of the curve: all the points now lie on the same straight line at potentials more positive than −1.4 V.

The influence of tetrabutylammonium is the result of two separate effects: adsorption at the mercury surface suppresses the emission current[84], but it also inhibits the oxidation of NO_3^{2-}, thus suppressing the decrease in photocurrent at positive potentials. The rate constant k_d for the decomposition of NO_3^{2-} in solution, and the transfer coefficient β of the electrochemical oxidation of NO_3^{2-}, have

been determined from the experimental results: $\beta \simeq 0.25$, $k_d = 6 \times 10^6\ s^{-1}$. A similar value of the transfer coefficient has been obtained by other workers [106,108].

A much lower value of the rate constant ($k_d = 10^4\ s^{-1}$) has been reported [106,108] from measurements of the emitted charge under pulsed illumination of the electrode. Those workers [106,108] ascribe the increase in charge in the presence of NO_3^- to electrochemical reduction of the OH radicals formed from the decomposition of NO_2^- by reactions (E) and (G); k_d was calculated from the kinetics of this growth of charge.

It is evident, from the examples considered in this Section, that the study of photoemission phenomena in aqueous solutions offers a wealth of information on homogeneous and heterogeneous processes in the layer of solution adjacent to the electrode.

3. Competing Solvated-electron Capture Reactions

Competing reactions take place in solution when several electron acceptors are present together. The competing acceptor method is widely used in radiation chemistry to determine relative rate constants. Barker and coworkers [29] have made a quantitative study of the photocurrent in the presence of two competing electron acceptors (A and B).

Acceptors		$10^{-10} k_A$, litre mole^{-1} s^{-1}	
A	B	photo-emission	pulse radiolysis
H_3O^+	N_2O	1.5	1.4
Zn^{2+}	H_3O^+	0.046	0.06
Cd^{2+}	N_2O	3.6	2.1
Ni^{2+}	N_2O	1.5	0.9
NO_3^-	N_2O	2.0	1.76
NO_2	N_2O	0.5	0.63

In the general case, the dependence of the photocurrent on the concentration of the two acceptors (c_A and c_B) can be written in the form

$$j = j_0(\nu_A k_A c_A + \nu_B k_B c_B)/(k_A c_A + k_B c_B)^r. \qquad (15)$$

In this expression k_A and k_B are the rate constants for the reaction of electrons with the acceptors A and B respectively, ν_A and ν_B are the stoichiometries for these reactions. The exponent r depends on the concentration of acceptors. At high acceptor concentrations $r = 1$; when both c_A and c_B are low $r = 1/2$. Eqn. (15) is strictly applicable if the stoichiometries ν_A and ν_B are independent of acceptor concentration. Furthermore, the product of the reaction of an electron with one of the acceptors must not undergo further reaction with the other acceptor.

It follows from Eqn. (15) that the ratio of the rate constants (k_A/k_B) can be determined by studying the variation of the photocurrent with the concentration of both acceptors. The absolute values of the rate constants can be deduced from the relative value if the rate constant of one of the competing reactions is known. Absolute values of the rate constant for the capture of a hydrated electron by various acceptors, measured by the photoemission variant of the method of competing reactions, are listed in the Table [29]. The values obtained by the pulse radiolysis method are also given for comparison.

In the calculations the absolute rate constant k_{N_2O} was taken, on the basis of radiation-chemical measurements, as 5.6×10^9 litre mole^{-1} s^{-1}. The satisfactory agreement between the two methods is evident from the Table.

VI. SOME NON-EMISSION PHENOMENA ASSOCIATED WITH THE EXTERNAL PHOTOEFFECT

As was stated above, photoemission is only one of the many photochemical effects which make up the "Becquerel effect". A brief description of some of these phenomena is appropriate here, because, like photoemission itself, they can be used to study the structure of the interface between an electrode and an electrolyte, and the kinetics of reactions at such an interface.

1. Anodic Photocurrents

To explain the photoeffect, Heyrovský suggested the formation of a charge-transfer complex between the surface of a metal electrode and molecules of solvent or solute decomposed under the influence of light. This explanation cannot be applied to a mercury electrode at potentials more negative than its point of zero charge, i.e. in the region of cathodic photocurrents. In this case, photoemission is a more probable process. But at more positive potentials, where emission is inconceivable and the observed photocurrents are usually of the opposite sign (i.e. anodic), Heyrovský's explanation is probably correct. Anodic photocurrents are observed in solutions of oxalic, chloroacetic, tartaric, and other organic acids and their salts [26]. The molecules of all these compounds contain the $-\overset{\overset{O}{\|}}{C}-\overset{\overset{X}{|}}{C}-$ group, where X denotes an electronegative substituent. When these species are adsorbed at the mercury surface a chemical bond is formed between the metal (acceptor) and the O or X atom (electron donors). The resulting bond can absorb light of greater wavelength than the compound originally in solution. On illumination the adsorption bond is broken, the electrons are transferred to the electrode, and the organic substance (in an oxidised form) is returned to the solution.

A similar mechanism was invoked [110] to explain the photoeffect at a platinum electrode under the influence of u.v. light.

The study of anodic photocurrents can yield valuable information on the energy spectrum of the surface electronic levels of the metal corresponding to the adsorbed particles.

2. Pulse Heating of the Electrode

According to Berg, light adsorption "excites" the electrode and (in the presence of a depolariser) enhances electrochemical reactions which are hindered in the dark. The concept of a "hot" electrode has been tested by looking for evidence of light-induced changes in properties such as surface tension and differential capacitance [70,111]. No significant change in the surface properties of mercury was observed on illuminating a mercury electrode with steady light from a super-high pressure lamp. However, a change in the differential capacity (due to the heating of the electrode and the adjacent layer of solution) has been observed by using very high energy light pulses.

In dilute solutions the differential capacity of the electrode is determined mainly by the capacity of the diffuse part of the double layer, and therefore decreases with increasing temperature. In the galvanostatic and the coulostatic regime a change in capacity produces a shift in the electrode potential; in the potentiostatic regime it produces a change in the current flowing in the external circuit. In both cases the sign of the effect depends on the sign of the charge on the electrode. Korshunov and coworkers [73] have proposed a method of measuring the zero-charge potential of metals based on this effect: as the (dark) potential of the electrode is varied, the sign of the photoeffect is found to change at a value of the potential corresponding to zero charge on the electrode. Long-wave light, which does not cause photoemission, is used in this experiment§.

Other interesting photoelectrochemical phenomena, on which we shall not dwell, include electrode reactions of light-excited depolariser molecules [5,112], photoemission of electrons from the surface of electrolyte solutions into the surroundings [113], and electro-reflection at the metal–electrolyte boundary [114-116].

VII. FUTURE PROSPECTS

The special properties of the metal–electrolyte interface (in particular, the independently variable potential of the electrode) offer a number of valuable facilities in studies of photoemission. Studies of this phenomenon in electrochemical systems can provide information on the electron density in the metal and its distribution, on the properties of the Fermi surface of the metal [117], and on the mechanism of light absorption by the metal surface.

Furthermore, photoemission studies have led to the solution of a number of purely chemical problems. For example, the structure of the electrical double layer and various adsorption phenomena have been studied in detail. The potential variation within the fixed part of the double layer can be investigated by monitoring deviations from the "five-over-two" law. Also, definite conclusions regarding the structure of the fixed part of the double layer can be based on data obtained from the study of photoemission into solutions.

Lastly, it is possible to study the behaviour of electrons in liquids, and in particular to measure the rate of solvation of electrons and the rate of capture of solvated electrons by acceptors and by the electrode surface.

Thus, the photoeffect at the metal–solution interface offers not only an insight into purely photoemission phenomena but also a powerful new method of studying the structure and properties of this interfacial boundary and the physicochemical processes of which it is the seat.

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Oxidation of Silicon

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Work on the oxidation of silicon in various gaseous media has been reviewed. Particular attention has been paid to the mechanism of formation and the kinetics of the growth of oxide films on silicon during high-temperature oxidation. Published data on the composition and structure of the resulting film of reaction products, the dependence of the rate of oxidation on the pressure of the oxidising medium, and the possible participation of silicon ions in the growth of the oxide film have been discussed. The bibliography contains 120 references.

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1. INTRODUCTION

The interest in oxide films on silicon is due to the development of semiconductor electronics with the use of these films to protect the surfaces of semiconductor devices and also as active and passive elements in solid silicon functional circuits.

The many methods for preparing these films have been for the most part the result of empirical research. In addition to methods involving the thermal[1-23] and anodic[24-30] oxidation of silicon, methods involving the deposition of silicon dioxide films from the gaseous phase have been developed. Methods of this kind which have found application include those involving the volatilisation of oxides of silicon in a vacuum[31-37], cathodic sputtering and sputtering in a high-frequency discharge[30,36-39], the pyrolytic decomposition of organosilicon compounds[30,41-43], and the chemical transport and hydrolysis of silicon halides[30,44-56].

When oxide layers are used as masks in processes of diffusion alloy-formation or the surface protection of a semiconducting device, the purity and continuity of the oxide are important, whereas when silicon dioxide is used as an active element, for example in MOS-structures (metal–oxide–semiconductor), the electrical properties of the film itself and more particularly of the interface between it and the semiconductor acquire considerable importance.

Such properties of the oxide film as the electrical conductivity and charge density in the bulk of the film and at the interface between it and the semiconductor, which determine the parameters of the device and their stability, depend chiefly on the conditions of formation of the oxide. It is the physicochemical conditions of the process (temperature, pressure, the oxidising medium, etc.), and hence of the formation of the oxide film, and the interface between it and the semiconductor, which determine its degree of stoichiometric and structural perfection and the related electrical properties of the MOS-structures.

Thus the detailed study of the mechanism and kinetics of the growth of oxide films, particularly in the initial stages of their formation, is of considerable importance for the production of films with required properties.

The present review deals with problems of the kinetics and mechanism of the thermal oxidation of silicon, which provides one of the basic methods for obtaining silicon dioxide films.

2. KINETICS OF THE GROWTH OF OXIDE FILMS ON SILICON

The initial stage of the reaction of silicon with oxygen when the silicon surface has been effectively cleaned should involve the adsorption of the gas on the surface. Subsequently, the oxygen may dissolve to some extent in the silicon, after which the production of oxide in the form of individual nuclei or a continuous film will take place.

In all the work dealt with in this review, the observation of the course of the high-temperature oxidation process was begun not with an atomically-clean silicon surface but with a surface carrying a thin oxide film, formed during the preliminary treatment of the specimens studied.

These films may have different thicknesses. The subsequent growth of the primary oxide film formed may obey different relationships, depending on its thickness, structure, and composition, and also on the actual conditions of oxidation.

The large number of studies of the kinetics and mechanism of the oxidation of various metals have been reviewed in a number of monographs[57-60], and they show that low-temperature oxidation in most instances is characterised by logarithmic or inverse-logarithmic relationships, whereas high-temperature oxidation most frequently shows a time dependence of parabolic type, deviations from which are observed in a number of instances in the initial stage of the oxidation. The parabolic law for high-temperature oxidation generally means that the rate of oxidation is limited by the rate of diffusion of the reacting components through the oxide film. A theoretical basis for this mechanism was proposed by Wagner[61,62]. His theory is based on the concept of conductivity in ionic crystals and semiconductors. The movement of ions through the oxide film is due to the cation concentration gradient which always exists as a consequence of the constant enrichment of the surface of the oxide layer in oxygen and of the internal interface in cations. Wagner's theory does not deal with the initial stages of the oxidation and is restricted to a consideration of the growth of oxide films after they have reached a definite thickness. The regular features of the initial stage of the oxidation have been interpreted in different ways by different authors. This problem will be discussed after an examination of published data on the kinetics of the high-temperature oxidation of silicon.

The kinetic features of the high-temperature oxidation of single crystals of silicon have been studied by various

methods by a number of authors over a wide range of temperatures and pressures.

Thus Atalla and coworkers [1] studied the stabilisation of the surface of silicon by oxide films grown at 1000° in an atmosphere of water vapour and oxygen.

McAdam and Geil [2] studied the growth of oxide films on silicon, using an optical method to measure the thickness of the oxide. They established that at temperatures in the range 500–950° the results can be described by the parabolic film-growth law:

$$\frac{dn}{dt} = \frac{k}{n} \quad (1)$$

where n is the number of molecules of oxygen reacting in time t, and k the oxidation rate constant.

Brodsky and Cubicciotti [3] studied the oxidation of silicon at p_{O_2} = 200 mmHg by recording the change in the oxygen pressure with time; they obtained at 950° and 1160° a parabolic relationship, and at 1015° and 1020° a logarithmic relationship of the form

$$W = k \lg(1 + at), \quad (2)$$

where W is the quantity of oxidant used in time t, and a and k constants.

The growth of the oxide according to a logarithmic relationship was attributed to the formation of a vitreous oxide of silicon, in which the concentration gradient of the diffusing particles changes not linearly but according to a relationship of the form $\partial c/\partial x = -c_0 \alpha e^{-\alpha x}$ (c_0 is the concentration of diffusing particles at a distance x from their starting point, and α a proportionality efficient). The estimated activation energy of oxidation is E = 26 kcal mole^{-1}.

Law [4] used a manometric method to study the kinetics of the oxidation of silicon at temperatures in the range 727–1027° at pressures of dry oxygen in the range 10^{-3}–5×10^{-2} mmHg. Under these conditions the rate of oxidation is described by a parabolic equation of the form

$$n = 2k\left(\frac{t}{n}\right) + c, \quad (3)$$

where n is the number of oxygen molecules which have reacted in time t, and c and k constants. According to Law's data, E = 36 kcal mole^{-1}.

Evans and Chatterji [5] studied the kinetics of the oxidation of silicon in dry oxygen by a gravimetric method and found that in the temperature range 1200–1400° the rate is given by a parabolic law (E = 43 kcal mole^{-1}). In their opinion, the straight lines shown in Fig. 1 do not, as might have been expected, pass through the origin of coordinates, because at all temperatures the rate of the process in the initial stage is greater than would be expected from a parabolic oxidation law.

Sah and coworkers [6] obtained a parabolic law for the oxidation of silicon in moist oxygen in the range 1200 to 1300° (E = 34 kcal mole^{-1}).

Ligenza and Spitzer [7] studied the oxidation of silicon by oxygen at p_{O_2} = 1 atm and 950°, and concluded that the kinetics of the oxidation can be described by the equation

$$x^2 = 8.4 \cdot 10^{10} \cdot p^{1/4}\left[\exp\left(-\frac{40000}{RT}\right)\right] \cdot t, \quad (4)$$

where x is the thickness of the oxide, Å; t the time, min; and p the pressure, atm.

Later, Ligenza [8] studied the oxidation of silicon in water vapour at a high pressure (25–500 atm) in the range 500–950°, and showed that the growth of the oxide film takes place linearly with time, and that its rate is directly proportional to the vapour pressure.

Yeh [9] used an optical method to determine the thickness of the growing oxide and established that the oxidation of silicon by water vapour at p_{H_2O} = 1 atm and 970° obeys a parabolic law.

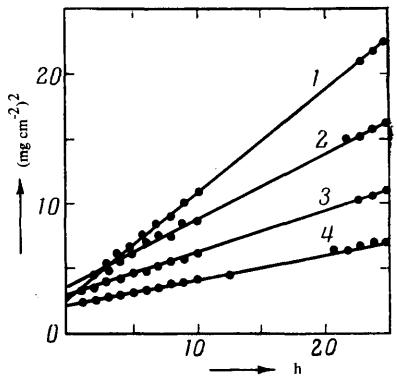

Figure 1. Oxidation of silicon [5]: *1*) 1360°; *2*) 1303°; *3*) 1255°; *4*) 1201°.

Claussen and Flower [10], using an ellipsometric method, found that the oxidation of silicon in dry moist oxygen or water vapour at 1200° also obeys a parabolic relationship.

A similar growth law for the oxide film on silicon in atmospheres of dry oxygen, moist oxygen, or water vapour in the range 1000–1200° was derived by Deal [11], who established that the rate of oxidation in water vapour is greater than that in moist or dry oxygen. The activation energy values obtained by Deal for the three oxidation conditions indicated are given in the Table.

Medium	Activation energy (kcal mole^{-1}) calculated from data	
	gravimetric	optical
Dry oxygen	28.4	30.2
Moist oxygen (95% H_2O)	21.4	20.8
Water vapour	20.0	19.9

Deal [11] noted that at ~1000° the growth of the film takes place according to the law

$$W^2 + k_1 W = k_2 t \quad (5)$$

where W is the quantity of oxide formed, t the duration of oxidation, and k_1 and k_2 constants.

The oxidation of silicon in dry oxygen and water vapour at elevated temperatures was studied by Edagawa and coworkers [12], who obtained the following experimental equations characterising the kinetics of the growth of the films: in an atmosphere of water vapour

$$x_0^2 = 3.35 \cdot 10^9 \cdot t \cdot \exp(-23000/RT) \quad (6)$$

and in an atmosphere of dry oxygen

$$x_0^2 = 4.84 \cdot 10^9 \cdot t \cdot \exp(-32200/RT) \quad (7)$$

where x_0 is the thickness of the oxide film, t the time, and R the gas constant.

Fuller and Streiter [13] studied the oxidation of silicon in an atmosphere of water vapour or dry oxygen in the range 700–1200°. To determine the thickness of the oxide layer they used an ellipsometer and a table of interference colours. In both media, for the reactions taking place below 1070°, they obtained a parabolic law of oxide growth with activation energy equal to 39 kcal mole^{-1}. The reactions taking place at higher temperatures are also characterised by a parabolic oxidation law, but with a lower activation energy.

Revesz and Zaininger [14] found that the oxidation of silicon in an atmosphere of water vapour obeys a parabolic relationship if the thickness of the film formed is greater than 3000 Å. A film of smaller thickness, in the opinion of the authors cited, grows according to a linear law.

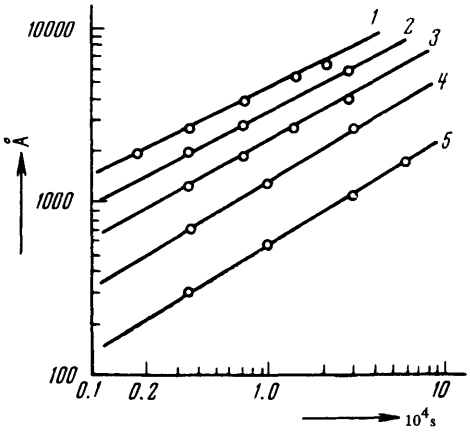

Figure 2. Oxidation of silicon [16]:
1) 1300°, *2*) 1200°, *3*) 1100°, *4*) 1000°, *5*) 900°.

Sladkova [15] used a polarimetric method to study the oxidation of silicon in air. In the range 300–560°, oxide could not be detected. In the range 560–950° the oxidation obeyed the linear law

$$d_1 = k_1\tau + d_0 \quad (8)$$

where d_1 is the thickness of the film, d_0 the initial thickness of the film, τ the time, and k_1 a constant. The value of k_1 depended on temperature: $k_1 = at^2 + b$, where t is the temperature, and a and b constants. In Sladkova's opinion, the oxidation of silicon in the range 950–1000° is described by the parabolic law

$$d_2^2 = k_2\tau + d_0^2 \quad (9)$$

where d_2 is the thickness of the film, d_0 the thickness of the original film, and k_2 a constant.

Evitts and coworkers [16], using an optical method, found the following relationships describing the rate of growth of oxides at temperatures equal to or greater than 1100° and a pressure equal to 1 atm:
for water vapour

$$x^2 = 1.21 \cdot 10^9 \cdot t \cdot \exp(-18400/RT) \quad (10)$$

and for dry oxygen

$$x^2 = 3.53 \cdot 10^9 \cdot t \cdot \exp(-30590/RT) \quad (11)$$

where x is the thickness of the oxide, Å, and t the time, s. The results [16] for the oxidation of silicon in dry oxygen are given in Fig. 2.

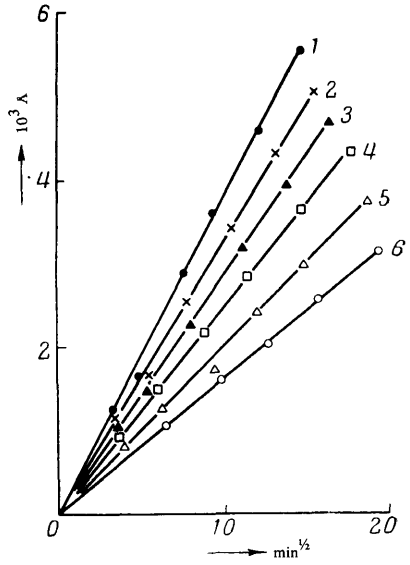

Figure 3. Oxidation of silicon [17]:
1) 1300°, *2*) 1247°, *3*) 1205°, *4*) 1150°, *5*) 1100°, *6*) 1050°.

Lukes and Schmidt [17] used an optical method to study the oxidation of single crystals of silicon in an atmosphere of dry oxygen at 1050° and 1300° and obtained a parabolic law for the oxide film growth (Fig. 3):

$$d^2 = kt, \quad (12)$$

where d is the thickness of the oxide film, t the duration of oxidation, and k a constant. They found that the temperature dependence of the parabolic rate constant k in Eqn. (12) was not exponential, but satisfied the relationship

$$k = A(T - T_0)^2 \quad (13)$$

where A is a constant, and $T_0 = 860°$ (from the experimental data).

The data of Deal and Grove [18] on the oxidation of silicon in dry oxygen, obtained by determining the thickness of the oxide by an optical method, are given on logarithmic coordinates in Fig. 4. The slope of the lines on the graph corresponds to the exponent n in the equation

$$x_0^n = kt \quad (14)$$

where x_0 is the thickness of the oxide film, t is the time, and k a constant.

It can be seen from Fig. 4 that the value of n at 1200° is close to 2, whereas at lower temperatures and smaller oxide thicknesses the value of n at first decreases to 1.5 and then increases again. Thus the data obtained by these authors cannot be described by a simple power law. The difference in the kinetics of the oxidation of silicon in dry

and moist oxygen is demonstrated in Fig. 5. The curve characterising the kinetics of the oxidation in dry oxygen intersects the axis of ordinates at $x_0 = 250$ Å. The authors conclude that this course of the curve is due either to the presence of an oxide film of definite thickness on the silicon surface before the start of the measurements or to the manifestation of a different oxidation mechanism in the first stage of the process. Since in the oxidation of silicon in moist oxygen a primary oxide film was not observed, the authors used the second alternative to explain the results obtained on oxidation in an atmosphere of dry oxygen. The rate of oxidation was higher at the start of the process in dry oxygen at 700° (Fig. 6).

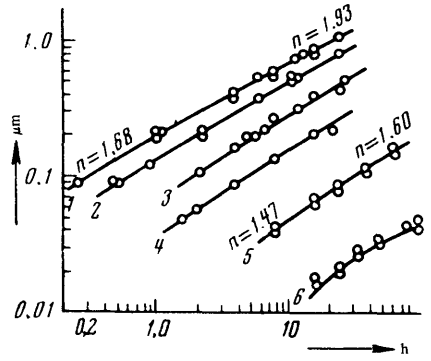

Figure 4. Oxidation of silicon in dry oxygen[18]: *1*) 1200°, *2*) 1100°, *3*) 1000°, *4*) 920°, *5*) 800°, *6*) 700°.

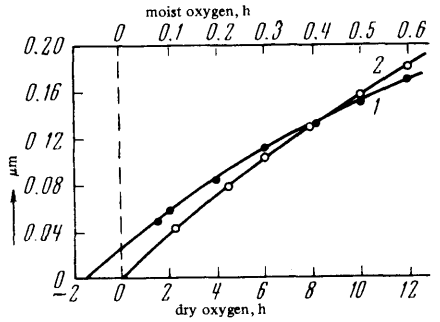

Figure 5. Oxidation of silicon in dry and moist oxygen[18]:
1) dry, *2*) moist.

Deal and Grove[18] consider that the kinetics of oxidation of silicon over a wide range of temperature and pressure by the action of oxygen or water vapour obeys a relationship of the form

$$x_0^2 + Ax_0 = B(t + \tau) \qquad (15)$$

where x_0 is the thickness of the oxide film, t the time, and A, B, and τ are constants for the oxidation.

According to Pliskin[19], the oxidation of silicon in an atmosphere of water vapour also obeys a linear–parabolic law.

Nakayama and Collins[20] studied the kinetics of the growth of films of SiO_2 on silicon in a mixture of water vapour and oxygen or argon in the range 850–1217° and partial pressures of water in the range 4.6–355 mmHg. In this temperature range the authors observed a mixed linear–parabolic oxidation law of the form

$$Ax + Bx^2 = t \qquad (16)$$

where x is the thickness of the oxide, t the time, and A and B constants. Hikaru and Dzenti[21] give data on the influence of the treatment of the surface of the specimen, the moisture content of the oxidising medium, and the crystallographic characteristics of the crystal plane studied, on the rate of oxidation of silicon. They did not observe any differences in the rates of oxidation of specimens subjected to mechanical and chemical polishing. The rate of oxidation increased with increase in the moisture content. In the range 995–1050° the rate of oxidation depended on the orientation of the crystal plane studied, as follows: $v_{[111]} = v_{[110]} > v_{[100]}$. It was found that the activation energy of oxidation changes on going to the temperature range below 1100°. The authors cited conclude that at low temperatures the mechanism of oxidation is different, and the growth of the oxide film does not follow a quadratic law.

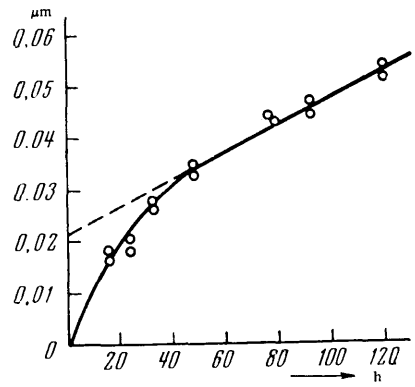

Figure 6. Oxidation of silicon in dry oxygen at 700°.[18]

According to the data of Mai[22], the growth of the oxide film in the successive oxidation of silicon in dry oxygen, moist oxygen, and water vapour at 1150° obeys a parabolic relationship, the rates of the corresponding processes decreasing in the order: $v_{\text{water vapour}} > v_{\text{m.o.}} > v_{\text{d.o.}}$

Burkhardt and Gregor[23] determined the volume of oxygen used in the oxidation from the position of a mercury seal in a measuring tube; adopting the interpretation of the oxidation put forward by Deal and Grove[18], they obtained a linear–parabolic relationship for the growth of oxide films as far as thickness of 5000–6000 Å.

3. MECHANISM OF FORMATION OF OXIDE FILMS

Analysis of published data on the thermal oxidation of silicon shows that at high temperatures the growth of the oxide film follows a parabolic time dependence, deviations from which have been observed by a number of authors[5,11,13,18,23] in the initial stages of oxidation.

Many authors try to explain the formation of the primary oxide films on silicon on the basis of the mechanism of formation of thin oxide films put forward by Cabrera and Mott[63]. This mechanism assumes that in the film of oxide formed on chemisorption, the electrons of the metal, moving independently of the ions, pass through the thin layer of oxide, either by a tunnel effect or as a result of thermionic emission, and react with oxygen on the outer surface of the film, that is at the oxide–gas interface, forming oxygen anions. Metal cations are formed correspondingly at the metal–oxide interface. As a result, in the opinion of the authors cited, a strong electric field, which facilitates the transfer of positive ions to the oxide–gas interface, is created inside the oxide film. The rate of ion transfer should show an exponential dependence on the field intensity, and the oxidation is described by a corresponding inverse logarithmic equation.

In a recent paper, Mott and Fehlner[64], taking into account the ideas of Eley and Wilkinson[65], dealt with the role of the structural factor in oxidation for the example where the growth of the oxide film involves the migration of oxygen through the oxide film.

Other authors[4,13] attribute the deviation from the parabolic law in the initial stage of the oxidation to the production of a space charge, in accordance with the ideas of Engell and Hauffe[66–68]. According to these ideas, exchange of charge carriers between the gas molecule being adsorbed and the semiconductor takes place on chemisorption, so that this stage leads to charging of the surface. As a result, a space charge is produced in the layer of the semiconductor next to the surface, leading to the manifestation of a diffusion potential, resulting from the difference in the mobilities of the electronic and ionic defects in the thickness of the oxide. In the opinion of this group of authors, a parabolic oxidation law should not be observed so long as the thickness of the growing layer is comparable with the region of the space charge influencing the ion diffusion responsible for the growth of the film.

Deal and Grove[18], using the model of oxidation proposed by Evans[57,69], suggest that for "short" times, the duration of which is determined by the specific conditions of the oxidation, a linear law of oxide growth should operate. Evans, however, in the interpretation of the equation which he derived, of the form

$$k_1 y^2 + k_2 y = k_3 t + k_4 \qquad (17)$$

where y is the thickness of the oxide film, t the time, and k_1, k_2, k_3, and k_4 constants, considered that for small values of t and y, Eqn. (17) becomes a simple parabolic equation, and at high values of t and y it may approach a linear equation.

Growth of the oxide film according to a linear law is possible if the oxide splits with the passage of time, as a consequence of a difference in the volumes of the oxide and the metal. In this instance, oxygen has free access to the metal surface, and the stage determining the rate of oxidation will be the reaction at the oxide–gas interface. It should be noted that a linear oxide growth law is also possible at very low oxygen pressures, when the oxygen being supplied is unable to compensate the loss of oxygen during its reaction with the cations passing through the oxide film, as observed, for example, by Gulbransen and coworkers[70], who made a gravimetric study of the oxidation of silicon at oxygen pressures equal to 9×10^{-3}, 4×10^{-2}, and 1×10^{-1} mmHg and temperatures of 1100, 1200, and 1300°. The authors cited put forward four equations to describe the reactions involved in the oxidation of silicon

$$Si_{(s)} + {}^1/_2 O_{2(g)} \rightleftarrows SiO_{(g)}, \qquad (18)$$

$$Si_{(s)} + O_{2(g)} \rightleftarrows SiO_{2(s)}, \qquad (19)$$

$${}^1/_2 Si_{(s)} + {}^1/_2 SiO_{2(s)} \rightleftarrows SiO_{(g)}, \qquad (20)$$

$$SiO_{2(s)} \rightleftarrows SiO_{(g)} + {}^1/_2 O_{2(g)}. \qquad (21)$$

A small increase in weight, indicating the formation of a layer of oxide on the surface according to Eqn. (19), was observed only at $p_{O_2} = 1 \times 10^{-1}$ and a temperature of 1100°. Under all other conditions, a decrease in weight as a result of the formation of the volatile monoxide according to Eqn. (18) was observed. Gulbransen and coworkers[70] established that the rate of oxidation is linearly dependent on the rate of flow and pressure of oxygen. They concluded that the rate of oxidation at low oxygen pressures is a function of chiefly the pressure and velocity of the gas stream, and is almost independent of temperature. In this case the rate of the process is determined by the transfer of gas to the surface of the specimen.

An analysis of the primary stage of the oxidation would be incomplete without consideration of the importance of the active sites on the metal surface, the role of which may be extremely significant, particularly in the examination of the influence of the pressure of the oxidising medium on the oxidation.

Arslambekov[71] has examined the kinetics of the formation and growth of the primary oxide film from the viewpoint of kinetic theory. The rate of the process in this instance can be represented by the equation

$$\frac{\partial n}{\partial t} = (N_0 + N_{\text{diff}} - n) \cdot \sigma \cdot Z \cdot e^{-E/RT} \qquad (22)$$

where N_0 is the initial number of active metal atoms on the surface, N_{diff} the number of active metal atoms coming out on the surface as a result of diffusion, n the number of metal atoms reacting, δ the effective cross-section of the metal atom–gas molecule reaction, Z the number of oxygen molecule collisions taking place on 1 cm² of the surface, and t the time.

The solution of this equation for low temperatures and low pressures, that is for the conditions under which the formation of thin oxide films can be followed, has the form

$$n = N_0(1 - e^{-kt}) \qquad (23)$$

where $k = 6 \times 10^6 \frac{p}{\sqrt{T}} \cdot e^{-E/RT}$ is the rate constant; p the pressure, mmHg; E the activation energy; and T the temperature, °K.

On the basis of the theoretical considerations developed in Refs. 71–73, Arslambekov put forward a mechanism for the formation of the oxide film, describing the interaction between oxygen and an atomically-clean metal surface, with allowance for local superheating.

In the elementary stage of the interaction of a gas molecule with a metal surface, all the heat of reaction is liberated in a negligibly small volume, and this leads to a local increase in temperature. The next gas molecule entering the local superheating zone undergoes reaction with a greater probability than that for the cold regions. This leads to additional liberation of heat and an increase in the temperature of the surface. The latter will increase until a steady state, in which the quantity of heat supplied by the reaction is equal to the quantity of heat removed by the thermal conductivity of the metal, is established.

At low oxygen pressures, the frequency of collisions against the surface is low, so that in the time interval

between two successive collisions of oxygen molecules in the same zone the heat from each elementary stage of the interaction is able to undergo complete scattering. Each new molecule of oxygen then reacts with a cold surface, so that the formation of the oxide film should take place relatively slowly, and the thickness of the layer formed may be very small (only several monolayers).

It should be noted that in all the above theories of formation of the primary oxide films, attention was not paid to the role of the crystal lattice type of the metal being oxidised and the oxide, or the crystal-chemical relationships between them. Allowance for the crystal-chemical correspondence between the structures of the metal and the oxide, however, reveals significant features of the actual mechanism of formation of oxide layers on metals.

According to Dankov's crystal-chemical theory of oxidation [74,75], the establishment of a stoichiometric relationship between the components takes place as soon as a monomolecular layer of oxide is formed. The characteristic feature of the primary stage of the oxidation is that in this stage there is direct contact between the oxygen molecules and the chemically non-combined metal atoms, whereas in the subsequent stages the O_2 molecules encounter the chemical compound M_xO_y on the surface.

A characteristic feature of the oxidation, observed when the reaction takes place at room temperature, is the attainment of a limiting oxide film thickness; this limit lies in the range of submicroscopic thicknesses. In the mechanism proposed by Dankov for the formation of oxide films of limiting thickness, it is assumed that the growth of the oxide film at moderate temperatures, in which diffusion of the components through the oxide is required, is made possible by the penetration of defect sites in the oxide lattice. The latter results from the non-coordinated growth of a large number of oxide blocks consisting of stoichiometric saturated formations.

On the basis of the theory that there is a gradual decrease in the concentration of the defects which are responsible for the diffusion and hence which determine the rate of formation of the oxide, Dankov derived an equation which characterises the change in the thickness of the oxide with time and which indicates the existence of an oxidation limit:

$$y^2 = \frac{2k''}{k}(1 - e^{-kt}), \qquad (24)$$

where y is the thickness of the oxide, k'' and k constants, and t the time.

A development of Dankov's principle of orientational and dimensional correspondence as applied to solid-phase chemical reactions was provided by the scheme proposed by Arkharov [76] for the nucleation of the primary crystal of a chemical compound. According to Arkharov, the reaction of a metal with a gas involves the formation of a supersaturated solid solution, in the volume of which the primary nucleus of the oxide phase is formed.

The reasons and conditions for the formation of nuclei of the oxide phase on a metal surface in its reaction with an oxidising medium have been examined by a number of authors [58,77,78].

The following scheme for the growth of oxide films on silicon in dry oxygen was proposed by Ono and coworkers [79]. In the initial moment of oxidation, isolated oxide units are formed around the defects in the silicon surface (impurity atoms, dislocations, lattice defects, etc.). Subsequently, each isolated unit expands, and its surface acquires a planar form. The upper layers of these regions consist of SiO_2, and the inner layers consist of a series of lower oxides of silicon. The secondary projections produced between the isolated oxide units on subsequent oxidation expand and join up with one another, and when the process lasts for a sufficiently long time they cover the Si surface completely.

Arslambekov and coworkers [80] give experimental data on the kinetics of the oxidation of silicon at temperatures in the range 700–1180° and oxygen pressures in the range 10–320 mmHg, obtained by continuous weighing on an automatic vacuum micro-balance. They also give a theoretical analysis of the kinetics of the growth of oxide films on silicon with allowance for the defects produced in the oxide film in the primary stage of the oxidation, and also with allowance for the possible counter-diffusion of oxygen and metal through the oxide. The experimental data are effectively described by the derived kinetic equation, which takes account of a number of possible stages in the high-temperature oxidation:

$$(Q + Q_0)^2 = 2kt + 2A\tau_a(1 - e^{-t/\tau_a}) + 2B\tau_b(1 - e^{-t/\tau_b}) + Q_0^2 \qquad (25)$$

where Q is the quantity of oxygen absorbed in the oxidation, Q_0 the quantity of oxygen absorbed in the primary stage of the oxidation, k the parabolic oxidation rate constant, t the time, A and B coefficients making allowance for the influence of the concentration of defects in excess on the diffusion of the components (oxygen and silicon respectively), and τ_a and τ_b the non-equilibrium defect relaxation time constants for oxygen and silicon respectively.

The accelerated growth of the oxide film at small thicknesses ($t < 3\tau$)—compared with the parabolic—which follows from the relationship derived by the authors cited, is due to the presence of an excess of structural defects produced in the primary stage of the reaction between silicon and oxygen. When the concentration of defects reaches the equilibrium value for the given temperature, when $t > 10\tau$, the exponential terms become much less than unity, and the growth of the oxide film will be described by a parabolic equation of the form

$$Q^2 + 2QQ_0 = 2kt + c \qquad (26)$$

where

$$c = 2A\tau_a + 2B\tau_b + Q_0^2 . \qquad (27)$$

4. COMPOSITION AND STRUCTURE OF OXIDE FILMS ON SILICON

The reliable determination of the mechanism of oxidation requires continuous measurement of the change in the weight of the specimen over a fairly prolonged period, and comparison with the composition and structure of the reaction products. The detailed analysis of the nature of the oxide films on silicon is made difficult by their amorphous structure, established by a number of authors [81–86] by X-ray and electron diffraction.

Pavlov and Shitova [87] made an electron diffraction study of films on silicon, produced by oxidation in water vapour under pressure (p_{H_2O} = 0.25 atm, temperature 650°) and in a high-frequency discharge plasma with tetramethoxysilane as starting material. Depending on temperature and pressure, crystalline silicon dioxide can exist in various structural modifications: quartz (α, β), tridymite (α, β, γ), and cristobalite (α, β) [88], which have been shown by X-ray diffraction [89] to be based on SiO_4 tetrahedra which are joined at their apices and are

arranged in space according to a definite law. In the cristobalite structure, closed cavities are formed, whereas in the tridymite structure, channels penetrating the entire framework are left. It has been shown[87] that irrespective of the method of production, all the films have an amorphous structure, in which the short-range order is identical to that in the structures of β-cristobalite and β-tridymite. Experiments on the diffusion of boron and phosphorus at 1200° gave very low values for the diffusion coefficients (10^{-15} cm^2 s^{-1}) for all types of film[90], and it was concluded that the cristobalite structure is the most probable from the energetic viewpoint.

Revesz[84] studied the structure of films obtained by different methods: thermal oxidation in moist or dry oxygen, anodic oxidation, and pyrolytic decomposition of tetraethoxysilane. In all instances the diffraction patterns contained only a diffuse ring or "halo" indicating that the oxide has an amorphous structure. Revesz considers that the small crystallites which may be formed in the initial stage of the growth of the oxide when the silicon surface carries projections and cracks facilitating the formation of nuclei of the crystalline phase are subsequently "displaced" to the oxide surface and no longer serve as crystallisation centres. He points out that the refractive indices and absorption of the films in the infrared range of the spectrum are very similar to those for vitreous silica, the structure of which is similar to that of cristobalite. In Revesz's opinion, the "vitreous" oxide formed is a non-crystalline chemically homogeneous material characterised by short-range order and the presence of Si–O bonds.

Thus according to modern theories[30,91], amorphous silica consists of a disordered three-dimensional network of silicon–oxygen tetrahedra, which are connected only through their apices, and not via edges or faces. The tetrahedra in quartz glass are similar to those in crystalline quartz, but in the glass they form a disordered network, and in crystalline quartz they form a regular lattice; even in quartz glass, however, many of the tetrahedra are grouped to form the hexagonal rings characteristic of crystalline quartz. According to modern theories of the vitreous state, the arrangement of the tetrahedra is not completely random[92]; the short-range order in the network of tetrahedra may be characterised by regions of crystallinity with dimensions from 10 Å to 100 Å. Thus the terms "quartz lattice", "vacancy", "interstitial atoms", etc. are used to describe the structure of the glasses.

In an examination of the problem of the phase composition of the oxide films formed on silicon, it must be borne in mind that since the free energy of the silicon–oxygen interface is different from that for the bulk of the material, there is a probability that compounds which are unstable in the volume of the material may be formed in this region. Thus the thermo-dynamic characteristics of the films formed on the surface may differ significantly from those of the same material in compact form.

The existence of the following oxides of silicon has now been established: SiO, Si_2O_3, SiO_2, and Si_3O_4[93].

Published data on the nature of solid silicon monoxide are contradictory. Most authors, on the basis of X-ray diffraction studies, regard it as an amorphous material[94-97]. Some workers consider that it is a fine mixture of silicon and silica (indistinguishable by X-ray diffraction[98-100], but direct proof for this hypothesis has not been given. Only two papers[101,102] describe SiO specimens with a cubic lattice with constant $a = 5.16$ Å.

Valuable information on the properties of silicon monoxide can be obtained by optical methods, particularly in the infrared range[103-106]. It has been noted[104-106] that the optical properties of a condensed film of silicon monoxide differ significantly from the properties of films of elementary silicon and of silicon dioxide. York[107] considers that data on the absorption spectra of silicon oxide films in the ultraviolet, visible, and infrared ranges can be used to establish quantitatively the proportions of the phases SiO, Si_2O_3, and SiO_2 in films obtained by condensation in a vacuum. According to Nishimura and coworkers[108], analysis of the infrared absorption spectrum indicates that the oxide films deposited in a high vacuum with a source at an elevated temperature contain SiO, whereas the films obtained in a low vacuum and with a source at a low temperature contain Si_2O_3. Litvinova and coworkers[93] report that it is possible that the phases Si_2O_3, Si_3O_2, and Si_3O_4 exist in the compact state in addition to the phase SiO. The materials studied were specimens of silicon oxides obtained by the condensation of SiO vapour in a vacuum. Films of oxides richer in oxygen than SiO were obtained under conditions in which small quantities of air were supplied to the vacuum chamber of the furnace. The compositions of the phases were established by high-precision chemical analysis and X-ray micro-analysis, and verified by carrying out the oxidation with continuous weighing. The authors cited concluded that the gaseous monoxide SiO, on condensation, can pass directly into the solid state, but that in order to prevent its disproportionation it is necessary to ensure a sufficiently high rate of cooling of the SiO vapour. In their opinion, the oxides SiO, Si_3O_4, and Si_2O_3 are stable only at high temperatures, have a high vapour pressure, and can exist indefinitely in solid form. albeit in a metastable state.

The explanation given by Sladkova[15] for the increase in the refractive index of oxide films on silicon from 1.48 to 1.55 is that in some instances the films formed on the silicon surface contain an SiO phase.

An attempt has been made[109,110] to establish the phase composition of the oxide films formed in the thermal oxidation of silicon in dry oxygen, by the analysis of data characterising the volatilisation of these films. Silicon itself, and some of its oxides, have an appreciable volatility. If the heats of evaporation of the individual phases differ significantly, it is sometimes possible, by carrying out studies over a wide range of temperatures, to reveal regions in which the kinetics of the overall process are determined by the volatilisation of one of these phases. In this instance, if the oxide film consists of several phases with different heats of volatilisation, inflections should be observed on the graphs giving the temperature dependence of the volatilisation rate constants on coordinates $\lg k$ against $10^4/T$. In both of the works cited, the analysis of the temperature dependence of the rate of volatilisation did in fact reveal three regions corresponding to volatilisation in the temperature ranges 810–1010, 1010–1082, and 1082–1150° (Fig. 7). The values of the heats of volatilisation calculated from the experimental data for these regions were found to be ~60, ~145, and ~117 kcal $mole^{-1}$ respectively. Microscopic analysis of the silicon surface after oxidation[110] showed that the oxide film had a marked defect structure, probably due to the change in the temperature conditions during oxidation and the long duration of the experiments. The presence of micropores and cracks in the oxide film probably also explains the fact that at about 950° the specimen showed a decrease in weight, due to the volatilisation of silicon monoxide present under a layer of silicon dioxide. This suggestion may also explain the difference in the data on the course

of the volatilisation of oxide films from a silicon surface in its initial stages [109,110].

Thus the oxide film on silicon, as on most metals, consists of several oxides: the outer layer consists of the dioxide, and the inner layer consists of silicon monoxide.

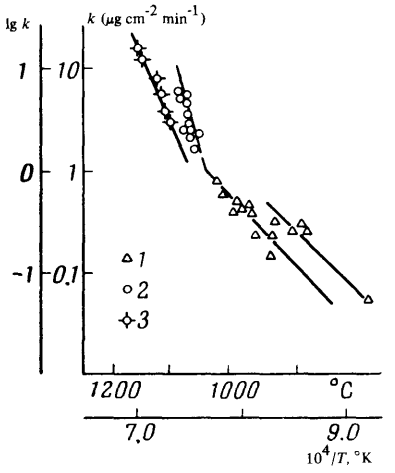

Figure 7. Volatilisation of silicon oxide films obtained by oxidation in dry oxygen at p_{O_2} = 40 mmHg in the range 816–916° for 44 h [110]:
1) volatilisation of SiO, *2*) volatilisation of SiO_2, *3*) volatilisation of Si.

5. DEPENDENCE OF THE RATE OF GROWTH OF OXIDE FILMS ON SILICON ON THE PRESSURE OF THE OXIDISING MEDIUM

A detailed understanding of the high-temperature oxidation of silicon requires a knowledge of the dependence of the reaction rate on the pressure of the oxidising medium.

If the rate of oxidation is limited by adsorption, the reaction usually depends markedly on the oxygen pressure. Under limiting conditions at very low oxygen pressures, the rate of oxidation is proportional to the rate of collision between oxygen and the surface, and hence to the oxygen pressure. At higher oxygen pressures the rate of oxidation is often proportional to $(p_{O_2})^{1/2}$. This is observed, in particular, in oxidations obeying the linear relationship, when the reaction rate is determined by processes beyond the limits of the phases.

Law [4] considers that the parabolic oxidation rate constant for thin oxide layers (100–1000 Å) is described by an equation of the form:

$$k = k_0 \ln p_{O_2} + \text{const} \qquad (28)$$

where k is the oxidation rate constant, and p_{O_2} the oxygen pressure.

A more marked dependence of the rate of oxidation of silicon on the pressure of oxygen, reflected by the empirical equation (29), was established by Arslambekov [109]:

$$x^2 = 1.1 \cdot 10^6 \cdot t \cdot p^{1/3} \cdot e^{-40000/RT} \qquad (29)$$

where x is the thickness of the oxide film, Å; p the pressure of oxygen, mmHg; and t the time, min.

6. NATURE OF THE DIFFUSING PARTICLES IN THE OXIDATION OF SILICON IN VARIOUS GASEOUS MEDIA

A number of papers [7,8,30,83,111–113] have been devoted to the investigation of the nature of the diffusing particles in the oxidation of silicon in various gaseous media.

Some authors [30] suggest that in the oxidation of silicon by water vapour, the first layers of oxide are formed by the chemisorption of water. Since these layers prevent further contact between water and silicon, the reaction takes place either between surface silicon atoms, combined in the crystal lattice, and water molecules, present in the interstices of the oxide, or between an intermediate silicon hydroxide group and silicon.

In the first instance the oxide is formed in the reaction

$$H_2O + Si{-}Si \rightarrow Si{-}O{-}Si + H_2 . \qquad (30)$$

In the second instance the following reactions take place: close to the gas–oxide interface

$$H_2O + Si{-}O{-}Si \rightarrow 2\,(Si{-}OH) , \qquad (31)$$

at the oxide–silicon interface

$$2\,(Si{-}OH) + Si{-}Si \rightarrow 2\,(Si{-}O{-}Si) + H_2 . \qquad (32)$$

In both reactions of oxide formation, described by Eqns. (30) and (32), the hydroxyl groups reacting with silicon must diffuse through the oxide layer in order to reach the oxide–silicon interface. It is assumed that the hydrogen, the rate of diffusion of which is fairly high ($D_{(H_2)_{1050°}} = 2.2 \times 10^{-6}$ cm² s⁻¹), diffuses through the oxide layer to the oxide–gas interface.

If a loose oxide layer is formed in the oxidation of silicon in an atmosphere of water vapour, the diffusion of hydroxyl groups or water molecules is facilitated. In this instance the process retarding the oxidation may be the reaction of the diffusing particles with silicon. Confirmation that the reaction rate is the factor limiting the oxidation can be provided, in the opinion of the authors cited, by the dependence of the rate of oxidation on the crystallographic characteristics of the surface being oxidised; this dependence is shown particularly clearly at high vapour pressures and low temperatures. It is found that $v_{[110]} > v_{[311]} > v_{[111]}$, where v represents the rates of oxidation of the corresponding faces.

The presence of impurities on the surface and in the volume of the semiconductor may lead to the production of pores of molecular dimensions, micro-cracks, dislocations, and other defects and inhomogeneities in the oxide. The pores and cracks make the oxide layer permeable to gases [115–118], and this must influence the regular features of the growth of the oxide.

In oxidation by water vapour, the presence of impurities in the volume of the silicon may influence both the rate of the surface oxidation and the diffusion coefficient of the reacting particles. For example, phosphorus influences chiefly the rate of the surface reaction: the surface containing a high concentration of the element is oxidised more rapidly than a surface containing a low concentration [118]. On silicon containing boron, the growing oxide "extracts" a large quantity of boron from the volume of the silicon [119]. The increasing defect nature of the oxide lattice leads to an increase in the rate of diffusion of the components of the reaction through the oxide.

Under conditions of prolonged oxidation at pressures of ~100 atm, dissolution of the oxide in water vapour is possible [8]. At even higher pressures, the silicon surface is etched as a result of the increased intensity of this process.

Study of the oxidation of silicon in a mixture of water vapour, oxygen, and argon[20] established that the concentration of water in the gas stream is the most important variable determining the rate of growth of the oxide at a given temperature. Change in the ratio of the partial pressures of water and oxygen may lead to a significant change in the kinetics of oxidation. Thus the activation energy of oxidation in moist oxygen decreases with increase in the concentration of water vapour. The process takes place much more rapidly in water vapour than in moist or dry oxygen, and the rate of oxidation in moist oxygen is greater than that in dry oxygen.

The nature of the diffusing particles in the oxide in the reaction of silicon with oxygen has been studied by various methods[83,112,113]. Thus Karube and coworkers[112] deposited the radio-active tracer ^{32}P on the oxidised surface of a specimen. The oxidation was then repeated under the same conditions (in a stream of oxygen at 1250°). The distribution of the diffusing particles was determined from the radio-activity values obtained by successively etching away layers of the oxide. The study was based on the following considerations: if silicon diffuses in the repeated oxidation, it will react at the gas interface, and the surface containing the radio-active tracer will again be covered by the growing oxide. If the process takes place as a result of the diffusion of oxygen, the chemical reaction will take place on the $Si-SiO_2$ interface, and the surface of the oxide obtained in the first oxidation will remain the gas–oxide interface. The results of the experiment confirmed the second mechanism, according to which the oxidation takes place with the transfer of oxygen through the oxide lattice.

Jorgensen[113] used a combination of methods involving the deposition of a Pt tracer on the surface and the application of an electric field. A layer of platinum with thickness 1 μm was deposited on the surface of a silicon crystal with a specific resistance of 1000 Ω.cm. A layer of silicon monoxide was deposited on the platinum and then oxidised to the dioxide. The position of the tracer was determined by measuring the resistance. If the resistance between the tracer and the silicon had remained unchanged on oxidation, this would have indicated that the platinum remains at the metal–oxide interface and that the oxidation product is formed under the platinum. The experiment showed that the resistance was equal to 4000 Ω before oxidation, and 6000 Ω after oxidation. On the basis of these results the author cited concluded that during the oxidation, the oxygen diffuses through the deposited layer of SiO, the platinum, and the layer of SiO_2 formed in the process, and then reacts at the oxide–silicon interface. To determine whether the oxygen diffuses in the oxide in the form of atoms or ions, Jorgensen carried out experiments, the results of which showed that the rate of oxidation is influenced by an electric field applied at right angles to the silicon surface. This increases the rate of oxidation when the silicon at the $Si-SiO_2$ interface is at a higher positive potential than that at the SiO_2-O_2 interface, indicating that oxygen diffuses in the form of negatively changed ions. Laverty and Ryan[120], however, carried out analogous studies at different oxygen pressures and concluded that in addition to the ionic component, neutral oxygen in molecular form takes part in the diffusion responsible for the growth of the oxide film.

Balk and coworkers[83] used electron microscopy to study the structure of a silicon surface subjected to thermal oxidation in dry oxygen and in water vapour, and established that the relief of the original silicon surface in the first stages is preserved in the outer layers of oxide, whereas the internal surface after removal of the oxide is smoothed. The explanation put forward by the authors cited for this phenomenon is that both with dry oxygen and with water vapour, the oxidation takes place at the silicon–oxide interface, so that the diffusing particles responsible for the growth of the oxide are oxygen particles.

In all the above work on the investigation of the nature of the particles diffusing through the oxide, the reaction of silicon with oxygen was carried out with gas at atmospheric pressure. While stating that the growth of the oxide films takes place under these conditions chiefly as a result of the diffusion of oxygen, the authors cited do not exclude the possibility of diffusion of silicon.

Arslambekov and coworkers[80], in an investigation of the influence of pressure on the kinetics of the oxidation of silicon, found that with decrease in pressure the activation energy of oxidation increases. The experimental results can be explained on the basis of the following considerations. At increased oxygen pressures the rate of oxidation of silicon is determined chiefly by the diffusion of oxygen through the oxide film. With change in the oxygen pressure there is a change in its concentration in the surface layer of oxide, and this leads to a change in the difference in the concentrations of oxygen at the gas–oxide and oxide–silicon interfaces. This should lead to a change in the overall diffusion stream, and hence to a change in the oxidation rate constant k. The difference in the concentrations of silicon at the interfaces, and the chemical potential gradient, are almost independent of the oxygen pressure. With marked decrease in the oxygen pressure in the system, the ratio of the diffusing atoms of silicon and oxygen taking part in the formation of the oxide film changes considerably. There are grounds for assuming that at a certain critical oxygen pressure in the system the quantity of oxygen diffusing in unit time may become commensurate with the quantity of silicon diffusing in unit time. Further decrease in the oxygen pressure may lead to a situation in which the process will be determined chiefly by the diffusion of silicon atoms. Since the activation energies for the diffusion of oxygen and silicon are different, we should also expect a change in the effective activation energy of the oxidation as a whole, as observed experimentally[80].

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The variety of complex phenomena observed in the oxidation of silicon explains the observed differences in the properties of the oxide films obtained under different conditions, and indicates the possibility of directed control of a number of these properties. This follows primarily from the dependence of the diffusion stream of silicon and oxygen on the conditions under which the process is carried out. In accordance with this, the zone which moves should be that in which the characteristic chemical reaction corresponding to the kinetic measurements takes place with the greatest probability. The distribution of heat in the oxide layer takes place accordingly.

Displacement of the regions in which the reaction takes place and heat is liberated should naturally influence the nature of the distribution of the stresses in the oxide and also the structural defects responsible for the electrical properties of the system.

The properties of oxide layers may also be influenced significantly by the conditions of the primary reaction of oxygen and silicon, the mechanism of which is also examined in this review.

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Influence of Metallic Additives on the Reduction of Solid Oxides

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The present review deals with one type of topochemical heterogeneous-catalytic reaction—the reduction of solid oxides by gaseous reducing agents (chiefly molecular hydrogen) in the presence of small quantities of metallic additives. Experimental data on the influence of these additives on the reduction of various oxides have been systematised, and the general regular features characteristic of these processes have been formulated. These regular features have been interpreted from the viewpoint of an electronic-chemical reduction mechanism. Methods for the practical utilisation of these reactions have been indicated. The bibliography contains 34 references.

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I. INTRODUCTION

Reactions involving the reduction of metal oxides by gaseous reducing agents (hydrogen, carbon monoxide, etc.) form the basis of many metallurgical processes, are widely employed in preparative inorganic chemistry, and are used for the preparation of various metallic and oxide catalysts.

Comparatively recently it was found that the rates of these processes are increased appreciably if the oxide being reduced contains a very small quantity of a foreign metal, such as platinum or palladium; in the presence of these additives, the temperature at which the reduction can be carried out is reduced considerably. Thus the addition of only 0.1 wt. % of metallic platinum to V_2O_5 lowers the temperature of the start of the reduction of V_2O_5 by molecular hydrogen by 180 deg[1].

An important characteristic feature of these systems is that the metallic additive under the conditions of the reaction does not form chemical compounds or solid solutions with the original oxide or the products of its reduction—it forms a distinct (usually highly dispersed) phase, separated by an interface from the phase of the oxide being reduced and its reduction products. The thermodynamic characteristics of the original oxide remain unchanged when the metallic additive is added. For example, the energies of the bonds formed by oxygen with pure V_2O_5 and with V_2O_5 containing 0.1 wt. % Pt are identical; this was proved experimentally by study of the adsorption-chemical equilibria, the temperature dependence of the equilibrium pressure of oxygen over V_2O_5,[2] and the rate of isotopic exchange of oxygen with V_2O_5.[3]

Thus the metallic additive, without influencing the thermodynamics of the reduction, increases its rate considerably, that is it catalyses the reduction. Since the catalyst (the metallic additive) and the reagents (the oxide being reduced, and the gaseous reducing agent) are in different phases, reactions of this type represent a unique form of heterogeneous catalysis.

These reactions are in some respects similar to gaseous heterogeneous-catalytic reduction processes; the rates of the latter are also increased by group VIII metals, which activate molecular hydrogen and other gaseous reducing agents. On the other hand, these reactions are heterogeneous topochemical reactions, in which one solid substance (the original oxide) is converted into another (lower oxide or metal); the reactions are characterised by certain specific features (nucleus formation, autocatalysis by the solid product, etc.).

The mechanism of the reduction of oxides in the presence of metallic additives is undoubtedly extremely complex. Its study is difficult, if only because the detailed mechanisms of heterogeneous catalysis and topochemical reactions are not yet clear. Nevertheless, the detailed study of the kinetics and mechanism of these reactions is opening up extremely interesting possibilities from both theoretical and practical viewpoints.

A fairly large amount of isolated experimental facts and observations providing evidence of the marked effect of metallic additives on the reduction of oxides, chiefly by molecular hydrogen, has now accumulated. The experimental data relating to different systems, however, are scattered—they have not been summarised from a single viewpoint, and indeed they have not until now been systematised.

This systematisation is undertaken in the present review, which attempts to reveal and where possible explain various common regular features characteristic of reactions of this type, and also to indicate methods for their practical utilisation.

II. METHODS OF PREPARING CATALYSTS, AND THEIR PHYSICAL PROPERTIES

Several methods for introducing a metallic additive into oxides to be reduced are known.

(1) Impregnation of the oxide with a solution containing a compound of the metal, followed by decomposition of this compound with the formation of the metal. Usually, the powdered oxide is impregnated with a solution of a compound such as H_2PtCl_6, $PdCl_2$, $AuCl_3$, etc., after which the powder is dried and heated to temperatures which ensure formation of the metal.

(2) Deposition of the oxide and metal on an inert carrier. The metal is first deposited on the carrier (Al_2O_3, SiO_2,

etc.) by the method described above, after which the specimen is impregnated with a solution of a salt which is decomposed to give the oxide to be reduced.

(3) Mechanical mixing; a) highly dispersed metal powder, for example platinum black, is mixed with the powdered oxide, and the mixture is shaped to form tablets; b) in a variation of this method, the oxide to be reduced is mixed with a powdered carrier (Al_2O_3, $BaSO_4$, etc.) on which the metal has been deposited beforehand. In addition to these basic methods, ion exchange[4] or spraying of the metal on to oxide granules[5] are also sometimes used.

Metals deposited even in small quantities on oxides or inert carriers are present chiefly in the crystalline state, in the form of fine crystals, the dimensions and distribution of which depend on the nature of the carrier, its surface area and porosity, the method of deposition and concentration of the metal, and the conditions of treatment[6]. Electron microscopy[7] has shown that in V_2O_5.0.5% Pt specimens the discrete platinum crystals do not penetrate into the V_2O_5 lattice or distort it, but are present in contact with the oxide. The direct deposition of the metal on the oxide ensures closer contact between the catalyst and the oxide being reduced than mechanical mixing.

III. CATALYTIC ACTION OF SMALL QUANTITIES OF METALLIC ADDITIVES ON THE REDUCTION OF OXIDES BY MOLECULAR HYDROGEN

1. Reduction of Vanadium Oxides

The catalytic action of very small quantities of platinum on the reduction of V_2O_5 was first established by Il'chenko and Yuza[1], who made a detailed study of the influence of various factors on the kinetics of this reaction†. The experiments were carried out by a gradient-free stationary–circulation method (the water formed was frozen out) under conditions free from the distorting influence of the macro-factors. The platinum was introduced into the specimens by method (1): its concentration was varied from 0.0005 wt. % to 0.5 wt. %, relative to the original oxide, the specific surface of which was 4.9 $m^2\ g^{-1}$.

The accelerating effect of platinum is shown even with trace quantities (0.0005%). The reduction of pure V_2O_5 begins at 420°. The addition of platinum lowers the temperature of the start of the reaction considerably (Table 1).

X-Ray diffraction and chemical analysis of specimens of pure and platinised V_2O_5, reduced to different extents, showed that in both instances the reduction takes place in three macro-stages:

$$3\,V_2O_5 + 2\,H_2 = V_6O_{13} + 2\,H_2O\,,$$
$$V_6O_{13} + H_2 = 3\,V_2O_4 + H_2O\,,$$
$$V_2O_4 + H_2 = V_2O_3 + H_2O\,.$$

The kinetic curves for the reduction have the S-shape characteristic of autocatalysis by a solid reduction product.

The addition of platinum increases the rates of all three macro-stages, but the catalytic action of platinum is greater at low degrees of reduction. In this range, which corresponds to the conversion of V_2O_5 into V_6O_{13}, the rate of reduction of platinised specimens containing up to 0.01% Pt is proportional to the concentration of the metallic catalyst and the hydrogen pressure to the first power. Increase in the platinum concentration (C_{Pt}) leads to a change in the kinetic relationships: at $C_{Pt} = 0.1\%$ the order with respect to hydrogen becomes less than unity, and at $C_{Pt} = 0.25\%$ a saturation effect is observed—further addition of platinum does not influence the temperature of the start of the reduction (Table 1).

Table 1. Dependence of the temperature of the start of the reduction of V_2O_5 by hydrogen on the concentration of platinum (hydrogen pressure 400 mmHg).

Platinum concn., wt.%	Temperature of the start of reduction, °C
0	420
0.001	360—370
0.01	300
0.1	240
0.25	220
0.5	220

The catalytic action of platinum begins to be shown at very low degrees of reduction, when the removal of oxygen from the oxide being reduced has not led to a phase transformation. Il'chenko and coworkers[2] studied the adsorption-chemical equilibrium

$$(O) + H_2 \rightleftarrows (\ ) + H_2O,$$

with the participation of V_2O_5, where (O) denotes oxygen of the oxide, and ( ) an oxygen vacancy; the quantity of oxygen removed does not exceed that corresponding to a monolayer. It was found that the addition of platinum, without altering the equilibrium constant for this process, leads to a sharp increase in the rate of attainment of equilibrium. Similar relationships were observed for V_2O_5 on which platinum had been deposited directly and for specimens prepared by mechanical mixing of V_2O_5 with $Pt/BaSO_4$.

Platinum also has a significant effect on the regular features of nucleus formation in the reduction of V_2O_5: in the reduction of the pure oxide, the nuclei of the solid product are produced according to a power law, whereas in the presence of platinum the nuclei are formed according to a more rapid exponential law[9]. An increase in the ease of nucleus formation in the presence of platinum is also revealed in the fact that the addition of platinum leads to a sharp decrease in the duration of the induction period observed in the reduction of V_2O_5.[1]

2. Reduction of Tungsten Oxides

Khoobiar[10,11] found that platinum has a marked catalytic action on the reduction of WO_3. He established that WO_3 powder, mixed with Pt/Al_2O_3 (0.5 wt. % Pt) is reduced by molecular hydrogen even at room temperature; under these conditions, pure WO_3 is not reduced and reacts with H_2 at temperatures above 400°.

A detailed study of the influence of added platinum on the reduction of WO_3 was made by Benson and coworkers[12], who used a gas-volumetric method. Most of their work was carried out with specimens obtained by grinding WO_3 powder with platinum black: metal concentration 2.5 wt. %, specific surface of metal 23 $m^2\ g^{-1}$, specific surface of WO_3 11.1 $m^2\ g^{-1}$ and 17.4 $m^2\ g^{-1}$.

† Even earlier, Yuza and Roiter[8] found that the rate of reduction of V_2O_5 by hydrogen was increased considerably after the V_2O_5 had been melted in a platinum crucible.

In the reaction of WO_3 with hydrogen, water was not liberated, and a pale-blue powder with the composition $H_{0.35}WO_3$ (the hydrogen analogue of the tungsten bronzes) was formed. Pure WO_3 begins to absorb hydrogen very slowly at 435°; in the presence of platinum the dry oxide begins to be reduced at 105°, and a specimen covered beforehand with a monolayer of water begins to be reduced at room temperature. Thus the catalytic activity of platinum is increased considerably in the presence of water adsorbed on the oxide surface.

The accelerating influence of platinum is more marked, the closer the contact between its micro-crystals and the surface of the oxide being reduced. Thus the rate of reduction is greater when the metal is deposited on WO_3 by impregnation than when the tungsten(VI) oxide is ground with platinum black, and much greater than when WO_3 powder is simply ground with platinum. An interesting feature is that the preparation of WO_3 specimens in platinum crucibles leads to an appreciable decrease in the temperature of the start of the reduction of this oxide, compared with specimens prepared in porcelain crucibles [13]. An analogous effect was observed for V_2O_5 (see p. 86).

Hegedüs and coworkers [13] made a detailed study of the influence of various metallic additives on the reduction of WO_3. The specimens were prepared by method (1) and contained 0.5 wt. % metal relative to W; the studies were made by a thermogravimetric method (the specimens were heated in a stream of gaseous reducing agent with continuous increase in temperature), with X-ray diffraction study of the solid products. Experimental data characterising the catalytic action of palladium, platinum, and osmium are given in Table 2.

Table 2. Influence of metallic additives on the reduction of WO_3 by a 30% H_2 + 70% N_2 mixture [13].

Additive	Temp. of the start of reduction, °C	Temp. at which $WO_{2.88}$ is formed, °C	Temp. corresponding to the end of the reaction, °C
Pd	284	345—529	768
Pt	290	351—527	779
Os	350	446—546	794
Pure WO_3	430	530	800

A strict quantitative comparison of the catalytic action of the different metals on the basis of Hegedüs' data [13] is difficult, since their surface concentrations might have been different, but it is clear that the order of activities of the additives is: Pd > Pt > Os. Neugebauer and coworkers [14] found that the activity of added palladium in the reduction of WO_3 is particularly high in the presence of water.

Unfortunately, the experimental data given by Hegedüs and coworkers [13] were not systematised and discussed. Analysis of these data led us to the following conclusions.

1. The accelerating action of the additives decreases with increase in the degree of reduction of WO_3 (Table 2). The temperature of the start of the reaction and the temperature of the start of the conversion of WO_3 into the blue β-oxide of tungsten ($WO_{2.88}$) is lowered appreciably in the presence of metals, whereas the temperature at which this change is complete is approximately the same as in the reduction of pure WO_3. Additives also have comparatively little influence on the temperature corresponding to the completion of the reduction.

2. Hegedüs and coworkers [13] also studied the influence of various other additives, in particular Hg, Al, Sn, Pb, Sb, and Bi, on the reduction of tungsten(VI) oxide. The additives were present in the original WO_3 specimens as the metal chlorides. The true chemical state and concentration of these additives under the conditions of the reaction were unknown; allowance must be made for the fact that the chlorides of these metals are volatile, and the metals themselves readily fusible, so that most of them (Hg, Sn, Pb, and Bi) are in the liquid state at the temperature of the start of the reduction. These additives (apart from Bi) do not accelerate the reduction of WO_3, and even retard it (Table 3).

Table 3. Influence of added readily fusible metals on the reduction of WO_3 by a 30% H_2 + 70% N_2 mixture [13].

Additive	Temp. of the start of reduction, °C	Temperatures at which $WO_{2.88}$ is formed, °C
Hg	433	521
Al	481	552
Sn	469	539
Pb	476	535
Sb	439	504
Bi	343	440—575
Pure WO_3	430	530

3. Reduction of Molybdenum Oxides

The influence of various metallic additives on the reduction of MoO_3 was studied by Hegedüs and coworkers [15], who used the same procedure as in the study of the reduction of WO_3. [13] The regular features observed in this instance were completely analogous to those found for the reduction of tungsten(VI) oxide. The addition of noble metals increases the rate of reduction of MoO_3 (Table 4), the catalytic activity decreasing in the order: Pd > Pt > Ag > Os. The addition of readily fusible metals (Hg, Al, Sn, Pb, Sb, or Bi) has little influence on the reduction of MoO_3.

4. Reduction of Nickel(II) Oxide

Verhoeven and Delmon [5] studied the reduction of NiO by hydrogen at 210–220° in the presence of added platinum, palladium, copper, gold, and silver. It was found that the first three metals increase the rate of the process considerably, and decrease sharply the duration of the induction period. The kinetic curves for the reduction are S-shaped, as in the reduction of pure NiO, that is the autocatalytic action of the solid product—metallic nickel—is also shown in the presence of the additives.

Added gold and silver have little influence on the rate of reduction of NiO, and added cadmium has a slight retarding action at 277–293°.

The accelerating action of palladium and platinum on the reduction of NiO by hydrogen was also demonstrated by Nowak and Koros [16]. In their experiments, both the metal and the oxide being reduced were deposited in small quantities on aluminium oxide. The catalytic activity of palladium was greater than that of platinum.

5. Reduction of Iron Oxides

Sancier and Inami[4] studied the influence of added palladium, platinum, copper, gold, and a palladium–gold alloy on the reduction of Fe_2O_3 (and Fe_3O_4) by hydrogen at 500°; the reaction rate was measured by the EPR method. The specimens for reduction were prepared by various methods: by depositing the metal and the oxide on Al_2O_3 or SiO_2 by impregnation; by mechanically mixing Fe_3O_4 and a carrier containing the metal additive; and by using a molecular sieve containing the metal cation and iron ions. The following order of catalytic activities was found: Pd > Pt > Cu ~ Pd–Au > Au.

Table 4. Influence of metallic additives on the reduction of MoO_3 by a 30% H_2 + 70% N_2 mixture[14].

Additive	Temp. of the start of reduction, °C	Temperatures at which MoO_2 is formed, °C
Pd	185	—
Pt	260	—
Ag	420	585—625
Os	500	625—645
Pure MoO_3	510	645

The activity of Pd–Au alloys containing 20 at. % and 60 at. % Au was found to be lower than that corresponding to the volume concentration of Pd; this was attributed to an increase in the concentration of gold on the surface compared with the volume. The rates of reduction of specimens obtained by the joint deposition of catalyst and oxide being reduced, and also by ion exchange, were greater than that for mechanical mixtures. According to Samchenko and Rusov[17], small quantities of platinum (0.01 wt. % and 0.1 wt. %) produce a marked increase in the rate of reduction of iron oxides (also containing K_2O, Al_2O_3, CaO, SiO_2, etc.) by a nitrogen–hydrogen mixture‡. At 450° and a pressure of 60 atm, the time required for a given degree of reduction to be achieved is much shorter in the presence of platinum. According to the data of Murata and Kasaoka[18], added copper increases the rate of reduction of Fe_2O_3 and Fe_3O_4 below 250°.

6. Reduction of Copper Oxides

The accelerating action of platinum on the reduction of copper oxide films was detected by Vorontsov and Koshkina[19]. In the absence of catalyst these films are reduced completely in 97 min at 200°, whereas in the presence of platinised platinum the reaction is complete in 7 s. In the presence of the catalyst the process is rapid even at 40°.

IV. GENERAL REGULAR FEATURES AND MECHANISM OF ACTION OF METALLIC ADDITIVES ON THE REDUCTION OF OXIDES BY MOLECULAR HYDROGEN

In the analysis of the above experimental facts, we observed various regular features characteristic of these processes.

1. An extremely high catalytic activity in the reduction of a given oxide is shown by palladium and platinum (usually, Pd > Pt); copper, and also osmium, are less active; silver and gold have little activity; and readily fusible metals—cadmium, mercury, lead, tin, and aluminium—are inactive.

2. The accelerating influence of metallic additives is particularly marked in the initial period of reduction, at low degrees of reduction; the active catalysts in a number of instances decrease the temperature of the start of the reaction by hundreds of degrees.

The action of the additives is also shown at high degrees of reduction, but to a smaller extent. If the reaction is carried out at a sufficiently high temperature, it is possible to achieve a greater degree of reduction in the presence of the metallic catalyst than in the absence of the additive (within the limits allowed by thermodynamics).

3. In those instances where the reduction of the pure oxide is autocatalytic, the autocatalytic action of the solid product is usually preserved in the presence of the additive.

4. Metallic additives decrease sharply the duration of the induction period and apparently alter the kinetics of nucleus formation.

5. The catalytic action of the additives (for very small quantities) is proportional to the metal concentration; at sufficiently high concentrations, a saturation effect is observed—further addition of metal has little influence on the course of the process.

6. The catalytic activity of a metal with respect to the reduction is greater, the closer its contact with the oxide being reduced and the greater the degree of dispersion. The direct deposition of a catalyst on the oxide being reduced gives better results than mechanical mixing. Nevertheless, the accelerating action of palladium and platinum is also shown in instances where the microcrystals of the oxide being reduced and the additive, deposited on an inert carrier, are separated in space.

7. The catalytic action of metallic additives is increased in the presence of water (this conclusion was reached by a number of authors[12,14]).

These regular features can be explained on the basis of the electronic-chemical theory of catalysis and reduction, proposed by Roiter[8] and developed by a number of authors[1,7,20].

According to this theory, the limiting stage of the reduction of an oxide by molecular hydrogen§ is usually the donor process of electron transfer from the adsorbed molecules of reducing agent (H_2) to the solid oxide; this process leads to a decrease in the oxidation state of the cations of the oxide and the formation of positive hydrogen ions, which subsequently react readily with negative oxygen ions with the formation of water.

If the oxide is in contact with micro-crystals of a metallic additive able to bring about the specific activation (ionisation) of hydrogen, the transfer of electrons from H_2 to the oxide is greatly facilitated, so that the rate of the overall reduction is increased.

In fact, the above order of decreasing catalytic activity of metallic additives with respect to the reduction of oxides agrees qualitatively with their ability to activate molecular hydrogen. Palladium and platinum adsorb hydrogen rapidly even at low temperatures and can dissolve hydrogen[21]; these metals are extremely active catalysts for

‡ This process gives the industrial iron catalyst for the synthesis of ammonia ("SA-1" grade contact catalyst).

§ It is assumed that the reduction is a quasi-steady-state reaction[22].

various gaseous reactions involving H_2 [23] and have the lowest overpotential for the cathodic liberation of hydrogen[24]. Copper has a lower catalytic activity with respect to gaseous reactions involving H_2, and silver and gold have little catalytic activity in these reactions[23]. Metals such as cadmium, mercury, aluminium, bismuth, lead, and tin have little activating effect on molecular hydrogen (very high overpotential for the cathodic liberation of hydrogen; low catalytic activity with respect to reactions involving H_2 [24]). It should also be borne in mind that the metals of this last group are readily fusible, and at the temperatures of the start of the reduction of oxides difficult to reduce (MoO_3, WO_3) most of them are in the liquid state. The liquid metal may flow over the surface of the oxide, blocking it and thus hindering the reaction of the oxide with the gaseous reducing agent; this explains the slight retarding action of these additives on the reduction of MoO_3 and WO_3 (pp. 48 and 49).

In the reaction of molecular hydrogen with Pd or Pt, dissociative adsorption takes place, and the adsorbed species exhibit surface mobility. Among the transition metals, the platinum metals have the lowest heats of chemisorption of hydrogen, that is the lowest metal–hydrogen bond strength[21]. According to Aston[25], hydrogen adsorbed on platinum is mobile at 7° and above; hydrogen dissolved in palladium is also mobile over a wide temperature range. It is natural to assume that hydrogen adsorbed on Pd or Pt can migrate from the palladium or platinum centres to the regions of the oxide in contact with these centres; if the micro-crystals of the metal and the oxide being reduced are deposited on the same inert carrier (for example Al_2O_3) and are at a certain (small) distance from one another, the hydrogen first migrates to regions of the carrier adjoining the metal and then to the oxide being reduced¶.

The possibility of surface diffusion in this way is proved by a number of experimental facts. It was established[26] that in the adsorption of hydrogen from solution on Pd/Al_2O_3 and Pt/Al_2O_3 specimens with a low concentration of metal (up to 1 wt. %), the number of hydrogen atoms corresponding to one metal atom at 25° is several times greater than unity. Since hydrogen is not adsorbed on the pure carrier, the only explanation for this result is that the hydrogen migrates from the palladium or platinum centres on to the carrier. An analogous interpretation of their results was put forward by Robell and coworkers[27], who showed that in the presence of small quantities of platinum (0.2% and 1%) the rate and extent of the adsorption of hydrogen and deuterium on carbon increase considerably. A similar result was previously obtained by Frumkin and Burstein[28]. The ability of hydrogen adsorbed on platinum to undergo surface diffusion is also indicated by the fact that small quantities of deposited platinum actively catalyse the exchange of deuterium and the hydrogen of the surface OH groups of aluminium oxide[29].

It is suggested that the increased rate of reduction of oxide containing adsorbed water in addition to platinum is due to an increase in the rate of diffusion of hydrogen, brought about by water, probably as a consequence of the formation of hydroxonium ions[12].

It is quite understandable that the closer the contact between the micro-crystals of the metallic additive and the granules of the oxide being reduced, the greater the ease of electron transfer from hydrogen to the oxide being reduced, through the metallic catalyst, on which hydrogen is ionised, and the greater the ease of diffusion of hydrogen from the palladium or platinum centres to the oxide surface.

In the initial period of the reduction, when the metallic catalyst is in direct contact with the oxide being reduced, the catalytic action of the metallic additive is naturally greatest and involves primarily a marked decrease in the temperature of the start of the reaction and a sharp increase in the initial rate of reduction. This effect is greater in the reduction of oxides difficult to reduce (V_2O_5, MoO_3, WO_3), for which the temperature of the start of the reaction is decreased by hundreds of degrees†.

The higher the concentration of additive, the greater the increase in the rate of activation of hydrogen and hence of the overall process. When a definite concentration of catalyst has been reached [for platinised vanadium(V) oxide this concentration is about 0.1–0.25%], the rate of the donor stage is increased to such an extent that it ceases to be the limiting stage. The slow stage of the reaction is then another process, probably diffusion in the solid phase or crystal-chemical transformations, since at increased concentrations of additive the reaction takes place at a low temperature. The presence of a metallic additive does not influence the rates of these processes, so that further increase in the concentration of catalyst does not lead to an additional increase in rate (saturation effect)[20].

Since the gaseous reducing agent is activated on the surface of the micro-crystals of the additive, the points of contact between it and the oxide being reduced become centres for the rapid production and growth of nuclei of the new phase. As a result, in the presence of active metallic catalysts there is a sharp decrease in the duration of the induction period and a change in the kinetics of nucleus formation, as observed in the reduction of V_2O_5.[9]

With increase in the degree of reduction of the oxide, the micro-crystals of the catalyst (Pd or Pt centres) are isolated to an increasing extent from the original oxide by a layer of solid reaction product—a lower oxide or metal. The catalytic action of the additive is also shown at this stage, since the transfer of electrons from the hydrogen, ionised on Pd or Pt, to the oxide being reduced cannot be prevented by a layer of semiconducting oxide or metal surrounding the palladium or platinum centres. The catalytic action of the additive becomes weaker, however, with increase in the degree of reduction. A possible reason for this is that the diffusion of hydrogen to the reaction surface, which is steadily moving further away, is hindered.

Judging from the form of the kinetic curves, the growth of the new phase takes place on a layer of solid product already present, that is the autocatalytic action of the reduction product is preserved in the presence of the metallic additive (if this product does not form a solid

¶ A heterogeneous–homogeneous reduction mechanism, in which H atoms are transferred from the platinum or palladium surface to the gaseous phase to start a chain reaction, is unlikely. Benson and coworkers[12] demonstrated this experimentally for the WO_3–H_2 system by using γ-radiation and an electric discharge to produce H atoms specially in the gaseous phase (reduction of WO_3 at 400° was not observed).

† Oxides which are readily reduced (such as Ag_2O and MnO_2) begin to be reduced at low temperatures even without a catalyst, so that in this instance the influence of metallic additives will apparently be less marked. Unfortunately, there is as yet no direct experimental evidence for this.

solution with the original oxide). Thus in this stage, two catalysts are operating—the metallic additive and the solid reduction product. The role of the first catalyst involves the activation of hydrogen, accompanied by the transfer of electrons to the oxide being reduced; the role of the solid product involves chiefly an increase in the ease of crystallisation of the new phase at the interface between it and the original oxide. In those instances where the reduction leads to the formation of metals such as Ni, Co, Fe, and Cu, which exhibit hydrogenating power, it is possible that they themselves play some part in the activation of hydrogen.

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The study of the influence of metallic additives on the reduction of solid oxides opens up interesting possibilities for the study of the mechanisms of reactions involving solid oxides.

An example is provided by the study of the mechanism of the catalytic oxidation of hydrogen on V_2O_5 and the reduction of this oxide by hydrogen. On the basis of kinetic data it was suggested that the limiting stages of the two reactions are analogous, both involving the donor process of hydrogen ionisation with the transfer of electrons to the oxide[6]. If this suggestion is correct, we would expect that when platinum is added to V_2O_5, the rate of the limiting stage would increase, so that the rates of both the catalysis and the reduction would increase. In actual fact, in the presence of added platinum the rate of reduction of V_2O_5 increases sharply[1], and the same additive also produces a marked increase in the catalytic oxidation of hydrogen on V_2O_5.[7] It was noted above that with high concentrations of platinum (0.1–0.25%) the donor stage is no longer the slowest stage in the reduction of V_2O_5, that is, the limiting stage is replaced. Analogously, in the catalytic oxidation of hydrogen on platinised V_2O_5 at a platinum concentration of 0.1%, the rate of activation of hydrogen increases to such an extent that the slow stage of the reaction becomes the acceptor stage of activation of molecular oxygen[20]. Thus the study of the influence of metallic additives in oxides assists in the investigation of the nature of the limiting stage in heterogeneous reactions involving these oxides.

Studies of this kind are also of assistance in the investigation of the mechanism of action of bifunctional reforming catalysts of the Pt/Al_2O_3 type containing small quantities of metal. It is often suggested that a necessary stage in these processes is the surface diffusion of hydrogen, adsorbed on platinum, to the aluminium oxide regions[11]. This idea has been used to explain the increased rate of hydrogenation of ethylene on a Pt/SiO_2 catalyst mixed with Al_2O_3.[30] Experimental proof of the possibility of this migration is provided by the ease of reduction of WO_3–Pt/Al_2O_3 specimens[11].

The use of metallic additives as catalysts for the reduction of solid oxides opens up extremely important practical possibilities for increasing the activity of catalysts, as indicated in our earlier paper[1].

The reduction of oxides by gaseous reducing agents is a widely used method for preparing catalysts, including industrial catalysts. Decrease in the temperature of reduction often leads to an increase in the surface area of the catalyst as a consequence of the decrease in sintering and recrystallisation and the associated increase in the efficiency of contact. The introduction of catalytically active metal additives such as Pd or Pt into the original oxide may decrease considerably the temperature of reduction and hence lead to an increase in the total activity of the catalyst.

Small quantities of copper decrease the temperature of the reduction of Fe_2O_3 [18] and at the same time increase the activity of the reduced iron catalyst for the synthesis of hydrocarbons from CO and H_2.[31] The last effect is possibly achieved to some extent during the preparation of the catalyst.

In some instances it is extremely important that the reduction of the oxide to the metal be complete, since the presence of even small quantities of oxide in the metallic contact catalyst has an unfavourable influence on its catalytic properties. The main difficulty is that it is the last portions of oxygen which are most difficult to remove from the oxide. The introduction of catalytically active additives makes it possible to overcome this difficulty and achieve complete reduction. This technique was used by Nowak and Koros[16], who reduced NiO in the presence of small quantities of added palladium and platinum to obtain a more active and selective catalyst for the isomerisation, aromatisation, and hydrogenolysis of n-heptane.

The most successful combination is evidently that for which the additive, while increasing the rate of reduction of the original oxide, also acts as a promoter for the catalyst when it is formed. Thus Pd and Pt additives not only increase the rate of formation of the nickel catalyst mentioned above, but also apparently promote it[16]. The addition of small quantities of palladium to the zinc–chromium oxide catalyst for the preparation of alcohols from CO and H_2 leads to an increase in selectivity with respect to the formation of methanol[32].

In conclusion it may be noted that many of the regular features formulated above may be of more general significance and may also be applicable to the reduction of oxides by reducing agents other than molecular hydrogen. Thus small quantities of added palladium increase sharply the rate of the reduction of V_2O_5 by carbon monoxide: pure V_2O_5 begins to be reduced at 575°, whereas the temperature of the start of the reduction of a V_2O_5–0.1% $Pd/BaSO_4$ specimen is 25°.[33] According to the data of Blejean and coworkers[34], the addition of Pd increases the rate of the reduction of V_2O_5 by *o*-xylene and ethylene. Unfortunately, the available experimental data on the reduction of oxides by reducing agents other than H_2 in the presence of metallic additives are extremely scanty and insufficient for detailed discussion.

The systematic accumulation of new experimental data on the catalytic reduction of oxides by molecular hydrogen is also extremely desirable. Detailed kinetic studies by modern methods, combined with X-ray diffraction study and chemical analysis of the oxide being reduced, and measurement of the surface areas of the additives and the oxide, are required; in each instance it is necessary to investigate the influence of various factors (temperature, the composition of the reaction mixture, the concentration, chemical character, and physical state of the additive, the degree of reduction of the oxide, etc.) on the rate of the process. An extremely interesting unresolved problem concerns the relationship between the catalytic action of a given additive and the chemical structure of the oxide being reduced and its solid reduction products.

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Reactions of Phosphoramidic Acids

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The mechanisms of the hydrolysis and solvolysis of phosphoramidic acids have been examined. The concepts of phosphoramidates as donors of the phosphate residue in phosphorylation reactions of acids, alcohols, and amines are discussed. The use of phosphoramidates as phosphorylating agents in synthetic chemistry and also their possible involvement in biological phosphorylation processes have been demonstrated.
The bibliography includes 142 references.

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I. INTRODUCTION

During the last decades derivatives of orthophosphoric acid have been continually attracting the attention of many organic chemists and biochemists in connection with the outstanding advances in the study of nucleic acids, protein, biosynthesis and the investigation of bioenergetics, the structure of complex phospholipids, phosphoproteins, etc. Many studies have been made on phosphoric acid esters and anhydrides, in particular pyrophosphates, triphosphates, and acyl phosphates. Nowadays, yet another type of phosphoric acid derivatives—phosphoramidates—has aroused considerable interest.

Phosphoramidates include phosphonocreatine, phosphonotaurocyamine, phosphonoarginine, and other phosphonoguanidines isolated from the muscles of various animals and involved in the formation of ATP and ADP in muscular contraction, (see, for example, Straub[1]). The study of biological phosphorylation involving these compounds promoted the use of phosphoramidates as starting materials in the synthesis of pyrophosphates and triphosphates, including nucleoside derivatives (nicotinamide-adenine dinucleotide, coenzyme A, ADP, ATP, etc.). On the other hand, the study of biological phosphorylation showed that it involves labile intermediate phosphoramidates, namely enzymes phosphorylated at the imidazole ring of the histidine residue.

The determination of the role of phosphonoimidazoles in enzymatic processes is closely related to the study of the effect of organophosphorus poisons, pesticides, insecticides, etc. Thus there are data showing that di-isopropyl phosphonofluoridate—an effective inhibitor of many enzymes with a powerful toxic activity—phosphorylates the imidazole residue of the enzyme (see, for example [O'Brien][2]). Many powerful poisons, insecticides, and pesticides are phosphoramidates (Tabun, Schradan, etc). The synthesis of many phosphoramidates with carcinostatic activity has been described (see, for example, Stock[3] and Burstone[4]). (P–N)-aminoacid derivatives of nucleotides constitute an interesting variety of phosphoramidates. There are data suggesting that DNA- and RNA-peptides with a P–N bond between the nucleotide and the amino-group of the peptide are involved in the formation of the structure and in the functioning of nucleic acids (see, for example, Shabarova and Prokofiev[6]). One of the approaches employed to establish the structure and role of phosphoramidates is the study of model compounds—synthetic nucleotidoamides. Many interesting facts were observed in these studies, significantly supplementing the available knowledge of the reactivity of phosphoramidates, particularly about the intramolecular catalysis of their reactions (see the reviews of Preobrazhenskaya and Shabarova[5] and Shabarova and Prokofiev[6]).

The amides of nucleotides have found a novel application for synthetic purposes: the use of the amide derivative of the nucleotide for the blocking of the phosphate group in the synthesis of the dinucleoside phosphate has been described[7]; a method has been proposed whereby the nucleotide can be fixed on a polymeric carrier in the synthesis of oligonucleotides via the formation of a phosphoramidic bond between the phosphate residues of the nucleotides and the amino-group of the polymeric carrier[8].

Yet another cause which has stimulated interest in recent years in phosphoramidates is the discovery of enzymes cleaving these compounds—the so called phosphoamidases.

Despite the important role of phosphoramidates and the large number of studies on their chemistry and biochemistry, there are virtually no reviews of such investigations. Phosphoramidates are briefly mentioned in a discussion of phosphoesters[9–14] are dealt with only in a single review by Peacock[15] and in a chapter in the book by Bruice and Benkovic[16].

II. THE STRUCTURE OF PHOSPHORAMIDATES†

Phosphoramidates, like other derivatives of orthophosphoric acid, have a tetrahedral structure in the ground

† For a more detailed treatment see Refs. 9, 13 and 14.

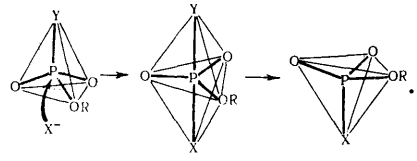
state having the phosphorus atom in the centre of the tetrahedron, and the four bonds directed to the vertides. The vacant 3*d* orbitals of the phosphorus atom may be involved in the formation of additional π bonds with the unshared electron pairs of nitrogen and oxygen (the so called $d_\pi-p_\pi$ conjugation). Thus the P–N and P–O bonds in phosphoramidates have some double-bond character[22]. This hinders attack by nucleophilic reagents and is shown particularly in a considerable resistance of phosphoramidates (in contrast to carboxylic acid amides) to the action of alkalis[17-21].

A necessary condition for nucleophilic substitution reactions at the phosphorus atom is the breakdown of $d_\pi-p_\pi$ conjugation in order to liberate the 3*d* orbitals of phosphorus and make them available for interaction with the *p* electrons of the nucleophilic reagent in the transition state.

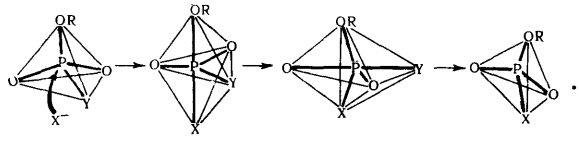
The most probable structure of the transition state in nucleophilic substitution at the phosphorus atom is a trigonal bipyramid[12-14,22]. Hence the entering and leaving groups can be located at the vertices of the bipyramid (a transition state of S_N2) type and the reaction takes place with inversion of configuration at the phosphorus atom. Such a transition state has been assumed for the majority of reactions of phosphoramidates on the basis of a study of nucleophilic substitution of optically active amido-derivatives of phosphoric acids (methyl *N*-cyclohexylphosphoramidothionate)[23] and also of intermolecular substitution reactions involving phosphoramidate derivatives with an additional amino-group[24].

However, these data do not fully exclude transition states of other types. The attack by nucleophilic reagents on the phosphorus atom can be facilitated if it is not directed along the P–N axis, since the unfavourable charge distribution then has a smaller effect[15]. This type of reaction is accompanied by so-called "pseudorotation", which is well known for phosphoesters (see, for example Refs. 25–28). As a result of pseudorotation, the nucleophilic reagent (X^-) attacking the phosphorus atom at an angle to the P–N axis passes from the plane of the base of the bipyramid to its vertex. Unfortunately, the stereochemistry of nucleophilic substitution at the phosphorus atom in phosphoramidates has been hardly investigated and therefore one can only speak of the possibility of "pseudorotation" in principle.

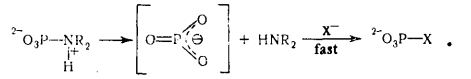
"Linear" substitution:



Substitution with "pseudorotation":



An extreme case of a trigonal bipyramid with an axial disposition of the entering and leaving groups is a transition state in which a labile intermediate metaphosphate is eliminated[24]. Its formation has been postulated for the reactions of many acyl phosphates, phosphoesters, and phosphoramidates, the common feature of which is the presence of a powerful electron-accepting substituent at the oxygen or nitrogen atom undergoing elimination and its marked dependence on the pK_a of the group eliminated[29]. Metaphosphate has a planar structure and therefore reactions involving it should take place with racemisation. However, the process has not been investigated for phosphoramidates. In reactions involving the intermediate metaphosphate, the rate-determining stage is unimolecular decomposition of the protonated phosphoramidate:

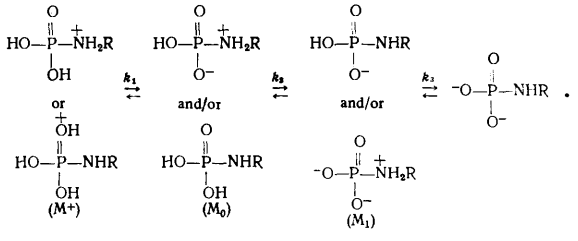


There are also many reactions in which a transition state, intermediate between the trigonal bipyramid and the planar metaphosphate[15,30-32] and characterised by a long P–N bond and a short bond between the phosphorus atom and the nucleophilic reagent being eliminated, has been postulated[30]. Such reactions exhibit the features of both bimolecular (in particular, the selectivity with respect to the nucleophilic reagent) and unimolecular reactions.

Table 1. Dissociation constants of phosphoramidic acids [and their esters]

Compound	pK_1	pK_2	References
Phosphoramidic acid	3.00	8.15	37
	4.6	7.7	17
	3.3	8.28	38
	2.83	8.03	39
	2.8	8.2	40
	2.72		15
	2.92	7.68	40
N-(*p*-Chlorophenyl)phosphoramidic acid	1.6	6.8	37
N-(*o*-Carboxyphenyl)phosphoramidic acid		7.25	32
N-(*p*-Carboxyphenyl)phosphoramidic acid		6.99	32
N-Acetylphosphoramidic acid	1.3	6.0	16
N-Benzoylphosphoramidic acid	1.99	6.42	41
	2.67	5.67	42
N-(*p*-Methylbenzoyl)phosphoramidic acid	2.04	6.20	41
N-(*p*-Nitrobenzoyl)phosphoramidic acid	1.97	6.24	41
Methyl *N*-cyclohexylphosphoramidate	3.1		43
Methyl *N*-cyclohexylphosphoramidothionate	3.1		18
Ethyl *NN*-diethylphosphoramidate		7.2	42
Phenyl *N*-benzoylphosphoramidate	1.9	13.4	41
N-Phosphorourethane	2.4	6.3	44

The reactions of phosphoramidates depend significantly on their degree of ionisation. Depending on the conditions and structure, phosphoramidic acids can exist in the form of the conjugate acid species (M^+), the neutral molecular (M_0), the monoanion (M_1), and the dianion (M_2). For example



Phosphoramidic acid may be protonated both at the nitrogen and at the phosphoryl oxygen. Its conjugate acid (M^+) is probably an equilibrium mixture of two forms: protonated at the oxygen and nitrogen atoms[33,34]. The neutral species (M_0) and the monoanion (M_1) can probably

exist in a zwitterionic form[35,36], and it is most likely that the derivatives of aromatic amines (for which $pK_a < pK_2$ for orthophosphoric acid) are protonated at the oxygen atom of the phosphate residue, while those of aliphatic amines (for which $pK_a > pK_2$ for orthophosphoric acid) exist mostly in a zwitterionic form[32] (Table 1).

III. HYDROLYSIS AND SOLVOLYSIS OF PHOSPHORAMIDATES

1. Hydrolysis of Phosphoramidates

The study of the hydrolysis of unsubstituted phosphoramidic acid as a function of pH showed[37] the presence of a plateau in the pH range 3.5–6.5; at higher pH the hydrolysis is retarded and at pH ≥ 10 phosphoramidate is virtually stable; at pH < 3 the rate of hydrolysis increases. These data show that the phosphoramidate dianion (M_2, $NH_2PO_3^{2-}$) is resistant to the action of water. The pH range 4.5–6.5 corresponds to the monoionic form (M_1), at lower pH the neutral form (M_0) makes a significant contribution, and at pH < 2 the cationic form (M^+) appears and the hydrolysis is acid catalysed.

When aromatic substituents are introduced at the phosphoramidate nitrogen, the profile of the curve relating the rate of hydrolysis of the phosphoramidate to pH hardly changes[45]. Only at pH < 3 is the hydrolysis of *N*-arylphosphoramidates somewhat slower than that of unsubstituted phosphoramidate. The explanation is probably that the electrons of the nitrogen atom are involved in conjugation with the aromatic ring, as a result of which the concentration of the active protonated form of the *N*-arylphosphoramidate (M^+) diminishes.

When powerful electron-accepting substituents (benzoyl[42], diphenylphosphoryl[42], benzenesulphonyl[46], and ethoxycarbonyl[44,46]) are introduced at the phosphoramidate nitrogen, the variation of the rate of hydrolysis with pH changes very significantly: the corresponding curves have a maximum at a pH of about 4 and at higher and lower pH the rate of hydrolysis falls sharply. Acid catalysis is as a rule not observed for these compounds[46,47] (*N*-benzoylphosphoramidate occupies an intermediate position: the acid catalysis of its hydrolysis occurs only in a very acidic medium[42]).

Probably acyl substituents, which are very powerful electron acceptors, hinder the protonation of the phosphoramidate and decrease the fraction of the neutral (M_0) and cationic (M^+) forms, which determine the rates of hydrolysis of the phosphoramidate at pH < 3.

There is no unanimous view at present concerning the possible reaction mechanisms. Therefore we present in Table 2 the suggested mechanisms of the solvolysis of various ionic forms of phosphoramidates according to different investigators and shall attempt to consider the motives which led them to give preference to a particular mechanism.

Phosphoramidic acid. The reactive ionic species are M_1, M_0, and M^+. Chanley and Feageson[37] attribute the activity of M_0 and M_1 to their ability to exist in a zwitterionic form. Conclusions concerning the solvolysis mechanism have been arrived at on the basis of a study of the composition of the solvolysis products in methanol–water mixtures: since for the monoionic form (M_1) the alkyl phosphate : phosphoric acid ratio is appreciably higher than the alcohol : water ratio in the reaction mixture, a bimolecular S_N2 (P) mechanism was assumed. This is consistent also with the catalysis of the solvolysis by pyridine and nicotine but not by the sterically hindered 2-methylpyridine.

However, Oney and Caplow[49] suggest a unimolecular solvolysis of the M_1 form of phosphoramidate, since it reacts at a rate close to that of the neutral form (M_0). They believe that with a bimolecular mechanism one should expect greater differences between the rates of solvolysis of the two forms owing to the more intense electrostatic repulsion of the nucleophilic reagent by the first form compared with the second.

Table 2. Suggested mechanisms of the solvolysis of phosphoramidates.

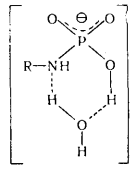
Compound	Ionic forms hydrolysed			Refs
	M^+	M_0	M_1	
Phosphoramidic acid	unimolecular bimolecular bimolecular *	unimolecular bimolecular	intermediate unimolecular bimolecular intermediate	15 48 37 11
N-Arylphosphoramidic acids	unimolecular * bimolecular	unimolecular bimolecular	unimolecular intermediate	37 11 32
N-Acylphosphoramidic acid			unimolecular * *	44 47 42

*The authors adduce data supporting both the unimolecular and bimolecular mechanisms without giving preference to either.

Cox and Ramsay[11] adduce evidence in favour of both the bimolecular and unimolecular mechanisms for the M_1 form of phosphoramidate. They suggest that, in the case of a direct attack by water on the monoanion (S_N2 mechanism), one should expect that phosphoramidate would react much more slowly than its aromatic derivatives. However, in fact phosphoramidate is hydrolysed approximately 10^3 times faster. On the other hand, if the solvolysis in aqueous alcohol proceeded via metaphosphate, the same ratio of alkyl phosphate and phosphoric acid should have been obtained as in the solvolysis of *p*-nitrophenyl phosphate under the same conditions, for which a unimolecular mechanism has been generally assumed. In fact phosphoramidate gives rise to approximately twice as much alkyl phosphate as does *p*-nitrophenyl phosphate[45]. Thus it is most likely that the solvolysis of the M_1 form proceeds via a transition state characterised by features of both the bimolecular and unimolecular mechanism. Peacock[15] arrives at this conclusion by considering the entropy of activation for the solvolysis of phosphoramidate.

A bimolecular solvolysis mechanism has been proposed[11,37,49] for the cationic form (M^+) of phosphoramidic acid in view of the lower yield of alkyl phosphate in solvolysis in aqueous alcohol compared with M_0 and M_1 (8, 44, and 72% respectively in 50% methanol[37,49]). However, the rate of hydrolysis of phosphoramidic acid is proportional to the Hammett acidity function H_0 and the corresponding plot has a slope of unity[17], which is characteristic of hydrolysis with elimination of metaphosphate[11]. Peacock is also inclined to favour the unimolecular mechanism[15].

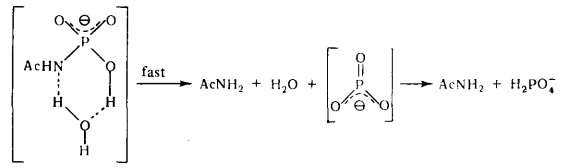
N-Arylphosphoramidates. A unimolecular solvolysis mechanism has been proposed for the monoionic (M_1) and neutral (M_0) forms of *N*-arylphosphoramidates, and it is suggested that M_0 is hydrolysed faster owing to the extremely high reactivity of its zwitter-ion[37]. However, in solvolysis in aqueous alcoholic mixtures with different alcohols different selectivities are observed compared with water[32]. This is inconsistent with the formation of free metaphosphate in the course of these reactions, since it cannot exhibit selectivity in relation to the nucleophilic reagent. On the other hand, the composition of the products in the methanol–water mixture is independent of the presence of an adjacent carboxy-group near the phosphoramidate group, which can be explained by a unimolecular mechanism[32]. In accordance with these data, it is suggested that the solvolysis of the monoanions of *N*-arylphosphoramidates includes a transition state with both unimolecular and bimolecular characteristics[32]. Possibly the hydrolysis of the monoanions involves the formation of a cyclic intermediate in which water participates[11,45], by analogy with that proposed for the hydrolysis of the monoanions of phosphate monoesters[50].



The neutral form (M_0) of *N*-arylphosphoramidic acids is selective with respect to the nycleophilic reagent in solvolysis in aqueous alcohol[32,37]. In addition, it is very sensitive to steric factors[32]. This suggests a bimolecular mechanism for the solvolysis of the M_0 form of *N*-arylphosphoramidic acids.

Examination of the solvolysis products in aqueous alcohol shows that the protonated form (M^+) is hydrolysed unimolecularly[37] (the alkyl phosphate : phosphoric acid ratio is close to the alcohol : water ratio in the solution). However, Benkovic and Benkovic[32] preferred a bimolecular pathway, including attack by the solvent on the protonated phosphoramidic acid. According to Cox and Ramsay[11], the linear relation between the rate of hydrolysis and the molarity of the acid which they observed[45] suggests that the hydrolysis of the M^+ form includes bimolecular attack by water, but the ratio of the products suggests that the reaction is unimolecular.

N-Acylphosphoramidates and *N*-phosphourethane. The reactive form of *N*-acylphosphoramidates and also of *N*-phosphourethane is the monoanion (M_1). The decrease of its proportion as both the dianion and the neutral form are formed retards the hydrolysis fairly markedly[42,44,47], which resembles somewhat the situation in the hydrolysis of monoalkyl phosphates[10]. The absence of an effect of nucleophilic (NaF, di-n-butylamine, butanethiol, aniline) and electrophilic (Ag^+, Cu^+) reagents on the hydrolysis of *N*-phosphonourethane[47] and the absence of exchange of the phosphoryl oxygen in the hydrolysis of *N*-phosphonourethane in $H_2^{18}O$ are inconsistent[47] with both unimolecular and bimolecular reactions. One of the possible mechanisms for the hydrolysis of *N*-acylphosphoramidates and *N*-phosphonourethane[41,42,47] is the cleavage of a hydrated cyclic intermediate, as in the hydrolysis of *N*-arylphosphoramidates examined above:



2. Hydrolysis of Phosphoramidate Monoesters

Phosphoramidate monoesters are cleaved at the P–N bond only in an acid medium[6,7,48,51–58]. The linear relation between the hydrolysis rate constant and the concentration of H^+ ions is evidence that the hydrolysis is acid catalysed[48].

The neutral forms of methyl phosphoramidate and unsubstituted phosphoramidic acid are both hydrolysed and solvolysed in 50% aqueous methanol at similar rates[48]. This finding indicates a bimolecular reaction mechanism for both compounds; in a unimolecular reaction involving an intermediate metaphosphate one would expect lower rates for the methyl ester because the resonance stabilisation of metaphosphate esters is more difficult than that of the metaphosphate ion. The bimolecular hydrolysis and solvolysis of phosphoramidate esters was demonstrated also for methyl *N*-cyclohexylphosphoramidate[43]: the lower yield of ethyl methyl phosphate (10%) in the solvolysis of this compound in 50% ethanol contradicts the formation of a highly reactive intermediate metaphosphate, which should not exhibit selectivity with respect to one of the nucleophilic reagents. However, in the catalysis of the solvolysis of methyl *N*-cyclohexylphosphoramidate by pyridine, for which the formation of active *O*-methylphosphonopyridinium has been suggested, the yield of ethyl methyl phosphate virtually corresponds to the content of ethanol in the reaction mixture, so that in this case one cannot rule out the possibility of the formation of an intermediate metaphosphate[43]. Thus it is extremely likely that the mechanism of the reaction of phosphoramidate monoesters depends on the type of groups eliminated, in other words on the substituents at the amide nitrogen.

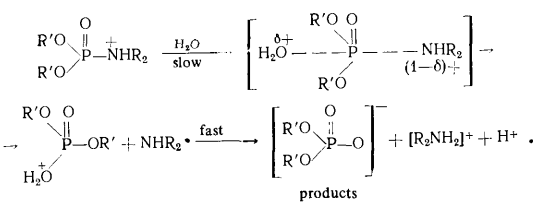
The view that the reactivity of phosphoramidates increases with the basicity of the initial amine[42,43,51], based on a study of the hydrolysis of three compounds (the piperidide, morpholide, and *p*-anisidide of adenosine 5′-monophosphoric acid)[51], has been very widely expressed in the literature. However, this conclusion contradicts the results obtained in the study of the hydrolysis of many other alkyl phosphoramidates[34,51,59,60], for which a decrease of reactivity with increasing basicity of the initial amine can be clearly traced.

In this connection a comparative study of the hydrolysis of many aliphatic and aromatic phosphoramidates derived from uridine 5′-monophosphate[61] is of interest. Comparison of the rates of hydrolysis of these compounds in 0.05 *N* HCl (37 °C) shows that the rate of hydrolysis of derivatives of weak amines (aromatic amines and 2,2,2-trifluoroethylamine, $pK_a = 1–5.7$) increases with the basicity of the initial amine, while the rates of hydrolysis of derivatives of strongly aliphatic amines ($pK_a = 9.34$ to 10.64) falls as the basicity of the initial amine rises. These results are consistent with the hypothesis of the dual effect of the substituent at the nitrogen atom on the hydrolysis of phosphoramidates[34]: on the one hand, electron-donating substituents promote the protonation of the

phosphoramidate, stabilising the positive charge generated, and, on the other hand, electron-accepting substituents facilitate the formation of the transition state, reducing the electron density at the phosphorus atom and promoting thereby nucleophilic substitution at this atom. Possibly[61] in the case of derivatives of weak amines the first effect predominates and therefore the rate of hydrolysis of the P–N bond increases as the electron-donating properties of the substituent become more pronounced. On the other hand, in the case of derivatives of strong amines the formation of the transition state is decisive and accordingly the rate of hydrolysis falls for more powerful electron-donating substituents.

3. Hydrolysis of Phosphoramidate Diesters

Phosphoramidate diesters are also hydrolysed at the P–N bond in an acid medium and are stable in an alkaline medium (see, for example, Sokolova et al.[62]). The study of the kinetics of the acid hydrolysis of phosphoramidate diesters, for 2,4-dichlorophenyl methyl *N*-alkylphosphoramidates, showed that the reaction is bimolecular and most probably involves direct attack on the phosphorus atom by the water molecule with simultaneous elimination of the amine[34]:



The results of a study of the hydrolysis of dimethyl phosphoramidate in D_2O and its solvolysis in 50% aqueous methanol[49] and also the results obtained in a study of the hydrolysis of dimethyl *NN*-dialkylphosphoramidates[60,63] are consistent with this mechanism.

Phosphoramidate diesters are much more stable in acid solutions than the corresponding phosphoramidic acids and phopshate monoesters[62,64–67]. In some cases, as a result of the stabilisation of the P–N bond in phosphoramidate diesters, the phosphate ester and not the phosphoramide bond is the first to be cleaved in an acid medium[34,64].

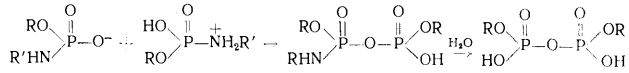
The reason for this change in the stabilities of the P–N and P–O bonds may involve[64] a change in the d_π–p_π – conjugation of the lone electron pairs of the nitrogen and oxygen atoms linked to the reaction centre and in the population of the 3*d* orbitals of the phosphorus atom in these compounds compared with phosphoramidic acids and phosphate monoesters. Conjugation of the electrons of the oxygen atom with the phosphorus atom in the P–OH and particularly the $P–O^-$ bond is known[22] to be much more pronounced than for the P–OR bond. This should have two consequences: firstly, a decrease of the stability of the P–O bond in phosphate diesters and secondly a decrease of the population of the 3*d* orbitals of the phosphorus atom in such diesters and consequently their greater accessibility to the electrons of the nitrogen atom, which should entail an increase in the stability of the P–N bond. The appreciably higher stability of diphenyl phosphoramidates compared with di-n-butyl phosphoramidates is consistent with these concepts[59]. It is also possible that the hydrolysis of phosphoramidate diesters is slower than that of the monoesters because, owing to the absence of a hydroxyl capable of dissociation in the phosphate residue of the diesters, their monomolecular hydrolysis via an intermediate metaphosphate is precluded.

IV. INTERACTION OF PHOSPHORAMIDATES WITH NUCLEOPHILIC REAGENTS

When phosphoramidates react with nucleophiles such as phosphoric acid and its esters, pyrophosphoric acid and its esters, carboxylic acids, amines, alcohols, etc., they can behave as donors of the phosphate group.

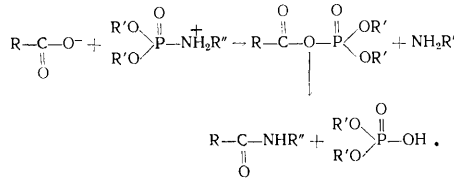
In the transfer of the phosphate residue from phosphoramidates to phosphoric acid or its esters, pyrophosphates are formed; if the nucleophilic agent is pyrophosphoric acid or its esters, triphosphates are formed. The formation of pyrophosphates from [unsubstituted] phosphoramidate was already observed in the previous century[68]. Later it was established that other phosphoramidates are readily converted into symmetrical pyrophosphates[51,67,69,70].

Kinetic studies showed that pyrophosphates are formed as a result of the attack by the phosphoramidate anion on the protonated molecule with elimination of one mole of the base[23,36,43,71]:



This reaction and also the known capacity of biological systems to employ phosphoramidates the so-called phosphagens, for example; phosphonocreatine, phosphonotaurocyamine, phosphonoglycocyamine, and phosphonolombricine (see, for example, Refs. 1, 72, and 73)—for the synthesis of pyrophosphates have served as a basis of preparative methods for the synthesis of pyrophosphates and triphosphates, including nucleotide coenzymes[69,74–77]. The most convenient amides of nucleotides for the synthesis of pyrophosphates are morpholides[51]. Many nucleoside polyphosphates have been synthesised from them. This problem has been considered in detail in monographs[78,79]. Mention should be made of those later studies[80] where the effect of reaction conditions on the yield of nucleoside diphosphate derivatives was investigated.

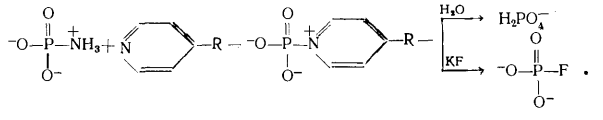
When the phosphate residue is transferred from phosphoramidate to carboxylic acids, acyl phosphates are formed[43,67,83]. Then the amine present in the reaction mixture (this may be a specially added amine[43,67,70] or the amine liberated as a result of the reaction between phosphoramidate and carboxylic acid[81]) can react with the acyl phosphate to form a carboxylic acid amide. When carboxylic acids are heated with phosphoramidate diesters and particularly with phosphoric triamide $PO(NH_2)_3$, the corresponding amides are formed in yields of 40–80%:[82]



The phosphate group in phosphoramidates can be transferred to another amine. The free phosphoramidic acids $(HO)_2PONR_2$ (R = H, Alk, or Ar) are least effective as phosphate donors in the phosphorylation of primary amines[19,39], probably because under conditions where

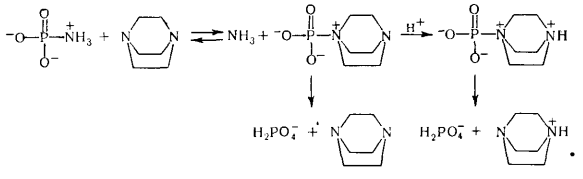
phosphoramidates are active the majority of primary amines are protonated and therefore cannot function as nucleophilic reagents. Nevertheless, the preparation of *N*-phosphonoaminoacids and *N*-phosphonopeptides using phosphoramidate as the phosphorylating agent has been described recently[84]. The phosphorylation of hydrazine in its reaction with phosphoramidate has also been described[39]

Phosphoramidate monoesters and particularly diesters are much more active as donors of the phosphate group, probably because of their higher p*K* values. However, the phosphate group is transferred only to weak amines. Thus methyl *N*-cyclohexylphosphoramidate and its thioanalogue enter into transamination reactions with 1-naphthylamine, 2,2,2-trifluoroethylamine, and *O*-methylhydroxylamine[23,43]. Among bases, the most effective acceptors of the phosphate group are tertiary bases[18], particularly pyridine and its homologues. Synthetic reactions are frequently carried out in pyridine (see the synthesis of pyrophosphates mentioned above), which is well known to catalyse the transfer of the phosphate group. The formation of an intermediate labile phosphonopyridinium ion has been frequently postulated in these reactions[18,37,85-90]. Its formation has been demonstrated in the reaction of phosphoramidic acid; in the presence of pyridine its hydrolysis is accelerated, and when fluoride ions are added, phosphorofluoridate is also formed[39]:



Pyridine derivatives catalyse also the hydrolysis of diisopropyl phosphorofluoridate and dimethyl phosphorofluoridate, 3- and 4-methylpyridines being more effective and 1-methylpyridine equally as effective as unsubstituted pyridine[85].

Other tertiary bases behave similarly, for example triethylenediamine is a still more effective catalyst (probably because of steric strain and the ready protonation of the second nitrogen atom, a more readily eliminated group is formed)[39]:



Phosphorylated tertiary amines can be useful phosphorylating agents in syntheses owing to their high reactivity and particularly because they remain reactive in an alkaline solution—under conditions where other phosphoramidates lose a proton and become inactive[39]. Examples of this kind are diphosphonoimidazole (see Section VI) and 4-methyl-*N*-phosphonopyridinium, which reacts completely with 0.5 M solution of methylamine at pH 11.7 in less than one minute[39].

An important problem in the chemistry of phosphoramidic acids is the transfer of the phosphate residue to the hydroxy-group of alcohols. The achievement of this reaction on a preparative scale would provide a method for the phosphorylation of alcohols which would be convenient for the following reasons: (a) the relative simplicity of the synthesis of the phosphorylating agent (phosphoramidate); (b) the possibility of storing it for a fairly long time; (c) the possibility of carrying out the reaction in an aqueous medium, this being particularly important in the phosphorylation of nucleosides and nucleotides, which are sparingly soluble in organic solvents. In this connection, a number of studies have been made on the solvolysis of phosphoramidates in water–alcohol mixtures. However, despite the fact that phosphoramidates effectively phosphorylate phosphates, carboxylic acids, and certain amines, in the vast majority of cases they proved to be unsuitable for the phosphorylation of alcohols[43,67]. This is because alcohols as a rule cannot compete as nucleophilic agents with water (hydrolysis) or with a second molecule of phosphoramidate (the formation of pyrophosphates). Thus, although in very dilute aqueous ethanol methyl *N*-cyclohexylphosphoramidate yields methyl phosphate (hydrolysis product) and ethyl methyl phosphate (ethanol phosphorylation product), in more concentrated aqueous ethanol considerable amounts of pyrophosphoramide are formed, the product being gradually hydrolysed, so that ultimately more than 90% of phosphorus is detected as methyl phosphate[43].

However, it is noteworthy that the ratio of the hydrolysis and phosphorolysis products depends considerably on the structure of the phosphoramidate, namely on the presence and nature of ester substituents at the phosphorus atom and of substituents at the nitrogen atom: the yield of methanolysis products depends on the introduction of a methyl group into the phosphate residue and amounts to 8, 21, and 12% for unsubstituted phosphoramidate, monomethyl phosphoramidate, and dimethyl phosphoramidate respectively[49].

The yield of phosphorylation products depends significantly on the reaction conditions, probably due to the specific mechanism of the solvolysis of phosphoramidate. But, in the solvolysis of the monoanionic form of phosphoramidate (bimolecular reaction), the ratio of the alkyl phosphate and phosphoric acid formed greatly exceeds the ratio of the alcohol to water in the reaction mixture[37]. This may be due to the greater nucleophilicity of alcohols compared with water. On passing to a unimolecular mechanism (for example acid-catalysed solvolysis), the effect of the nucleophilicity of the reactant diminishes and there is a corresponding decrease of the percentage of phosphorolysis. Until recently, the formation of alkyl phosphate and phosphoric acid in the solvolysis of phosphoramidates in water–alcohol mixtures in proportions close to those of the alcohol and water was regarded as evidence of a unimolecular mechanism involving the formation of an intermediate metaphosphate[37]. However, it was shown recently that the product ratio depends to a considerable degree on the nature of the group eliminated even when the mechanisms are known to be identical[29,91] and on the nature of the alcohol[29]. The latter finding had been explained previously by steric factors, but this explanation is invalid, since in the phosphorylation of amines significant differences as a function of the structure of the group are not observed. It has been suggested that the difference between the reactivities of alcohols can be due to a non-static distribution of solvent molecules in the solvation shell around the phosphate group[29], the degree of solvation in the transition state being apparently important[49]. This suggests that phosphoramidates are in principle unsuitable for the phosphorylation of alcohols with a bulky alkyl group.

However, the role of the alcohol alkyl group is abolished in the phosphorylation by phosphoramidates derived from tertiary amines. Above it was already mentioned that

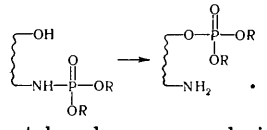
pyridine derivatives catalyse the reactions of phosphoramidates with phosphates and amines by forming active phosphorylating compounds. This is also observed in the reaction of phosphoramidates with alcohols. Thus in the solvolysis of methyl *N*-cyclohexylphosphoramidate in aqueous ethanol (50 mole %) in the presence of pyridine, the yield of ethyl methyl phosphate increases to 40% compared with 8% in the absence of pyridine[43].

N-Benzoylphosphoramidate proved to be an effective phosphorylating agent for alcohols on a preparative scale. It was used successfully in the phosphorylation of ethyl and benzyl alcohols, cyclohexanol and phenol (yield 40–80%); ethanolamine was phosphorylated to 2-aminoethylphosphoric acid. The reaction was carried out in the presence of triethylamine; the highest yields were obtained when it was used in an equimolar amount in relation to the phosphoramidate[41].

Thus apart from the phosphonoimidazoles, which will be discussed separately in Section VI, only phosphoramidates with powerful electron-accepting substituents at the nitrogen atom are of preparative value as phosphorylating agents for alcohols.

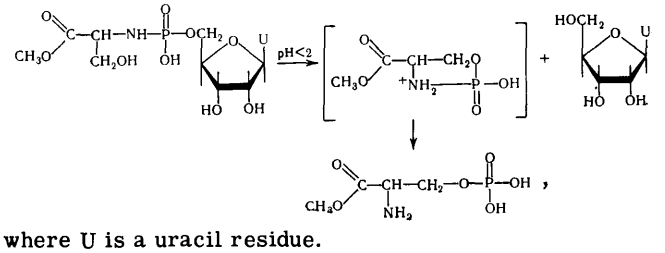
The situation is different when the phosphoramide group and the alcoholic hydroxyl are near one another in space: the intramolecular phosphorylation of hydroxy-groups is achieved under a wide variety of conditions and with high yields. It is possible to distinguish two types of reactions.

1. The amino-group of a hydroxylated compound is phorphorylated. In this case intramolecular phosphorylation results in N → O migration of the phosphate residue:



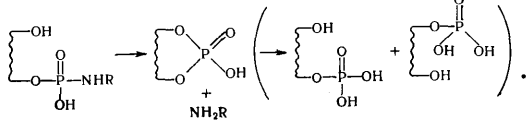
These reactions take place as a rule in an acid medium (see, for example Plapinger and Wagner-Jauregg[92]).

The finding that intramolecular phosphorylation of hydroxy-groups by phosphoramidates takes place only with esterified phosphono-derivatives is striking[18]. This phenomenon is attributed to the necessity for a cyclic intermediate, which in the case of monoesters and diesters can be formed fairly readily as a result of transesterification whereas in the case of a non-esterified phosphate group its formation is difficult[18]. N → O migration of this kind with transesterification in the acid hydrolysis of (P–N)-serine derivatives of nucleotides has been described[93]:

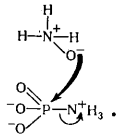


where U is a uracil residue.

2. The hydroxy-compound contains a second OH group esterified by the phosphoramidate residue. In this case intramolecular phosphorylation leads to the elimination of the amine and the formation of a cyclicphosphate, which under sufficiently severe conditions may be hydrolysed further to the monophosphate[7,94–98]:



Among other nucleophilic reagents capable of reacting with phosphoramidates, hydroxylamine should be mentioned. A study of its reaction with unsubstituted phosphoramidate at pH 7 established that it attacks the phosphorus atom via its oxygen atom rather than the nitrogen[39]:



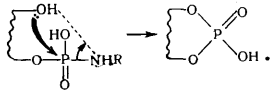
The reaction of hydroxylamine with phosphoramidates has been suggested for the specific cleavage of nucleotido-(P–N)-peptides[99,100]. When they are treated with hydroxylamine at pH 5, hydroxylamine derivatives of nucleotides are formed together with peptides, and the latter can be determined quantitatively by conversion into dinitrophenyl derivatives[99]. *N*-Methylhydroxylamine proved to be more reactive and *O*-methylhydroxylamines less reactive than unsubstituted hydroxylamine[100], in agreement with the mechanism described above.

Finally, phosphoramidates react with hydrogen halides. Hydrogen fluoride is the most reactive in this process. It reacts with any phosphoramidate, in contrast to hydrogen chloride and hydrogen bromide, which reacts only with *NN*-disubstituted phosphoramidates[101,102].

In aqueous solutions phosphoramidates react with fluoride ions to form phosphorofluoridates, rapidly in a weakly acid medium[17,103] and slowly in neutral and alkaline media[39]. Phosphorofluoridate is formed from phosphoramidate and potassium fluoride in the presence of pyridine or triethylenediamine, which are responsible for the nucleophilic catalysis of the transfer of the phosphate residue[39] (see pp. 58, 59).

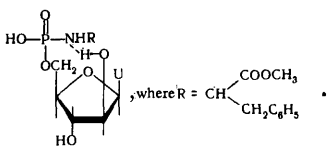
V. GENERAL INTRAMOLECULAR ACID CATALYSIS OF THE REACTIONS OF PHOSPHORAMIDATES

The transfer of the phosphate residue from the amino-group to the hydroxy-group with formation of cyclicphosphates, described in the preceding sections, probably constitutes a special case of general intramolecular acid catalysis in which the hydroxy-group behaves as a proton donor for the amide nitrogen, disrupting the $d\pi$–$p\pi$ conjugation between nitrogen and phosphorus and increasing the electrophilicity of the latter[93,98]:



In the majority of the examples quoted above, general acid catalysis involving the hydroxyl-group leads to a sharp change in the properties of the phosphoramidates: the P–N bond becomes labile not only in acid but also in neutral and alkaline media. In other cases, catalysis by the hydroxyl group can lead only to an increase of the reactivity of phosphoramidates in an acid medium. Thus the methyl ester of 1-B-D-arabofuranosyluracil 5′-phospho-(P–N)-phenylalanine is hydrolysed faster at pH 1–5 than the corresponding ribose derivative, probably

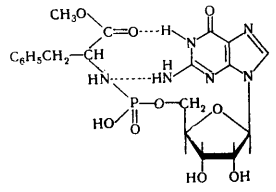
because in the former the 2'-OH group is in the *cis*-position relative to the 5'-P–N bond and may protonate its nitrogen atom[96]:



Apart from the hydroxy-group, the undissociated carboxy-group can function as a proton donor in the general intramolecular acid catalysis of reactions of phosphoramidates. Thus *o*-carboxylphenyl phosphoramidate is hydrolysed faster (in the monoanionic and neutral forms) than the corresponding *p*-carboxyl-derivative[32]. A similar effect of the carboxyl group is observed in the hydrolysis of phosphonocreatine[104].

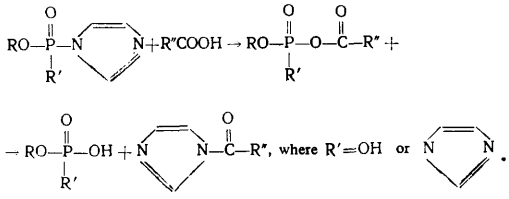
The increase of the reactivity of the P–N bond as a result of the catalytic effect of the amino-group as the proton donor is observed in the hydrolysis of phosphonohistidines. Histidine derivatives are less stable than the corresponding imidazole derivatives both in hydrolysis and in the transfer of the phosphate residue to imidazole derivatives, the P–N bond in the 1-position of the imidazole ring being the most labile. The protonated α-amino-group is responsible for the increase in the lability of phosphonohistidines[84,105].

An intramolecular acceleration of the hydrolysis of the phosphoramide bond by the amino-group has been observed also for 5'-guanylyl-(P–N)-phenylalanine[57]:



VI. IMIDAZOLE DERIVATIVES OF PHOSPHORIC ACID

Imidazolides occupy a special place among phosphoramidates. They are distinguished by high reactivity towards nucleophilic reagents of various types. Thus phosphonoimidazole monoesters and diesters give quantitative yields of pyrophosphates in reactions with phosphoric acids and its esters[108-109]. In the reaction with carboxylic acids, phosphonoimidazole monoesters and also the esters of phosphoric acid di-imidazolide yield acyl phosphates, which react further with the liberated imidazole, forming acylimidazole and a phosphate monoester[107,108]:



Among phosphoramidates, phosphonoimidazoles are the most active donors of the phosphate residue towards amines. Phosphonoimidazole and its esters phosphorylate aromatic and aliphatic amines, the latter reacting more readily[107,108,110,111]. Diphosphonoimidazole is particularly effective in the phosphorylation of amines. It phosphorylates primary aliphatic amines at alkaline pH. Diphosphonoimidazole can be used to prepare phosphoramidic acid (75%) and to phosphorylate aminoacids[40,112], ethanolamine, aromatic amines, *p*-aminobenzoic acid, and sulphanilic acid[18].

Phosphonoimidazoles are even more effective phosphorylating agents towards alcohols, phosphonoimidazole esters being the most reactive[107,108,111].

Evidently (see Sections VI and V) the intramolecular phosphorylation of an alcoholic hydroxyl by phosphonoimidazoles would be most effective. In this connection, the synthesis of dinucleoside phosphates on a polynucleotide matrix by the reaction of the nucleotide imidazolide with the nucleoside is exceptionally interesting[113-115]. The complementary interaction of polyuridylic acid with a mixture of *N*-(5'-adenylyl)-imidazole and adenosine ensures relative positions of the phosphoramide group and the alcoholic hydroxyl resembling those in the intramolecular reaction, as a result of which the phosphate residue is transferred from imidazole to the hydroxy-group of the nucleoside, i.e. a dinucleoside phosphate ApA is formed (yield 41%).

Thus phosphonoimidazoles are the most active donors of the phosphate residue in the phosphorylation of phosphates, carboxylic acids, amines, and alcohols. On the other hand, imidazole is the most effective acceptor of the phosphate group from phosphoramidates[18,39,116]. This has served as a basis for a preparative method of phosphorylating imidazole by phosphoramidic acid[84,105].

The imidazole residue can be phosphorylated not only by phosphoramidates but also by phosphonoimidazoles. Examples of this are the reaction between diphosphonoimidazole and histidine with formation of phosphonohistidine and the hydrolysis of 1-phosphonoimidazole, where one molecule probably phosphorylates another[18] and also the conversions of 1-phosphonohistidine into the corresponding 3-derivatives[84], for example: 1-phosphonohistidine + histidine → histidine + 3-phosphonohistidine; 1-phosphonohistidine + α-*N*-acetylhistidine → histidine + α-*N*-acetyl-3-phosphonohistidine.

The unique capacity of phosphonoimidazoles to function as effective donors and acceptors of the phosphate residue probably constitutes the basis of their catalytic effect in the reactions of many phosphoric acid derivatives. Thus imidazole catalyses the hydrolysis of phosphoramidate[18,39,116], *p*-nitrophenyl phosphate[31], dialkyl phosphorofluoridates[35], and ethylene methyl phosphate[117]. It has been suggested[85] that the catalytic properties of imidazole can be accounted for by the intermediate formation of phosphorylated imidazole. Indeed, the exceptional lability of di-isopropylphosphonoimidazole—the potential intermediate in the hydrolysis of di-isopropyl phosphorofluoridate—has been demonstrated. In a bicarbonate buffer at pH 7.6 at 30°C it hydrolyses to the extent of 50% in 2.7 h and 100% in 13 h.[85]

The catalytic activity of imidazole in reactions *in vitro* suggests that phosphonoimidazoles may be intermediates in the reactions of phosphorylated compounds *in vivo*. Imidazole in the form of the histidine residue enters into the active centres of transphosphorylation enzymes. Phosphonohistidine has been isolated in many cases. The involvement of histidine is particularly likely, since its *N*-1-phosphono-derivative is much more labile than *N*-1-phosphonoimidazole[84]. As stated above (see section V), this is associated with the effects of the histidine side chain, namely its protonated amino-group, which is

close to the *N*-1-position. In protein the histidine amino-group is of course most likely to be combined in a peptide chain, but the labilisation of the P–N bond of phosphono-imidazole may be induced by the amino-group of another aminoacid located in its vicinity owing to the specific conformation of the enzyme. Evidently, in principle, there is then a possibility of the activation of both phosphor-amide groups, in the 1- and 3-positions of imidazole, and the specific result will be determined by steric factors.

It is interesting to note that phosphonoimidazole itself is not more reactive than phosphoramidic acid but its esters are much more reactive towards nucleophilic attack. One may suppose therefore that phosphonohistidine partici-pates in enzymatic processes associated with the transfer of the phosphate ester residue (for further details, see Section VIII).

VII. INTERACTION OF PHOSPHORAMIDATES WITH ELECTROPHILIC REAGENTS

General and specific acid catalysis (see Sections V and III) and catalysis by metal ions are special cases of elec-trophilic catalysis. Catalysis by metal ions (Zn^{2+}, Mn^{2+}, Fe^{3+}, Co^{2+}, and Cu^{2+}) has been described for phospho-guanidines—natural phosphagens[118]. It is known that *in vitro* they are much more stable than simple phos-phoramidates. This is because of the delocalisation of the positive charge at the amide nitrogen. The catalytic effect of the metal ion consists in preventing the delocalisation by the formation of a phosphoramidate–metal cation com-plex[72,73,118].

Electrophilic catalysis has been investigated in detail in the hydrolysis of phosphoramidates in the presence of formaldehyde, pyridoxal, and hypochlorite[30], nitrous acid, and isopentyl nitrite[119]. The role of such catalysts is probably the conversion of the amino-group into a more readily eliminated group. For example, the following mechanism has been suggested[30] for the hydrolysis of phos-phoramidate in the presence of formaldehyde:

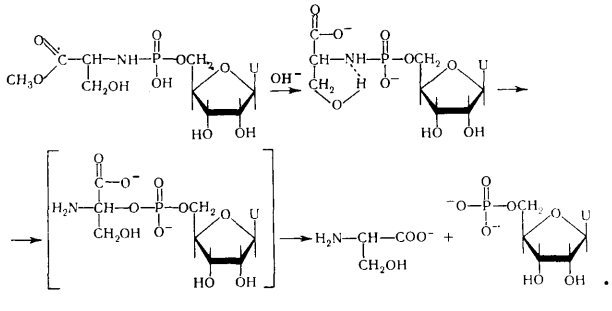
$$^{-2}O_3P\overset{+}{N}H_3 + HCHO \overset{\text{fast}}{\rightleftharpoons} {}^{-2}O_3P\overset{+}{N}H_2CH_2OH\,,$$

$$^{-2}O_3P\overset{+}{N}H_2CH_2OH + HCHO \overset{\text{fast}}{\rightleftharpoons} {}^{-2}O_3P\overset{+}{N}H(CH_2OH)_2\,,$$

$$^{-2}O_3P\overset{+}{N}H_2CH_2OH \rightarrow H_2PO_4^- + NH_2CH_2OH\,,$$

$$^{-2}O_3P\overset{+}{N}H(CH_2OH)_2 \rightarrow H_2PO_4^- + NH(CH_2OH)_2\,.$$

Electrophilic catalysis combined with nucleophilic catalysis, particularly when they take place intramole-cularly, is most effective in relation to phosphoramidates. For example, in the case of 5′-uridilyl-(P–N)-serine[93] and other nucleotidoamines containing the OH group capable of approaching the amide nitrogen[97], combined electro-philic and nucleophilic catalysis results in the lability of the P–N bond in an alkaline medium:



VIII. PHOSPHORAMIDATES AS INTERMEDIATES IN BIOLOGICAL PHOSPHORYLATION REACTIONS

The exceptional sensitivity of phosphoramidates to nucleophilic and electrophilic catalysis and in particular to combined intramolecular nucleophilic and electrophilic catalysis suggests that they can play the role of active intermediates in biological phosphorylation processes.

A number of enzymes cleaving phosphoramidates, the so called phosphoamidases (here we are not considering phosphagens), have been described. However, hitherto in all cases the phosphoamidase activity has been merely supplementary to the main activity of the enzyme—usually phosphoesterase of phosphotransferase activity[120–127]. Only ribonucleoside 5′-phosphoamidase from mammalian tissue extract has not so far shown any additional activity[128]. Phosphoamidase activity is also shown by certain proteo-lytic enzymes[127].

The phosphoesterase and phosphotransferase activity of phosphoamidases and the fact that free phosphoramidates have not been detected in biological systems, synthetic compounds being employed as substrates in enzymatic reactions, suggest that the phosphoamidase activity of the enzymatic preparations described is a kind of artefact reflecting certain details of the mechanism of enzyme action.

Possibly, in phosphoesterase and other reactions, intermediate enzyme–substrate compounds of the phos-phoramidate type are formed and this is why the enzymes are capable of cleaving phosphoramidates when these are supplied in a finished form.

The phosphorylation of the enzyme protein during the reaction has been described for a number of enzymes[129–142]. For certain enzymes involved in nucleic acid metabolism, it has been suggested[110,127,138–140] that the substrate can interact initially with the active centre of the enzyme, forming intermediate active nucleoside 5′-phospho-enzyme derivatives. In many cases it has been suggested that phosphate adds to the imidazole moiety of the histidine residue[105,129–135,142]. Phosphonohistidine was also isolated from mitochondria and from a preparation of succinate thiokinase and was identified by reference to a synthetic specimen of 3-phosphonohistidine[105]. However, subse-quently the exceptional case of the transfer of the phosphate residue from the 1-position of histidine to various acceptors, including the *N*-3-position in histidine, was demonstrated. Thus the problem of the site where histi-dine is phosphorylated in the enzyme remains open[84].

In connection with the possibility of the formation of enzyme–substrate complexes with a P–N bond between the fragments, synthetic phosphoramidates can be regarded as models of such complexes. The differences between them and natural phosphoramidates consists in the fact that the enzyme has been replaced by an amine residue as a donor of amide nitrogen. If the phosphoramidate can approach the active centre of the enzyme without affecting sifnifi-cantly its structure, there is a possibility of nucleophilic-electrophilic activation of the phosphoramidate site with participation of the functional groups of the enzyme, which under "normal" conditions acts on the enzyme's own phosphonoimidazole system. Ultimately, when a phos-phate acceptor is present, transphosphorylation takes place, while in the absence of a specific acceptor the phos-phoramidate is hydrolysed. This hypothesis has been discussed in detail for ribonucleoside 5′-phosphoamidase and it was suggested that, like other phosphoamidases, this enzyme has no independent importance and its activity is based on the formation of intermediate phosphoramidate structures in the synthesis of hydrolysis of internucleotide bonds of RNA.[61]

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Polytriazines

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The review deals with studies on the synthesis and properties of polymers containing the *s*-triazine ring in the main chain (polytriazine). These polymers have found large-scale application in many branches of engineering. Attention has been concentrated on studies dealing with the preparation of thermostable and heat resistant polymers based on *s*-triazine derivatives and also new and novel methods of synthesising these polymers, particularly such as the polycyclotrimerisation and polycyclocondensation reactions.

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I. INTRODUCTION

Polymers containing the cyclic *s*-triazine group in the main chain have been attracting attention for a long time. As early as in the 1930's a melamine-formaldehyde polymer was obtained by the polycondensation of melamine with formaldehyde[1] and subsequently found large-scale industrial application.

Recently there has been a considerable increase of interest in polymers containing *s*-triazine rings because the majority of polymers of this kind exhibit high thermal stability owing to the aromaticity of the *s*-triazine ring[2-4].

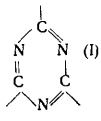
Polymers containing *s*-triazine rings may be obtained in two ways: (1) by the polycondensation or polymerisation of monomeric *s*-triazine derivatives and (2) by the polycyclotrimerisation of nitriles or by the polycyclocondensation of nitrile derivatives (iminoethers, amidines, etc.). Since the synthesis and properties of melamine-aldehyde polymers have been thoroughly reviewed[5-12], we shall not consider here (with some exceptions) studies dealing with triazine polymers of this type.

In the present review attention will be concentrated on problems of the thermal stability of polytriazines and also new, novel methods of their synthesis.

II. POLYTRIAZINES OBTAINED BY THE POLYCONDENSATION AND POLYMERISATION OF MONOMERIC *s*-TRIAZINE DERIVATIVES

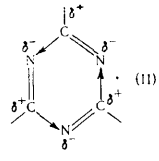
1. Polycondensation of Monomeric *s*-Triazine Derivatives

As mentioned above, *s*-triazine behaves like an aromatic compound[2-6]. It consists of a six-membered cyclic system of alternating N and C atoms:



(I)

which resembles the benzene cyclic system. The nitrogen atoms in *s*-triazine are more electronegative than the carbon atoms and the carbon–nitrogen bond tends to undergo type (II) polymerisation:



(II)

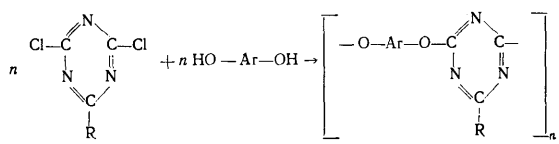
Apart from the χ-electron system, the *s*-triazine ring contains six unpaired electrons of the nitrogen atoms. Calculation of electron density in *s*-triazine[13] showed that it is 1.179 at a nitrogen atom and 0.821 at a carbon atom. This is probably the reason for the fundamental differences between the *s*-triazine and benzene systems: the *s*-triazine ring is less aromatic[14-16]. This is shown, in particular, by the lower chemical stability of the *s*-triazine system compared with the benzene ring.

Studies on *s*-triazine showed its inability to undergo electrophilic substitution reactions characteristic of benzene (nitration and sulphonation), so that it was impossible to synthesise nitro-derivatives of cyanuric chloride[2]. This can be explained only by the reduced electron density at the carbon atoms of *s*-triazine and the same explanation is also given for the greater mobility of the halogen atoms in its halogeno-derivatives, particularly of chlorine atoms in cyanuric chloride, which distinguishes the latter from benzene derivatives.

Cyanuric chloride and dichloro-*s*-triazines readily enter into substitution reactions with various compounds and therefore they constitute the main starting materials for the synthesis of polytriazines.

A number of polyesters—poly(aryl cyanurates)—with enhanced heat resistance and thermal stability have been

synthesised by the reaction of cyanuric chloride and dichloro-*s*-triazines with various bisphenols[17-35]:



Depending on the functional groups in the initial *s*-triazines, both linear soluble and cross-linked insoluble poly(aryl cyanurates) were obtained.

Thus Nakamura and coworkers[17] synthesised poly(aryl cyanurates) by the interfacial polycondensation of di-(4-hydroxyphenyl)propane with 2-R-4,6-dichloro-*s*-triazines, where R = OCH_3, $OCH_2CH{=}CH_2$, OC_6H_5, $N(C_2H_5)_2$, $N(CH_2CH{=}CH_2)_2$, $N(CH_2)_5$, $N(C_6H_5)_2$, C_6H_5, $PhNSO_2C_6H_4CH_3$, or Cl. Some of the poly(aryl cyanurates) obtained are crystalline and soluble in chloroform, *o*-dichlorobenzene, etc., films being formed from the solutions.

Cross-linked polymers[18-20], insoluble in the usual solvents but decomposing in hot alkalies and amines, have been synthesised by the interfacial polycondensation of cyanuric chloride with bisphenols [resorcinol, quinol, 4,4′-dihydroxybiphenyl, di-(4-hydroxyphenyl)methane, and di-(4-hydroxyphenyl)propane]. Vigorous thermal degradation of these polymers begins about 450°C.

Nakamura and coworkers[21,22] synthesised a number of poly(aryl cyanurates) using 2-diphenylamino-4,6-dichloro-*s*-triazine and various bisphenols and also a phenol-formaldehyde resin of the novolak type. The polymer based on di-(4-hydroxyphenyl)propane (dian) proved to have the highest molecular weight. It was found that the temperature of the onset of decomposition of the poly(aryl cyanurate) synthesised depends little on the type of the initial diol and is in the range 320–360°C (for an average molecular weight of about 5000). The majority of polymers dissolved in chloroform and nitrobenzene, but polymers based on quinol, 4,4′-dihydroxybiphenyl, di-(4-hydroxyphenyl)propane, and di-(4-hydroxyphenyl) sulphone were partly soluble only in nitrobenzene. Polymers with a fairly high molecular weight (in excess of 5000) are capable of forming colourless transparent films with high mechanical strength and a characteristic absorption in the ultraviolet.

Seta and Nakamura[23] obtained and successfully employed as dyes and stabilisers for various resins coloured poly(aryl cyanurates). Triazine dyes of this kind are synthesised by the polycondensation of diazo-derivatives of dichloro-*s*-triazine with bisphenols such as di-(4-hydroxyphenyl)propane, fluorescein, aurin, etc. The low-molecular polymers of different colours thus obtained (η_{inh} between 0.09 and 0.6 dl l^{-1}) proved to be readily soluble in chloroform, dimethylformamide (DMF), and dimethylacetamide.

In a later study Nakamura and coworkers[24] investigated the effect of the structure of poly(aryl cyanurates) on their thermal and mechanical properties. A large number of dichloro-*s*-triazines with 35 different substituents R in the ring were employed as the starting materials together with the following initial bisphenols: quinol, 4,4′-dihydroxybiphenyl, di-(4-hydroxyphenyl)methane, di-(4-hydroxyphenyl)propane, 4,4′-dihydroxybenzophenone, di-(4-hydroxyphenyl)sulphone, and phenolphthalein. The polymers obtained had high inherent viscosities (η_{inh} up to 3.52 dl g^{-1}) and their softening temperatures were in the range between 200° and more than 360°C. The authors established that the temperature of the onset of decomposition of these poly(aryl cyanurates) in air depends greatly on the structure of the substituents R in the triazine ring and is in the range 300–400°C. Poly(aryl cyanurates) with substituents such as $N(C_6H_5)_2$, $N(C_6H_5)$(β-naphthyl), C_6H_5, etc. have the highest temperatures of the onset of decomposition. Poly(aryl cyanurates) based on phenolphthalein, 4,4′-dihydroxybenzophenone, and di-(4-hydroxyphenyl) sulphone are distinguished by high thermal stability.

Poly(aryl cyanurates) based on phenolphthalein and 2-diphenylamino-4,6-dichloro-*s*-triazine were described simultaneously by Devdariani and Kutepov[25], but they had less satisfactory thermal characteristics (softening temperature 160–210°C, temperature of the onset of decomposition 250–300°C) than those synthesised by Nakamura and coworkers[24], probably due to the lower molecular weights of the polymers synthesised (η_{inh} = 0.08–0.12 dl g^{-1}).

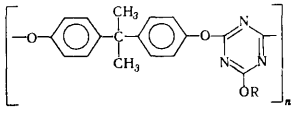
Vinogradova and Frenkel'[26] obtained poly(aryl cyanurates) by the high-temperature polycondensation in solution of 2-amino-4,6-dichloro-*s*-triazine with the anilide of phenolphthalein and 9,9-di-(4-hydroxyphenyl)fluorene in the presence of potassium or sodium carbonate. The polymer based on 9,9-di-(4-hydroxyphenyl)fluorene had η_{inh} = 0.18 dl g^{-1} in sulphuric acid and a softening temperature in excess of 320°C.

Later Anderbert and Neel[27] achieved under similar conditions the polycondensation of substituted dichloro-*s*-triazines $C_3N_3Cl_2R$ (R = NC_5H_{10}, C_6H_5, or OC_6H_5) with quinol, 4,4′-dihydroxybiphenyl, di-(4-hydroxyphenyl)sulphone, and di-(4-hydroxyphenyl)propane. The poly(aryl cyanurates) obtained had softening temperatures between 270° and 380°C and a temperature of the onset of decomposition (according to thermogravimetric data) in the range 305–415°C. These temperature characteristics of the polymers depend both on the structure of the substituent in the triazine ring and on the structure of the initial bisphenol. The poly(aryl cyanurates) based on 2,4-dichloro-6-phenoxy-*s*-triazine and quinol showed the highest thermal stability (380° and 415°C respectively)[27].

Korshak and Kutepov and coworkers carried out the high-temperature condensation of 2-anilino-4,6-dichloro-*s*-triazine with di-(4-hydroxyphenyl)propane and other bisphenols in solution[28-30] and in the melt[31], and established that, together with the main reaction, there is a homocondensation side reaction leading to the formation of three-dimensional products. When employed as hardening agents for epoxy-resins, the resulting oligomers and polymers increased the thermal stability of the resins[30,31].

Korshak, Kutepov, and coworkers[19,20,25,28-31] synthesised poly(aryl cyanurates), based on substituted dichloro-*s*-triazines [R = C_6H_5, $N(C_6H_5)_2$, $N(C_2H_5)_2$] and bisphenols such as 2,2-di-(4-hydroxyphenyl)propane, 2,2-di-(3-chloro-4-hydroxyphenyl)propane, 2,2-di-(2,5-dichloro-4-hydroxyphenyl)propane, and phenolphthalein as well as bisphenols containing various substituents at the central carbon atom, by high-temperature polycondensation in ditolylmethane in a stream of inert gas at 180–240°C. It was established that, depending on the structure of the substituents at the central carbon atom, the reactivity of bisphenols decreases in the series H, H > CH_3, C_6H_5 > H, C_6H_5 > C_6H_5, C_6H_5.

Breed and Elliott [32] synthesised two poly(aryl cyanurates) with the following structures by the polycondensation of substituted dichloro-*s*-triazines:

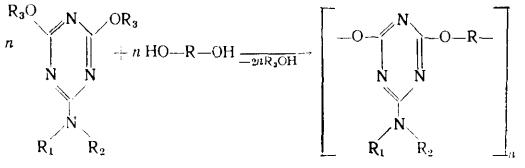


where R = $(CH_2)_4CH_3$ and $CH_2(CF_2)_4H$.

According to thermogravimetric analysis of polymers with similar inherent viscosities (0.89 and 1.24 dl g^{-1}), the polymer with the fluorinated substituent in the triazine ring has a higher thermal stability. Thus at 400°C the poly(aryl cyanurate) with R = $(CH_2)_4CH_3$ loses in air 19% of its weight (heating rate 6 deg min^{-1}) and 30% in an inert atmosphere (heating rate 3 deg min^{-1}), while the poly(aryl cyanurate) with R = $CH_2(CF_2)_4H$ loses only 3% of its weight in air and 3% in an inert atmosphere.

Anderbert and Neel [33,34] obtained linear polytriazines by the polycondensation in a high-boiling solvent at 200–240°C of substituted dichloro-*s*-triazines (R = NC_5H_{10}, C_6H_5, and OCH_3) with di-(4-hydroxyphenyl) sulphone, 2,2-di-(4-hydroxyphenyl)propane, 4,4′-dihydroxybiphenyl, and quinol. The resulting polymers were soluble in aniline, hexamethylphosphoramide, *N*-methylpyrrolidinone, etc. The polytriazines had a high softening temperature (270 and 585°C) and a temperature of the onset of decomposition in an inert atmosphere in the range 260–420°C.

Many polymers containing the *s*-triazine ring were obtained by the transesterification of dialkoxy-*s*-triazines with glycols [36]. The transesterification reactions proceed according to the mechanism



where R_1, R_2, and R_3 were varied from H to C_4H_9 and the glycols were ethylene glycol, di- and tri-ethylene glycols, hexa- and deca-methylene glycols, and also higher polyglycols with molecular weights up to 400.

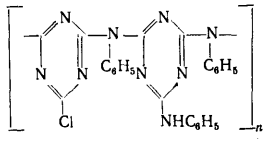
The degree of reaction was 85–90% and the polymerisation coefficient n = 4–5. The polymers were synthesised *in vacuo* at 80–160°C, the alcohol formed in the course of the reaction being distilled off. It has been noted that the transesterification reaction takes place in stages and at a high temperature infusible and insoluble polymers may be formed. Nakamura and coworkers [37–39] carried out the polycondensation of 2-R-4,6-diphenoxy-*s*-triazines, where R = OCH_3, OC_2H_5, $OCH_2CH{=}CH_2$, $N(C_2H_5)_2$, $N(CH_2CH{=}CH_2)_2$, $N(CH_2)_5$, $N(C_6H_5)_2$, *m*-$C_6H_3(CH_3)_2$, and Cl, with 2,2-di-(4-hydroxyphenyl)propane at 180–270°C in the presence of cadmium acetate. Low-molecular-weight linear polymers with a polymerisation coefficient of 3–10 were obtained. All the polymers, except that with R = Cl, were soluble in chloroform and dimethylformamide and had softening temperatures in the range 120–270°C. On further heating in the presence of dicumenyl peroxide, the polymers with R = $OCH_2CH{=}CH_2$ and $N(CH_2CH{=}CH_2)_2$ become cross-linked and insoluble.

Nakamura et al. [40] obtained linear polytriazines by heating (220–240°C) 2-amino-4-6-diphenoxy-*s*-triazine with 2,2-di-(4-hydroxyphenyl)propane *in vacuo*. It was established that in the first stage the reaction is of second order with an activation energy of 16.7–17.8 kcal $mole^{-1}$. Further heating of the polymer to 270°C without catalyst or in the presence of cadmium acetate leads to the formation of a cross-linked product, probably as a result of the elimination of phenol when phenoxy- and amino-groups interact. The authors [40] showed that the last reaction is identical with the homocondensation of 2-amino-4,6-diphenoxy-*s*-triazine on heating, since both processes are of second order and have similar activation energies (40.3–47.8 and 42.7 kcal $mole^{-1}$ respectively). The thermal stability of the cross-linked polymer thus obtained is somewhat higher than that of the product of the cross-linking of the linear polymer by paraformaldehyde, dimethyl terephthalate, tolylene di-isocyanate, etc.

Polyamides, polyimides, polyureas, and other classes of polymers obtained from triazine derivatives are distinguished by high thermal stability and heat resistance. Depending on the functional groups in these derivatives, polymers with both linear and three-dimensional structures can be obtained, as in the case of poly(aryl cyanurates).

One of the main starting materials for the synthesis of polymers of this type is cyanuric chloride and its various derivative, which Sheehan et al. [41] were the first to employ for this purpose.

Thus Ehlers and Powers [42] described the synthesis of thermostable polytriazyleneimides from cyanuric chloride and 2,4,6-triphenylamino-*s*-triazine, whose structure may be represented by the following formula:

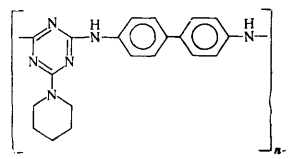


Thermostable and chemically stable polymers have been obtained by the polycondensation of cyanuric chloride or dichloro-*s*-triazines with various aromatic diamines [19,20,26,27,42–46].

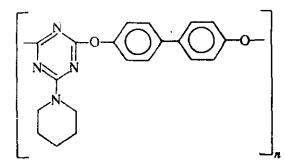
Triazine-containing polymers based on 2-amino-4,6-dichloro-*s*-triazine and hexamethylenediamine, *p*-phenylenediamine, and anilinephthalein have been described [26]. The polycondensation was carried out in a stream of nitrogen in n-butyl alcohol in the presence of triethylamine (12 h with a gradual increase of temperature from 85° to 115°C) or in decalin in the presence of sodium carbonate (at the boiling point of the solvent for 18 h). The polymers of hexamethylenediamine and *p*-phenylenediamine, synthesised in n-butyl alcohol, had inherent viscosities of 0.13 dl g^{-1} (in dimethyl sulphoxide) and 0.14 dl g^{-1} (in sulphuric acid) respectively. Their softening temperatures were 290–320°C and about 450°C respectively. The polymer based on anilinephthalein had a softening temperature of 260–270°C and was more soluble than the above polymers (it was soluble in dimethyl sulphoxide, dimethyl formamide, and dioxan). The polyamide based on hexamethylenediamine and synthesised in decalin was infusible and insoluble.

Andebert and Neel [27] carried out the high-temperature polycondensation of various dichloro-*s*-triazines with diamine derivatives or related compounds such as piperazine hydrochloride, benzidine, 2,4-diamino-6-phenyl-*s*-triazine, and hexamethylenediamine in decalin. It is noteworthy that the polyamides greatly surpass (by 100–150°C) in both heat resistance at thermal stability the poly(aryl cyanurates) with comparable structures obtained

in the same study[27]. Thus the polyamide based on benzidine,



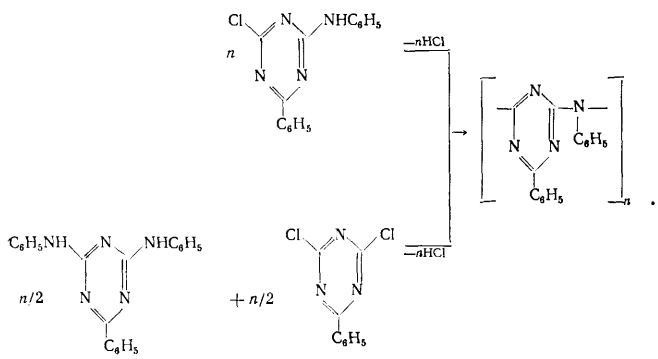
has a softening temperature at 470°C and begins to decompose *in vacuo* at 460°C (η_{inh} = 0.32 dl g^{-1}), while the corresponding temperatures for the poly(aryl cyanurate) having a similar structure and based on 4,4′-dihydroxybiphenyl,



are 315–320° and 365° respectively (η_{inh} = 0.23 dl g^{-1}).

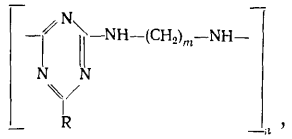
Polycondensation of 2,4-diphenoxy-6-chloro-*s*-triazine with di-(4-aminophenyl) sulphone yielded a polymer melting at 360°C and stable on heating in air to 400°C.[43] Among polymers of this type, polyperfluoro-4,4′-diphenylmelamine proved to be the most thermostable[44]. It is stable up to 500°C but at 700°C in air it loses 63% of its initial weight.

Ehlers and Ray[45] established that it is more convenient to employ chloro-derivatives of *s*-triazine rather than phenoxy-derivatives in the polycondensation with the aim of obtaining linear polytriazyleneimides:



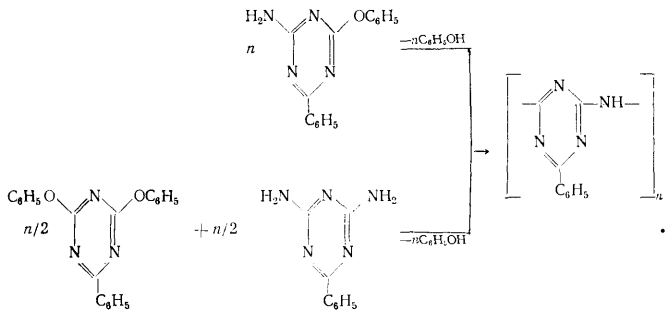
They also established that the polycondensation is best performed in an inert atmosphere at 200–250°C without reducing the pressure; the latter condition is necessary owing to the ease of sublimation of the initial monomers at a high temperature (about 200°C), while at a 150°C the reaction hardly occurs. It was shown that acids, alkalies, peroxides, and HCl acceptors do not affect the molecular weight of the polymer formed. It is noteworthy that the polymers containing terminal and side chain chlorine atoms are hydrolysed in air, becoming brittle and insoluble. Attempts have been made to replace these chlorine atoms by phenoxy-groups by treating the polymer with phenol, but the polymer decomposed under these conditions.

Infusible and insoluble polymers thermostable up to 400°C are formed in the high-temperature homocondensation of a number of amino-derivatives of *s*-triazine[45]. The most thermostable of these proved to be the polymer obtained from 6-anilino-4-chloro-2-phenyl-*s*-triazine. It loses 5% of its weight at 400°C and not more than 25% at 900°C. Polymers containing guanamine units separated by aliphatic bridges were obtained by the polycondensation of cyanuric chloride or its derivatives with aliphatic diamines:



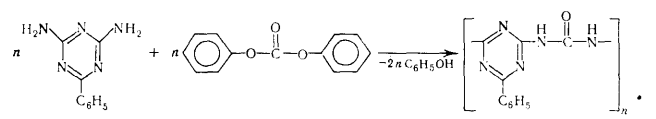
where R = Cl, C_6H_5, a monoamine residue, etc. and m = 6–12.[26,27,47]

Linear soluble polyamides containing *s*-triazine rings were obtained by the homocondensation of 4-amino-6-phenoxy-2-phenyl-*s*-triazine or by the reaction of 4,6-diphenoxy-2-phenyl-*s*-triazine with guanamines[48,49]:



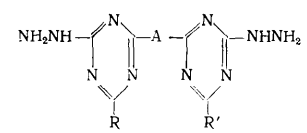
The transamination reaction was performed in an atmosphere of nitrogen above the melting point of the monomers; the optimum reaction temperature is 260–300°C. Polymers with maximum molecular weights (according to viscometric data) are obtained when the synthesis is carried out at a reduced pressure. The homopolymer of 4-amino-6-phenoxy-2-phenyl-*s*-triazine and a polymer based on 4,6-diphenoxy-2-phenyl-*s*-triazine and benzoguanamine have the same physical properties, which is evidence of the identity of their structures. This is also confirmed by infrared spectroscopic data.

The polymer obtained by the polycondensation of 2,4-diamino-6-phenyl-*s*-triazine with diphenyl carbonate exhibits a high heat resistance[48]:



It is soluble in sulphuric acid and melts at 350°C.

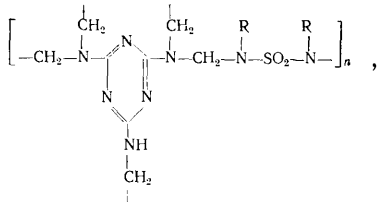
Insoluble polymers are formed in the homopolycondensation of 2,4-diamino-6-phenoxy-*s*-triazine and 2-amino-4,6-diphenoxy-*s*-triazine[50,51]. Gehm et al.[52] obtained film-forming polymers with viscoelastic properties by the interaction of linear polyhydroxy-compounds, modified using isocyanate (M = 750–6000), with compounds of the type:



where R and R′ = H, Cl, alkyl, aryl, etc. and A is a bivalent diamino-residue linked via N atoms to the *s*-triazine rings, for example a diamino-residue with 2–12 carbon atoms in the chain.

Polymers with high thermal stability and resistance to oxidation were obtained by heating a mixture of dihalogeno-derivatives of aromatic compounds (for example *p*-dichlorobenzene) and 2,4,6-tri-(*p*-chlorophenyl)-*s*-triazine with sulphur in the presence of alkali or alkaline earth metal carbonates, sulphides, and oxides[53]. The decrease of the weight of the resulting polymers was 3.3% after heating for 100 h at 300°C and 5.3% after 20 h at 400°C.

Polymers with the following structure were obtained by the polycondensation of formaldehyde with sulphamide or its mono- and di-alkyl-substituted derivatives (RNH–SO_2–NH–R) and melamine[54,55]:



where R = CH_3, t-C_4H_9, etc. These polymers lose 25% of their weight at temperatures up to 225°C; the N–H and N–SO_2 bonds in the polymers persist up to 225°C; the *s*-triazine ring does not break down up to 300°C.[54]

Kabaivanov and Alaminov achieved the synthesis of low-molecular-weight thermoplastic resins by the polycondensation of phenol, formaldehyde, and cyanuric acid in the presence of both acid[56] and alkaline[57] catalysts. They established that the reaction proceeds via the formation of hydroxymethyl derivatives of cyanuric acid. Articles made from the resulting Resol resins are distinguished by high thermal stability, water resistance, good mechanical strength, and incombustibility.

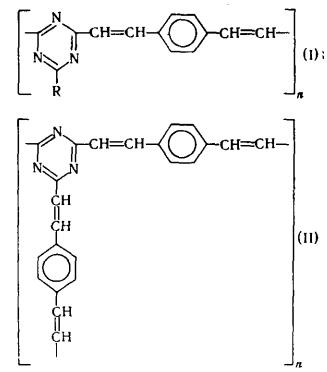
The same authors[58,59] obtained resins based on cyanuric acid, 2,2-di-(4-hydroxyphenyl)propane, and formaldehyde. The polymers were synthesised in an acid medium with different proportions of the initial components. The polycondensation reaction was investigated spectroscopically. It was shown that cyanuric acid reacts in the keto-form; at 130°C methyl ether groups are formed predominantly, rearranging at a higher temperature (170°C) to methylene bridges with liberation of formaldehyde[60].

A characteristic feature of the majority of the polytriazines discussed above is the presence in the macromolecular chain of heteroatoms (O and N) linking the *s*-triazine rings either directly with one another or via another group.

Next we shall consider studies on the synthesis and properties of polytriazines in which the *s*-triazine rings are linked via hydrocarbon groups.

Greth and coworkers[61,62] described the synthesis of polymers with a system of conjugated double bonds containing *s*-triazine rings in the chain and investigated some of their properties. The authors undertook the synthesis of these polymers on the basis of the fact that the *s*-triazine ring is an aromatic system with a high resonance energy and therefore polytriazines should have a high thermal stability.

Polycondensation of 2,4-dimethyl-6-phenyl-*s*-triazine, 2-methoxy-4,6-dimethyl-*s*-triazine, and 2,4,6-trimethyl-*s*-triazine with terephthalic dialdehyde yielded linear (I) or cross-linked (II) conjugated polytriazines[61,62]:

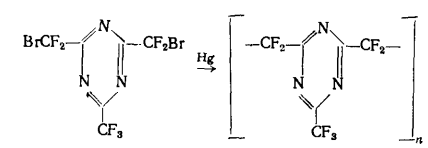


where R = C_6H_5 or OCH_3. Polymers of type (I) begin to decompose in a stream of nitrogen at 380°C (4% weight loss) and decompose vigorously at 530°C; at 730°C they lose 40% of their weight. In oxygen the polymer loses at 380°C only 4% of its weight but at 700°C its combustion is complete.

A polytriazine of type (II) loses 8% of its weight at 500°C in a stream of nitrogen, 30% at 700°C, and 40% at 875°C. The degradation of this polymer in a stream of oxygen begins, like that of polymer (I), at 380°C and at about 600°C its combustion is complete[63].

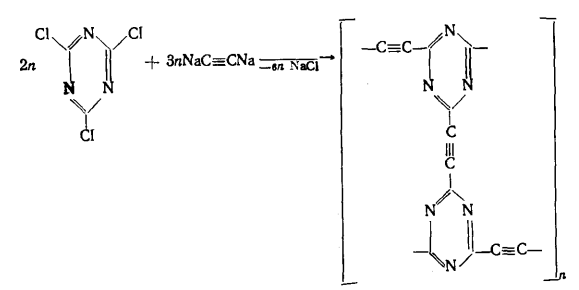
Nitriles, which are usually formed in the depolymerisation of low-molecular-weight triazines, were not detected in the degradation products of polytriazines[63].

Linear polyperfluoroalkylenetriazine polymers, which are of considerable interest as high-temperature elastomers (temperature at the onset of decomposition about 400°C, see below—pp. 72–74), were synthesised by the polycondensation of difunctional fluorinated triazine monomers containing an active halogen[64] at 250–300°C in the presence of metallic mercury. The reaction of 2,4-di(bromodifluoromethyl)-6-trifluoromethyl-*s*-triazine takes place according to the mechanism:



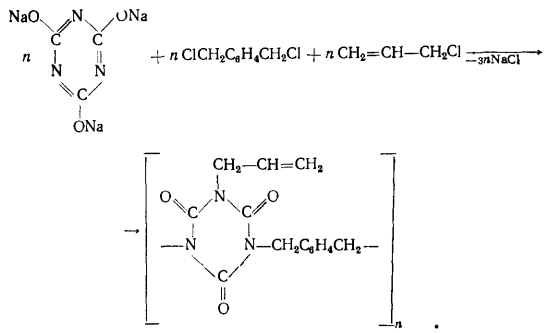
Above 40°C the resulting polymer exhibits rubber-like properties.

Paushkin et al.[65] obtained polymers by the polycondensation of cyanuric chloride with sodium carbide by the reaction



The infrared spectrum of the polymer has absorption bands in the region of 1540 and 1570 cm^{-1} which in all probability characterise the triazine rings in the polymer.

Fusible and soluble polymers with a softening temperature of about 200°C and containing isocyanurate rings in the chain were synthesised by the joint polycondensation of allyl chloride and *p*-xylylene dichloride with sodium cyanurate[66]:



2. Polymerisation of Monomers Containing the *s*-Triazine Ring

As already mentioned at the beginning of the review, one of the common methods for the introduction of the *s*-triazine ring into the polymer chain is by polymerising monomeric *s*-triazine derivatives. Depending on the functional groups in the unsaturated triazine derivatives, both linear and three-dimensional polymers may be obtained.

Data have been published both on the homopolymers of unsaturated *s*-triazine derivatives[67-76] and on their copolymers with other unsaturated compounds[68,71-73,76-90]. *s*-Triazine derivatives are as a rule introduced into copolymers to improve their thermal stability. Moreover, the presence of a large number of unsaturated functional groups in the triazine ring promotes the formation of a large number of cross-links, which also lowers the rate of thermal degradation of highly-structured polymers based on them.

One of the most widely used unsaturated monomers containing the *s*-triazine ring is triallyl cyanurate[77-88,91]. It is readily miscible with unsaturated polyesters and therefore has come to be widely used as a modifying and structure-forming agent in alkyd resins[77-85].

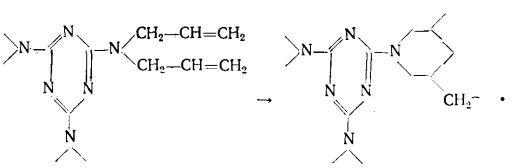
According to the data of Cohen and Cypher[86], who investigated the copolymers of poly(ethylene glycol maleate) and poly(diethylene glycol maleate) with diallyl phthalate, isophthalate, and terephthalate and with triallyl cyanurate, the thermal stability of the copolymers varies in the following sequence as a function of the monomer employed in the copolymerisation: triallyl cyanurate > diallyl terephthalate > diallyl isophthalate > diallyl phthalate. The high thermal stability of copolymers with triallyl cyanurate is due, according to the authors, to the thermal stability of the *s*-triazine ring in the initial monomer. In the same study[86] it was shown that the replacement of the allyl group in triallyl cyanurate by the ethoxy-group does not alter the thermal stability of the polymer: the methyl group decreases and the β-hydroxyethyl group sharply increases the thermal stability of the polymer. This finding was explained by the increase in the number of substituents in the monomer as a result of the side reaction involving the formation of dimeric cyanurate. Another explanation may be the involvement of the hydroxyethyl group of the monomer in the cross-linking of the polyester.

There are data on the use of triallyl cyanurate also for other purposes, for example for the preparation of transparent materials used to make lenses and other articles[87]. The products of the transesterification of triallyl cyanurate with glycols are used as plasticisers for a number of resins[87,88]. Oswald[91] stabilised halogen-containing polyolefins with cyanurates or isocyanurates. It was found that chlorinated polyethylene stabilised with 0.5–10% of triallyl cyanurate does not change over a period of 1 h at 200°C.

Linear triazine polyesters with allyl groups in the side chain were obtained by the transesterification of triallyl cyanurate with glycols in the presence of sodium methoxide as a catalyst[88]. Linear unsaturated triazine polyesters were synthesised only in the very initial stage of the reaction; when the degree of reaction is more than 0.15, polymers with three-dimensional structures are formed exclusively.

The synthesis of unsaturated polyesters by the copolymerisation of alkenyl alkyl esters of cyanuric acid with unsaturated aliphatic and alicyclic hydrocarbons in the presence of radical polymerisation initiators has been reported[79,88].

Gillham and Petropolous[67] investigated hexa-allylmelamine polymers. Piperidine rings alternating with *s*-triazine rings may be formed in the radical polymerisation of hexa-allylmelamine by the reaction



Owing to the high degree of cross-linking, these polymers have good mechanical properties and a high thermal stability. The polymers are stable up to 370°C on heating in air and up to 400°C on heating in nitrogen. Their thermal stability is higher than that of polymers based on triallyl cyanurate. Transparent plastics based on hexa-allylmelamine are stable in air up to 260°C

Oligomeric unsaturated polyesters based on hexa(hydroxymethyl)melamine, partly esterified with allyl alcohol and maleic acid, have been described[92].

There are also literature data on the modification of unsaturated polyesters by compounds based on *s*-triazine. Thus the use of cyanuric acid and its derivatives as modifying components has been described[93].

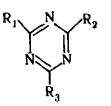
Widmer[89] described the synthesis and structure of new resins suitable for the preparation of varnishes, based on the allyl ether of hydroxymethylmelamine and its copolymers with vinyl monomers. The varnishes obtained from these resins dry rapidly and the coatings are distinguished by high hardness and resistance to solvents.

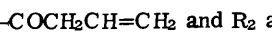
Kugel and coworkers[68] achieved the synthesis of 2,4-dimethyl-6-vinyl-*s*-triazine by the pyrolysis of the corresponding acetoxyethyldimethyl-*s*-triazine, polymerised it, and investigated the properties of the polymer. They found that the initial monomer polymerises at 20°C under the influence of free-radical initiators (benzoyl peroxide, etc.) or radiation, and readily copolymerises with styrene, methyl methacrylate, and acrylonitrile. The kinetics of its copolymerisation with styrene and methyl methacrylate have been investigated. The homopolymer softens at 105°C and readily dissolves in water and the usual organic solvents, with the exception of aliphatic hydrocarbons.

Pyrolysis of the corresponding acetoxyethyl- or acetoxyisopropyl-*s*-triazine also yielded 2,4-diethyl-6-isopropenyl-6-methyl-2,4-divinyl-, 2-butyl-4,6-divinyl-, 2,4,6-trivinyl-, 2,4-di(trichloromethyl)-6-vinyl-, 2,4-di(pentabromoethyl)-6-vinyl-, and 2,4-di(pentafluoroethyl)-6-isopropenyl-*s*-triazines[76]. They have been homopolymerised and copolymerised with alkyl acrylates, styrene, vinyltoluene, and other monomers in the presence of radical initiators. These homopolymers may be used in the manufacture of thermostable sheets and fibres.

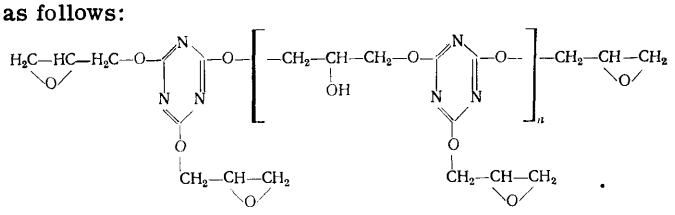
Vinyl derivatives of guanamines—2,4-diamino-6-(α-vinyloxyalkyl)-*s*-triazines[69] and acylamino-*N*-(vinyloxyalkyl)guanamines[70]—are polymerised in the presence of strong acids (H_3PO_4) or are used for polycondensation with formaldehyde. The copolymerisation of hexahydro-1,3,5-triacryloyl-*s*-triazine with styrene, vinyl acetate, methyl methacrylate, and acrylonitrile has been investigated[90]. There are various patent data on the vinyl esters, amides, and other derivatives of *s*-triazine[71-73] which form homopolymers and copolymers with vinyl monomers.

Holtschmidt[75] obtained polytriazines with a high thermal stability by radical polymerisation of compounds of the type



where R_1 =  and R_2 and R_3 = R_1, H, halogen, etc.

Poly(glycidyl cyanurates)[94-99], obtained by the reaction of cyanuric acid with epichlorohydrin or of cyanuric chloride with 2-hydroxymethyloxiran, have been described[94-99]. The initial product was triglycidyl cyanurate, which subsequently forms poly(glycidyl cyanurate) resins. The general structure of such resins can be represented as follows:



(where n = 0 - 2).

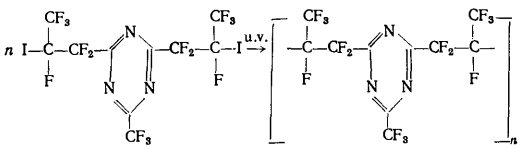
Usually poly(glycidyl cyanurate) resins contain between 0.8 and 10% of chlorine, which is evidence of an incomplete conversion of the chlorohydrin groups. In order to reduce the chlorine content, the resin is subjected to additional dehydrochlorination with a solution of alkali, which makes it possible to increase the number of epoxy-groups. Poly(glycidyl cyanurate) resins, hardened with the usual hardening agents employed for epoxy-resins, have a higher thermal stability and lower dielectric losses at high temperatures than ED-6 epoxy-resin.

Apart from the polymers of triglycidyl cyanurate, the polymers of other epoxy-derivatives of *s*-triazine have been described[100-104].

Three-dimensional polymers insoluble in organic solvents are obtained by heating a mixture of cyanuric acid with the di-isocyanate esters $R(NCO)_2$, $R-PO-(NCO)_2$, or $R-P(NCO)_2$, where R is an aliphatic or aromatic group. The reaction is carried out in the presence of an excess of cyanuric acid. The polymers are stable up to temperatures in excess of 300°C.[105]

Nakamura and coworkers[37-39] described a method for the preparation of novolaks containing *s*-triazine rings with unsaturated side groups: 2,4-diallylamino-6-chloro-*s*-triazine was allowed to react with phenol, t-butylphenol, and novolak. Polycondensation in the presence of alkali at 100–105°C yielded unsaturated products with different molecular weights and different numbers of functional groups. Such polymers may be hardened with radical-polymerisation initiators or may be structured with methyl methacrylate and styrene.

Griffin[64] investigated the possibility of using the polyrecombination reaction for the synthesis of polyfluoroalkyltriazine polymers. In particular, these polymers are formed by the following mechanism when di(iodoperfluoroalkyl)-*s*-triazines are exposed to ultraviolet light:



Thermostable elastomers were obtained in this way. However, owing to the high cost of the monomers, this method of preparing fluorinated triazine elastomers cannot as yet compete with other syntheses of these polymers (see below—pp. 72–74).

III. POLYTRIAZINES OBTAINED BY POLYCYCLOCONDENSATION AND POLYCYCLOTRIMERISATION REACTIONS

In contrast to the methods of preparation of polytriazines described above, where the *s*-triazine ring was introduced with the initial monomers, this section deals with the formation of the *s*-triazine ring in the course of the synthesis of the polymer. Since in this case polytriazines (and also other polymers) may be formed by polycondensation or polymerisation reactions in which three functional groups of the initial monomers must be involved at once, these reactions have been called, following the suggestion of V. V. Korshak, polycycloconden-sation and polycyclotrimerisation respectively.

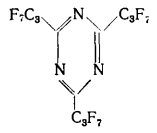
The synthesis of polytriazines (as well as other polymers) by these two methods has been widely used only in recent years. However, the high promise of these syntheses is already evident.

The advantages of the synthesis of polymers by polycondensation and particularly by polycyclotrimerisation include the possibility of the specific synthesis of both highly structured polymers, the rings of which are separated by various bridging groups, and linear polymers. The polycondensation or polymerisation may be interrupted at the oligomer stage, the oligomers being processed by the usual methods.

1. Polycyclocondensation of Nitrile Derivatives

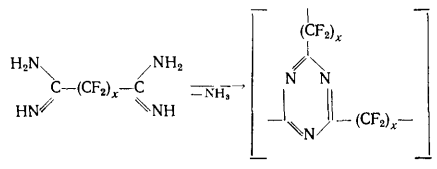
As already stated above, the polycyclocondensation reaction has only comparatively recently come to be widely employed for the synthesis of polytriazine polymers. This method of polycondensation became particularly interesting in connection with Brown's discovery of the class of polyperfluoroalkylenetriazine elastomers with high thermal stability and physicomechanical parameters[106-108].

Fluorocarbon elastomers are known to be stable for a long time at temperatures not exceeding 300°C. At the same time the exceptionally high resistance of perfluoroalkyltriazines with the structure[109]

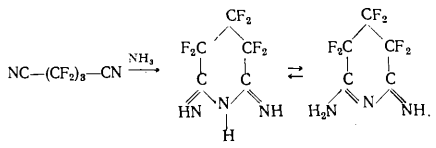


to thermal oxidation suggested that the problem of increasing the thermal stability of fluoro-polymers may be solved by introducing *s*-triazine rings into their structure. Perfluoroalkylenetriazine polymers, which combine a high thermal stability (about 400°C), exceeding the thermal stability of fluorocarbon elastomers by about 100 deg, with resistance to strong oxidising agents and radiation, constitute such a system[64,106-108,110-122].

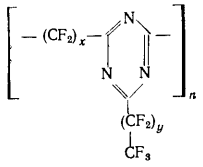
Cross-linked polymeric products containing repeating units of the above type were obtained by the thermal cyclisation of perfluoroalkylenediamidines[108]. The polycondensation of the starting materials takes place with the evolution of ammonia according to the following mechanism:



The initial diamidines were obtained by the action of ammonia on perfluoroalkyldinitriles. Perfluoroglutaronitrile yields a cyclic product—perfluoroglutaroimidine:



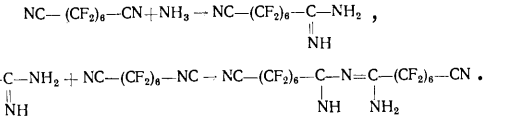
The polycondensation is usually carried out in the melt, solid infusible polymers being formed. Polymers with the following structures have been obtained from a mixture of mono- and di-functional reactants:



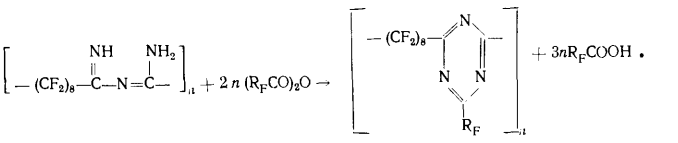
The physicomechanical properties of the cross-linked polymers of this structure depend greatly on the proportions of the initial reactants, i.e. both rubber-like materials with low strength and rigid non-elastic polymers may be obtained. The tensile strengths of these polymers vary as a rule in the range 7–35 kgf cm^{-2} with an elongation on rupture of about 100%.[108,115]

Cross-linked polyperfluoroalkylenetriazine polymers have a high thermal stability; they remain stable on heating to 420°C.[108,115] The polymers are also resistant to the action of hydrocarbon fuel and other liquid media employed in aviation up to a temperature of about 370°C; promising results have been obtained as regards their resistance to radiation[64].

It has been suggested that the development of methods for the synthesis of linear non-cross-linked triazine polymers will yield materials with improved physicomechanical properties. For this purpose, a study was made of the possible synthesis of polymers by the direct action of ammonia on the dinitrile, omitting the stages involving the synthesis and isolation of the diamidine[113]:



Together with the monocyanoamidine, a diamidine can also be formed as an intermediate. The low-molecular-weight products formed in the second stage of the reaction may be more numerous than shown in the above scheme. However, it is important that the polymerisation reaction in the presence of ammonia may be divided into two consecutive stages—the addition of ammonia to the nitrile with formation of the amidine and the addition of the latter to the nitrile in the growing chain of the imidoylamidine polymer. By adding a solution of the imidoylamidine polymer to the anhydride of a perfluoroalkanecarboxylic acid, a triazine polymer is obtained by the following mechanism:

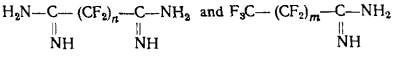


Best results were achieved when the anhydrides of trifluoroacetic, perfluorobutyric, and perfluorocaprylic acids were employed[113]. The resulting high-molecular-weight perfluorotriazine polymers were rubber-like materials soluble in ethyl perfluorobutyrate, ethyl acetate, and di(trifluoromethyl)benzene. The glass temperatures of the polymers varied in the range between −17° and −5°C. Rapid degradation began at 420°C.

Graham[119] obtained from the triazine elastomers vulcanised materials with a high strength and thermal stability up to 315°C. The polyimidoylamidine necessary for the synthesis of the elastomers was obtained by the copolymerisation of the dinitrile and diamidine of perfluorosebacic acid.

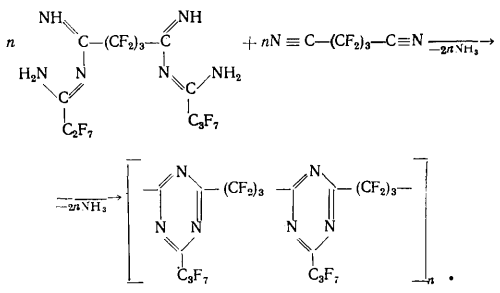
When this polymer reacted with an excess of perfluorobutyric acid anhydride, with an excess of a mixture of perfluorobutyric acid anhydride and cyanoperfluorobutyryl chloride, or a mixture of the anhydride of perfluoroacetic acid and cyanoperfluorobutyryl chloride, triazine elastomers, containing perfluoroalkyl side groups, were synthesised. The vulcanised triazine polymers are resistant to the action of strong acids but are decomposed by strong bases. The mechanical strength of these vulcanised materials, determined at an elevated temperature or after thermal ageing, is close to that of fluorocarbon vulcanisate but, in contrast to the latter, these materials remain flexible at 300° and 370°C.

Polymers with high thermal stability and satisfactory dielectric properties were obtained by the joint polycondensation of the monomers

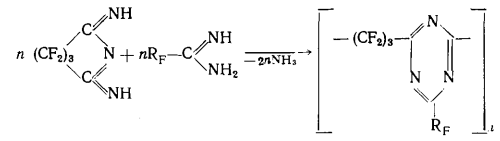


where $n = 2-4$ and $m = 2-3$, followed by vulcanisation with *p*-phenylenediamine, benzidine, triethylenetetramine, and other compounds[116].

In order to synthesise linear polyperfluoroalkylenetriazine polymers with a linear structure, a study was also made[64] of the reaction between di(perfluorobutylimidoyl)-perfluoroglutaroamidine and the dinitrile of glutaric acid:



Fedotova and Dolgopol'skii obtained polymers based on C_2–C_7 perfluoroalkylamidines and perfluoroglutaroimidines according to the mechanism



where R_F = CF_3, C_2F_5, C_3F_7, C_4F_9, or C_6F_{13}, in an attempt to elucidate the effect of the size of the perfluoroalkyl group of the monoamidine on the joint polycondensation and properties of the perfluoroalkylenetriazine polymers[120].

The principle of the method of synthesis of linear perfluoroalkylenetriazine polymers, proposed by Brown[107,108,121], is based on the joint polycondensation of mono- and di-functional perfluoroamidines. Monoamidines suppress to a considerable degree the structure-formation process but nevertheless they do not eliminate it owing to the considerable difference between the reactivities of mono- and di-functional monomers. Fedotova and Dolgopol'skii[120] showed that, starting with the C_4 amidine, the size of the perfluoroalkyl substituents has almost no influence on the properties of the polymers and the conditions of their synthesis. Moreover it was established that low-molecular-weight polymers with $[\eta]$ = 0.04–0.07 dl g^{-1}, obtained with the molar ratio monoamidine : diamidine = (1.6–1.8) : 1, are cross-linked by perfluoroglutaroimidine with formation of insoluble high-molecular-weight polymers thermostable up to 400–420°C.

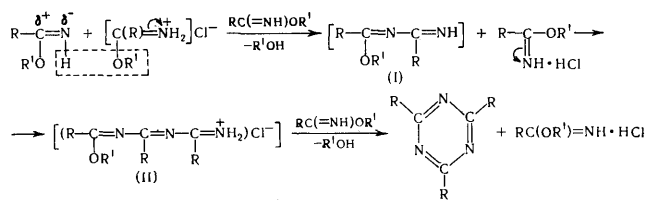
The polycondensation of pentafluorobenzamidine with perfluorophthalodiamidine has been described[114].

Kardash et al.[118] investigated the thermal degradation at 400–500°C of polyperfluorotriazine polymers, obtained by the copolycondensation of the diamidine of perfluorosebacic acid with perfluorobutyramidine and of perfluoroglutarodiamidine with perfluoroacetamidine. The thermal stabilities of these polymers were compared with that of polytetrafluoroethylene and it was shown that the introduction of *s*-triazine rings into the fluoromethylene chains enhances their thermal stability. However, this effect decreases to some extent in polyperfluorotriazines owing to the presence of amide groups, which increase the initial rate of degradation of the polymers. The formation of amide groups in such polymers is possible both in the synthesis of the polymers itself and during their storage, since perfluoroalkyl derivatives of *s*-triazine are hydrolysed on prolonged storage in air. The presence of amide groups in the polymers was confirmed by infrared spectroscopy (showing the C=O absorption band at 1735 cm^{-1} and the absorption bands at 3430, 3160, and 1680 cm^{-1}, which are characteristic of the NH_2 group in amides). The principal gaseous degradation product of polyperfluorotriazines is tetrafluoroethylene. In addition, hexafluoropropene, carbon dioxide, and silicon tetrafluoride, formed evidently when the CF_3 radicals react with the glass of the reaction vessel, have been identified. The liquid degradation products are low-molecular-weight analogues of polyperfluorotriazines. The water formed on decomposition of the amide groups hydrolyses the *s*-triazine rings and the radicals induce their polymerisation with formation of the azomethine structure $[-\underset{\displaystyle R}{\underset{|}{C}}=N-]_n$, as in the polymerisation of 2,4,6-tri(trifluoromethyl)-*s*-triazine under the influence of radicals[109]. On the other hand, in the absence of radical sources, 2,4,6-tri(trifluoromethyl)-*s*-triazine is stable up to 500°C.[109]

Polyperfluoroalkylenetriazine elastomers are regarded as promising raw materials for the preparation of fuel tanks, electrical insulation, and rubber components of hydraulic systems operating at temperatures in the range 300–400°C.[64]

The application of perfluorinated triazine rubbers in aviation and space engineering has been described[117]. It has been stated that elastomers based on *s*-triazine, with the triazine groups linked by perfluoroalkyl units, are processed by the usual methods using standard equipment[110].

Yakubovich and coworkers[123-128] obtained polytriazines with aliphatic, aromatic, and perfluorinated aliphatic bridges between the *s*-triazine rings by the polycyclotricondensation of the corresponding iminoethers. They employed the diethyl and dimethyl esters of bisiminoadipic, bisiminoterephthalic, bisiminoperfluoroglutaric, and bisiminoperfluoroadipic acids as the starting materials for the preparation of polytriazines. Non-fluorinated iminoethers are readily cyclised in the presence of catalytic amounts of their hydrochlorides, while the fluorinated analogues react also in the absence of catalysts. Yakubovich et al.[125] believe that the condensation of iminoether groups to the *s*-triazine rings proceeds via a series of consecutive stages leading to the formation of a linear "dimer" (I) and "trimer" (II). The resulting hydrochloride of the linear "trimer" (II) cyclises to the more stable *s*-triazine system according to the mechanism[129]

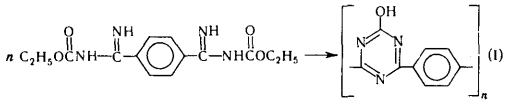


One may suppose that the electrophilicity of the carbon atom in iminoethers is insufficient to ensure the addition of a second iminoether molecule at the C=N double bond and the free bases of the iminoethers are not cyclised. When the reaction mixture contains the hydrochloride of the iminoether, in which the electrophilicity of the carbonyl carbon atom is higher than in the iminoether itself owing to the appearance of a positive charge at the nitrogen atom (the 'onium nitrogen) in $C{=}\overset{+}{N}H_2Cl$ and the associated considerable shift of the π-electron pair of the double bond, the reactivity of the system increases.

The replacement of hydrogen atoms by fluorine in the alkyl group of bisiminoethers increases the electrophilicity of the carbonyl carbon atom so much that condensation with the initial formation of the "dimer" and then of triazine derivatives occurs even in the absence of a catalyst[128].

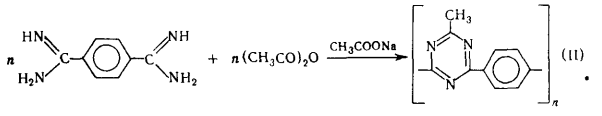
As mentioned above, for the formation of linear triazine polymers it is necessary that in the synthesis of the *s*-triazine ring one position in the latter should be occupied by a stable side group and the remaining two should participate in the formation of the polymer chain.

On this basis, Greth and Elias[61,63,130] obtained linear polytriazines by the thermal decomposition of the diethyl ester of terephthalamidine-*NN*-dicarboxylic acid:



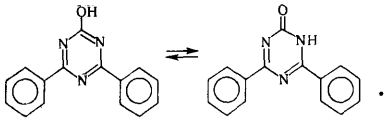
(I)

and by the interaction of terephthalamidine with acetic anhydride:



(II).

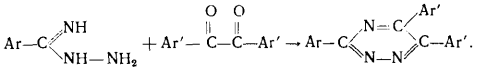
The structure of the resulting polymers was demonstrated chemically and by infrared spectroscopy (absorption bands characteristic of the *s*-triazine ring at 1540, 1450, and 1360–1390 cm^{-1}). An intense absorption band in the region of 1660 cm^{-1}, showing that these compounds may be present in the tautomeric keto-form, was observed in the spectra of poly-2-hydroxy-4,6-diphenyl-*s*-triazines:



Contrary to the authors' expectations, polytriazines obtained in this way had a much lower thermal stability than polymers synthesised by the same workers from methyltriazines and terephthalic dialdehyde[63], which were described above (see Section I, p. 70).

The temperature of the onset of decomposition in nitrogen of type (I) polymers is in the range 250–300°C. They lose 65% of their weight at 500°C and 85% at 850°C. The thermal decomposition of type (II) polymers takes place in two stages: in the first stage the decrease in weight is 12% between 200° and 325°C and in the second stage the polymer loses 50% of its weight on subsequent heating to 800°C.

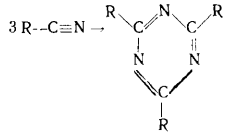
In recent years a large number of polymers with symmetrical triazine rings were synthesised and investigated; polymers containing asymmetric triazine rings were unknown until recently. A recent communication[131,132] reported the synthesis of model compounds containing asymmetric triazine rings from hydrazidines and α-diketones:



Hergenrother[133] employed this reaction to synthesise high-molecular-weight soluble poly-*as*-triazines. When 2,6-pyridinediyldihydrazidine was allowed to react with *pp'*-oxybis(phenyleneglyoxal hydrate) and *pp'*-oxydibenzil, poly[3,3'-(2'',6''-pyridinediyl)-5,5-(*pp'*-oxydiphenylene)di-(*as*-triazine)] (PT) and poly[3,3'-(2'',6''-pyridinediyl)-5,5'-(*pp'*-oxydiphenylene)di-(6-phenyl-*as*-triazine)] (PTP) were obtained. The polycondensation was carried out in *m*-cresol solution at 200°C. The resulting polymer solutions were employed without additional purification to prepare sheets, coatings, adhesives, etc. ($\eta_{log} = 0.5 = 1.25$ dl g^{-1}). The softening temperatures of the polymers were in the range 300–340°C, while according to thermogravimetric data PT and PTP exhibit the same resistance to thermal and thermo-oxidative degradation—the thermograms have a single inflection at 400°C in air and at 450°C in helium. The polymer specimens heated at 316°C for 200 h lost between 3 and 8% of their weight.

2. Polycyclotrimerisation of Monomers Containing C–N Groups

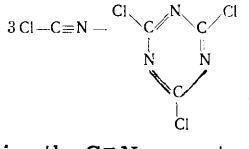
The capacity of nitriles for polymerisation with formation of triazines (the cyclotrimerisation reaction of nitriles) via the mechanism



was already known in the previous century[134,135].

Numerous subsequent studies established that the cyclotrimerisation reaction is more readily undergone by nitriles with electronegative substituents in the α-position relative to the nitrile group. Electronegative substituents in the α-position give rise to a comparatively low electron density at the carbon atom of the nitrile group and hence an enhanced electrophilic reactivity of such nitriles[136–138].

Thus chlorocyanogen is readily cyclotrimerised in the presence of various catalysts with formation of cyanuric chloride[137,139,140]:

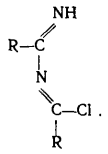


Compounds containing the C≡N group tend to form a stable cyclic trimer because trimerisation involves the loss of the enthalpy of the π bond and in addition the cyclic trimer is stabilised because of the combination of the most favourable valence angles (about 120°)[15,141] with the planar structure of the ring[15,141,142], which allows the formation of a $p\pi-p\pi$ aromatic system. The high stability of the ring in *s*-triazine is shown by the fact that many *s*-triazine derivatives do not polymerise at temperatures up to 500°C.[41]

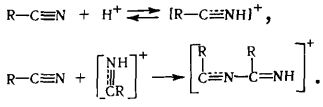
The cyclotrimerisation of nitriles may be accelerated by many catalysts. Thus the halides of coordination-unsaturated metals are active catalysts of this reaction. The presence in the C≡N: group of nitriles of a lone electron pair and also of electron-donating π bonds promotes the addition of Lewis acids to the electron pair of the nitrogen with the formation of highly electrophilic molecular compounds. Probably the addition to the nitrile of more than one equivalent of the electrophilic compound is due to the formation of the so called π-complexes[143].

Grundman et al.,[144] who investigated the mechanism of the synthesis of *s*-triazines from nitriles in the presence of hydrogen halides, showed that a compound of the nitrile

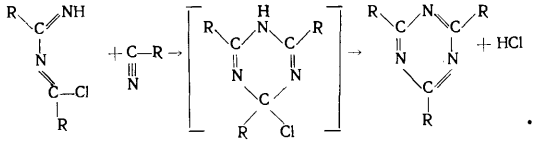
with the hydrogen halide of the type of a substituted imino-chloride,



is formed as an intermediate in this reaction. The formation of the substituted imino-chloride may be regarded as a nucleophilic reaction of the nitrile group, where the electrophilic agent is the same nitrile:

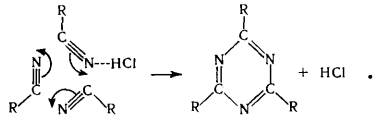


The reaction of the imino-chloride with a third nitrile molecule takes place similarly. Grundman[144] regards the interaction of imino-chlorides with nitriles as diene synthesis reactions:



However, the treatment of the adduct $2CCl_3CN.HCl$ with acetonitrile does not yield the expected *s*-triazine, although the joint cyclotrimerisation of trichloroacetonitrile with acetonitrile in the presence of hydrogen chloride leads to the formation of the corresponding di(trichloromethyl)methyl-*s*-triazine[144].

Zil'berman[138], who considered the cyclotrimerisation of nitriles, proposed a different mechanism for the formation of *s*-triazine. He believes that the reason for the comparative ease of formation of *s*-triazines may be cyclic electron transfer via the mechanism



Both the free nitrile and its complex with hydrogen halide are involved in the formation of triazines by this mechanism.

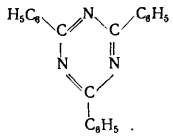
Hydrogen halides are most often employed as agents inducing the cyclotrimerisation of nitriles[136] but alkaline and acid agents, such as sulphuric and chlorosulphonic acids, Lewis acid, etc. can also serve as catalysts[136,145].

The cyclotrimerisation of benzonitrile in the presence of acid agents with formation of triphenyl-*s*-triazine (cyaphenine) has been known for a very long time[134,146-148].

Recently Kargin, Kabanov, and coworkers[149-154] carried out a number of studies on the polymerisation of nitriles via the C≡N bond in order to obtain conjugated azomethine structures. With benzonitrile as an example, they investigated the mechanism of the formation of both linear polyconjugated structures and of a cyclic trimer (triphenyltriazine).

Although the aim of these studies was not to obtain polytriazine structures, nevertheless they are of undoubted interest for the elucidation of the formation of polymers by polycyclotrimerisation and therefore some of them must be considered in this review.

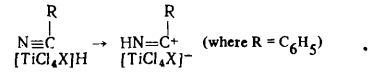
The mechanism and kinetics of the polymerisation of benzonitrile complexes in the presence of compounds such as titanium tetrachloride, zinc chloride and boron trifluoride have been investigated[150]. It has been found that, when benzonitrile complexes are heated, two types of products are formed. One of them is a polymer with an azomethine structure, $[-C(C_6H_5)=N-]_n$, and the other is a benzonitrile trimer (cyaphenine):



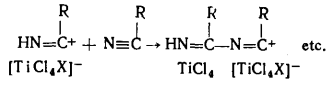
It was established that the rate of reaction and the ratio of the products formed are significantly influenced by small amounts of promoting agents such as proton-containing substances (inorganic acids, water, amides, organic acids) and organic compounds with mobile halogen atoms, for example benzoyl chloride, benzyl chloride, etc.

When the complex of benzonitrile with BF_3 is heated for 10 h at 250°, 275°, and 300°C, only the trimer with traces of a polymer is formed. The same result was obtained with the benzonitrile complex of zinc chloride. If, on the other hand, a proton initiator (HPO_3) is introduced into the reaction mixture, a polymer is formed in both cases[150].

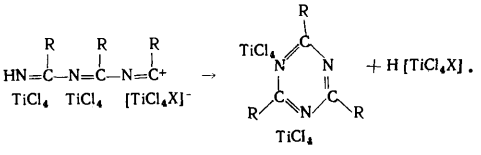
When the pure complex $(C_6H_5CN)_2.TiCl_4$ is heated in the presence of metaphosphoric acid below 300°C, the reaction proceeds at an appreciable rate, but the sole reaction product is triphenyl-*s*-triazine. At a higher temperature, a polymer is formed[153]. On the other hand, when an organic promoting agent (benzoyl chloride) is added to the system, a polymer is formed at an appreciable rate even at 270°C. The authors explain these results as follows. The centre for chain initiation is the complex $[TiCl_4X]H$ formed when the complex-forming agent reacts with the proton-containing additive:



Chain propagation takes place as follows:

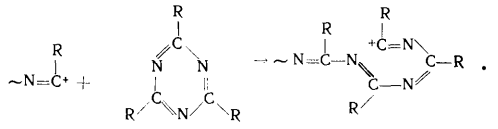


The formation and accumulation of the trimer in the initial stages of reaction can be explained by the fact that, after the addition of the third monomer molecule, there is a possibility of the formation, in addition to chain propagation, of a stable six-membered ring with regeneration of the initial initiating proton complex:



The consumption of the trimer can be accounted for by its polymerisation at an elevated temperature with the

opening of the triazine ring under the influence of the carbonium ion of the growing linear chain, which in fact leads to the formation of a polynitrile chain:

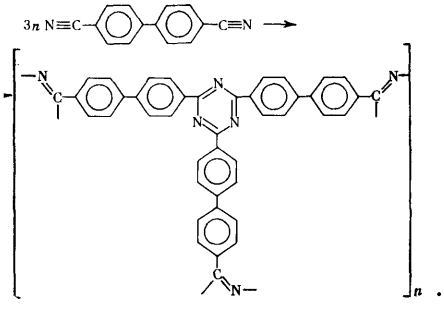


In order to test the hypothesis of the involvement of the trimer in the reaction, a study was made of the possibility of its polymerisation as a complex with $TiCl_4$, which would indeed result in a polymer with an azomethine structure.

The difference between the effects of proton-containing acids (HX) and aprotic organic acids (RX) on the linear polymerisation of benzonitrile consists in the fact that the aprotic acids are in this case more powerful promoting agents. This may be due to the higher rate of ring opening following the attack by the R^+ ion, which is a more powerful electrophilic agent than the proton[155], and to the decrease of the possibility of the cyclisation of the linear trimer when RX is employed.

Free-radical polymerisation of triazine rings is known to occur in the presence of a source of either free radicals or complex-forming agents[156]. The nature of the substituents in triazines then has a significant influence on the stability of the ring. Thus triazines with electronegative substituents (CCl_3, CF_3, and C_3F_7) form a polyene chain with conjugated double bonds $[-\underset{\displaystyle R}{\underset{|}{C}}=N-]_x$ in the presence of a source of free radicals at 250–300°C, while triazines with electropositive substituents (CH_3, C_2H_5) are polymerised only at 520°C.[156]

The cyclotrimerisation of nitriles with the aim of synthesising polytriazines was achieved for the first time by Anderson and Holovka[44], who obtained thermostable polymers with triazine rings from aromatic dinitriles under the influence of chlorosulphonic acid:

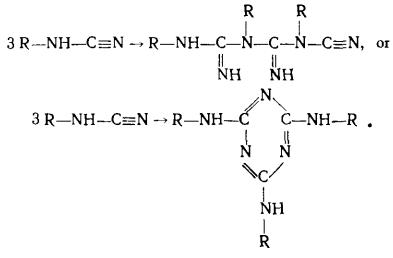


The polycyclotrimerisation of, for example, 4,4′-dicyanobiphenyl was continued until the characteristic absorption band of the C≡N bond disappeared from the infrared spectra of the polymer. In order to confirm the structure of the polymer obtained from 4,4′-dicyanobiphenyl, it was hydrolysed in the presence of concentrated hydrochloric acid and biphenyl-4,4′-dicarboxylic acid was identified. According to thermogravimetric data, the polymer synthesised exhibits a high thermal stability up to 350–400°C.

For comparison, Anderson and Holovka[44] synthesised a number of aromatic melamine polymers by the polycondensation of cyanuric chloride with aromatic diamines. All the polymers showed a high thermal stability (up to 400°C) and the polymer based on ring-fluorinated aromatic diamines was stable up to 500°C.

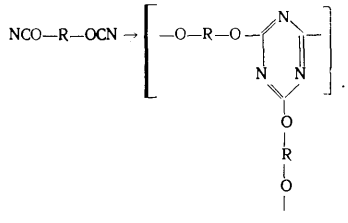
The polymerisation of 2,4,6-tricyano-*s*-triazines, which may result in the formation of both polyazomethine and polytriazine structures, has been reported[157]. These polymers, which have semiconducting properties and are used to manufacture thermistors, are obtained by heating a mixture of 2,4,6-tricyano-*s*-triazine in an excess of quinoline at the boiling point of the latter.

Sugino et al.[158–163] obtained polymers from alkylenedicyanamides with the general formula $N\equiv C-NH-(CH_2)_m-NH-C\equiv N$, where m = 4–10. Compared with nitriles having a similar structure, the C≡N groups of cyanamides are much more reactive, which may be due to the higher electrophilicity of the carbon atoms in this group. Alkylenedicyanamides are readily polymerised below 100°C and slowly at room temperature with formation of infusible and insoluble polymers. The authors believe that the polymers obtained may have the structure of polydicyanodiamides or polymelamine, which may be represented as follows for monocyanamide as an example:



Cyanamide polymers may be used to prepare ion-exchange resins, transparent plastics, coatings, and also adhesives for glass, metals, ceramics, and wood[159–163]. The strength of the joint produced by sticking together glass with these polymers is 400 kgf cm^{-2}.[162,163]

Grigat et al.[164,165] obtained cross-linked poly(aryl cyanurates) by the polycyclotrimerisation of various dicyanate esters of bisphenols via the mechanism

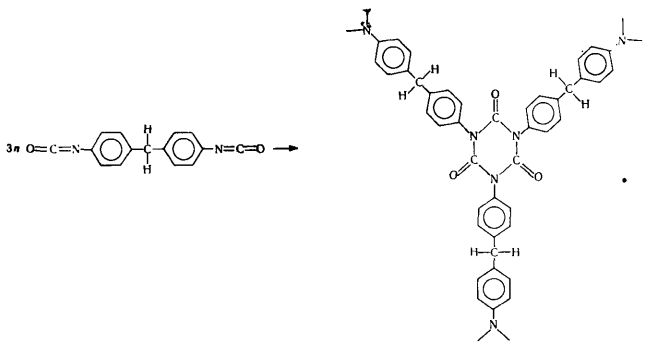


The starting materials employed were the dicyanate esters of resorcinol, quinol, 2,2-di-(4-hydroxyphenyl)propane, and 2-nitroresorcinol. The resulting cross-linked poly(aryl cyanurates) had fairly satisfactory physicomechanical properties [specific impact strength about 20 kgf m cm^{-2}, ultimate bending strength 1300–1800 kgf cm^{-2}, thermal stability (after Martens) up to 212–240°C].

The polycyclotrimerisation process was carried out in several stages. In the initial polymerisation stages fusible and soluble pre-polymers were obtained, and were converted into an infusible and insoluble state on heating to 200–250°C.

The presence of stable aromatic systems between oxygen atoms (–R–) in similar structures promotes the synthesis of polymers with even higher heat resistance and thermal stability[166].

Ball et al.[167] described the results of technical tests on a rigid isocyanurate foam plastic, which they obtained by the cyclotrimerisation of di(isocyanatophenyl)methane:



The cyclotrimerisation reaction was regulated by basic catalysts. The temperature of the onset of decomposition of the isocyanurate foam plastic is in the region of 300°C according to thermogravimetric analysis in air. The isocyanurate foam plastic exhibits a higher fire resistance than the usual urethane foam plastics, due to the formation on its surface under the influence of flames of a carbonaceous fibrillar network, reproducing the initial structure of the foam. The isocyanurate charcoal formed breaks down very slowly even at 1200°C.

The kinetics of the cyclotrimerisation of di-isocyanates were investigated by Petrov et al.[168] using infrared spectroscopy. They studied the "pre-polymer" obtained by the reaction of one mole of low-molecular-weight polybutadiene (M = 4000) containing terminal OH groups with two moles of 2,4-tolylene di-isocyanate. The catalyst components were glycidyl phenyl ether and benzyldimethylamine in different molar proportions.

The authors showed that the cyclotrimerisation of isocyanate groups is a quasi-unimolecular reaction up to a conversion of 70–90%. The rate of cyclotrimerisation is directly proportional to the product of the initial concentrations of the tertiary amine and the epoxy-derivative of the olefin.

It has been suggested that the cyclotrimerisation reaction is a special case of anionic polymerisation[168].

The results obtained were explained by Beitchman's stepwise mechanism[169], according to which the addition of the first, second, and third isocyanate molecules (M) to the catalytic complex (N) takes place in the same manner:

$$N + M \xrightarrow{k} NM,$$

$$NM + M \xrightarrow{k} NM_2,$$

$$NM_2 + M \xrightarrow{k} M_3 + N.$$

However, it was noted that, although according to Beitchman's mechanism the closure of the isocyanate rings with elimination of the catalyst is most likely in the trimer stage, other reactions are possible in principle, for example the partial formation of the dimer or of a linear polymer.

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The s-triazine ring, which has aromatic properties, exhibits high thermal stability, approaching that of the benzene ring[41,170]. Therefore, when polytriazines contain fairly thermostable groups (phenyl groups, fluorinated aliphatic chains, etc.) binding and surrounding the s-triazine rings, the polymers show enhanced thermal stability.

The ready availability of the starting materials for the synthesis of the majority of polytriazines and also the versatility of the synthetic reactions (particularly the use of polycyclotrimerisation and polycyclocondensation reactions) have promoted a large-scale practical application of these polymers in the newest branches of engineering, where materials with enhanced thermal stability and heat resistance are required. Polytriazines are used as thermostable elastomers, as binders for reinforced plastic, adhesives, coatings resistant to ultraviolet irradiation, etc.

During the preparation of the manuscript for the press, a number of interesting studies on the synthesis and properties of polymers containing s-triazine rings were published.

Polycondensation of monomeric s-triazine derivatives yielded polyesters[171-179], polyamides[180-183], and other polymers of different classes[184-192]. The thermal degradation of certain polymers containing triazine rings in the chain was investigated[193-197].

New data were published on the synthesis and properties of triazine polymers synthesised by the polymerisation of unsaturated side groups[198-209] and polymers obtained by the migration copolymerisation[210-217] of s-triazine derivatives.

Interesting results are reported in studies published recently on the polycondensation of nitrile derivatives[218-228].

A number of studies have been made on the linear polymerisation of nitriles[229-232] and the polymerisation of s-triazine rings with formation of polymers having the azomethine structure.

New results have also been obtained in the study of the polycyclotrimerisation of nitriles of different structures[235-239], cyanate esters[240-242], and isocyanates[243-250].

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Contemporary State of the Problem of the Polymerisation and Copolymerisation of Alkene Sulphides [Epithioalkanes]

L.A.Korotneva and G.P.Belonovskaya

Studies of the polymerisation and copolymerisation of alkene sulphides, including those published in 1971, are reviewed. The literature is classified according to the nature of the action of the catalytic systems—polymerisation under the influence of anionic and cationic excitants, modified organometallic compounds, and charge-transfer complexes. A separate chapter gives the results of studies on the copolymerisation of thio-oxides. 176 references.

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I. INTRODUCTION

The polymerisation and copolymerisation of cyclic sulphides (alkene sulphides, thio-oxides, episulphides, thiirans, thioethanes) has only recently attracted the attention of investigators, but every year the number of papers dealing with these problems increases. The problem is of interest both theoretically as regards the formation of polymers by the opening of heterocycles, and also from the standpoint of the practical use of a new class of polymers which contain monosulphide bonds in the main chain. Unlike their oxygen analogues—the cyclic oxides, the polymerisation of which has been studied in sufficient detail and many polymer compositions based on which have found wide practical application—information about the polymerisation and copolymerisation of cyclic sulphides, and also the physicochemical properties of the polymers formed has been unsystematic until recently and in several instances only qualitative.

Nevertheless, the available published information shows that the formation of a polymeric chain in opening cyclic thio-oxides is quite unique and the crystalline and rubbery polymers and copolymers which are formed exhibit a series of valuable working properties, above all increased radiation resistance, high adhesion and dielectric properties, specific in relation to various solvents, increased resistance to oxidants, etc.

A feature of the behaviour of cyclic sulphides, and in particular of thiirans, in nucleophilic and electrophilic reactions, which appears in ionic polymerisation, is connected with the specific structure of their molecules, examined in detail in several contemporary reviews[1-5]. In this connection we thought it undesirable in the present review to state the physicochemical properties of the cyclic sulphides and compare them with the properties of other small heterocyclic compounds.

II. POLYMERISATION OF ALKENE SULPHIDES

Over a long period of time the existence of thiirans was demonstrated only on a basis of a study of the structure and composition of the polymeric products formed in attempts to synthesise them by various methods[6,7]. The ease of opening of the ring of the α-thio-oxide to form polymeric compounds led Grishkevich-Trofimovskii[7] to conclude that they could not exist in the free state. Later Délépin, who was the first to succeed in synthesising and isolating the simplest α-thio-oxides in the pure state, showed their extreme ability to polymerise under the influence of various agents.

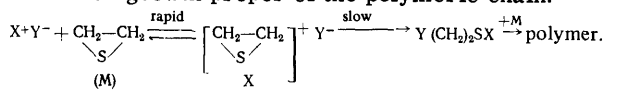
After the development of simple universal methods of synthesising the thiirans from oxides[12], and cyclic carbonates[13,14] interest in this class of compound increased greatly and in addition to the investigation of the physicochemical properties of the thio-oxides papers also appeared on the study of their polymerisation—mainly the simplest and most accessible thiirans—ethylene sulphide [thiiran or epithioethane (Ed. of Translation)] and propene-sulphide [1,2-epithiopropane (Ed. of Translation)]—which are relatively stable when pure at low temperature[4].

An attempt to polymerise thiirans under the influence of radical type initiators did not give positive results[15,16]; only for perfluorinated α-thio-oxides was the possibility of polymerisation under the influence of free radicals demonstrated, brought about by the breaking of a C–S bond[17]. The first papers dealing with the study of the ionic polymerisation of thiirans appeared in 1954, but systematic investigations in this field began to appear in the sixties. The Table gives information about the polymerisation of alkene sulphides in the presence of various catalytic systems. The most interesting investigations dealing with the polymerisation of the thio-oxides can be classified into four main groups according to the type of catalytic system used: polymerisation under the influence of anionic inducers, modified organometallic compounds, cationic inducers, and charge-transfer complexes. A separate section gives the principal results of work on the copolymerisation of alkene sulphides.

This classification is extremely provisional because in the variety of initiating systems often within the framework of qualitative observations it is difficult to draw a boundary between the individual groups of inducers according to the mechanism of their action. Thus, for the α-oxides[86] and α-thio-oxides[87-89] it is known that the $Zn(C_2H_5)_2-H_2O$ system can be cationic or coordination-anionic, depending upon the ratio of the components and in excitation polymerisation but in the induction polymerisation of propene sulphide with a charge-transfer complex the nature of the initiation and growth processes of the polymeric chain are different.

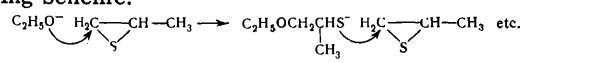
1. Polymerisation of Alkene Sulphides under the Influence of Inducers of the Anionic Type

The polymerisation of alkene sulphides in the presence of Lewis bases can be represented as a succession of reactions: (1) the addition of a molecule of the monomer to the inducer with the formation of an active centre, and (2) the successive addition of the monomer to the mercaptide formed—growth proper of the polymeric chain:



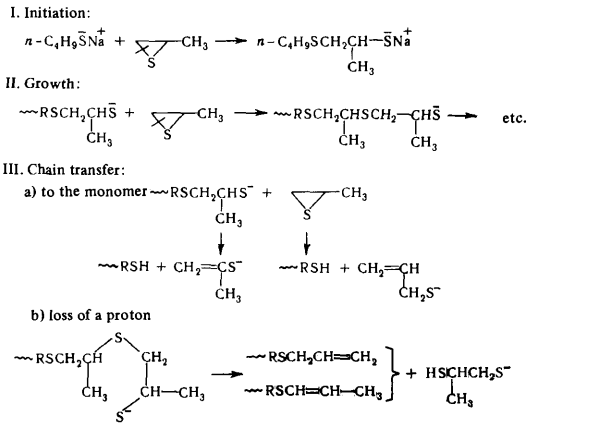
Reactions of this type are close to the break-free polymerisation of monomers of the vinyl series. The principle of the polymerisation of α-thio-oxides which corresponds to ideas about the "living" polymers, was described in a series of papers [16,22,23,38–42,57,70,74,90].

Marvell and Weil [34] obtained low-molecular-weight polypropene sulphide poly(epithiopropane) under pressure at 95–100°C in the presence of an alcoholic solution of sodium ethoxide and represented this process by the following scheme:



Culvenor and coworkers [91] also associate the polymerisation of ethylene sulphide under the action of NaOH or other alkali agents (NaX) with the formation of $NaSCH_2CH_2OH$ (X); they showed that the α-thio-oxides do not polymerise when the molecule of the attacking agent is constructed so that the product of its condensation with one molecule of the monomer is a stable cyclic compound (for example, trithiocarbonate in the reaction of ethylene sulphide with thiourea or thiocyanates).

In 1964 Ishii and coworkers [35], in studying the polymerisation of propene sulphide (PS) in the presence of various organometallic compounds showed that the alkoxides effective for the induction of the polymerisation of α-oxides (sodium, iron, and titanium ethoxides; aluminium 2-propoxide, Pr^i_2AlOH) are not effective in the polymerisation of episulphides and suggested that Marvel's results [34] are due to the presence of traces of moisture in the system and hydrolysis of the alkoxide. In the same work Ishii showed that sodium, cadmium, zinc, copper, nickel, cobalt, and iron mercaptides at 0–80°C are capable of bringing about the polymerisation of PS with the formation of viscous oils. The use of polar solvents increased the rate of the process. They used infrared spectroscopy to show the presence of C=C groups in the polymer, which allowed them to propose a scheme for the polymerisation of PS by an anionic mechanism which includes a chain transfer reaction:



The same investigators studied the polymerisation of PS under the influence of $Al(C_2H_5)_3$, $Zn(C_2H_5)_2$, and $Al(C_2H_5)Cl$ [35] at 0°C and showed that the presence of water in the system reduces the catalytic activity of the inducer.

Catalytic systems used for initiating the polymerisation of alkene sulphides.

Initiating system	Monomer	Reference
Ultraviolet, γ-radiation, peroxides diazo-compounds	CHS, perfluorinated and unsaturated episulphides	17–19
Organic and dilute mineral acids	ES, PS, BS, CHS, TE, TECH	9–11, 16, 20, 21
Lewis acids: BF_3, PF_5, SbF_5, $BF_3O(C_2H_5)_2$; $AlCl_3$; $TiCl_4$, AsF_5	PS, ES, TE, 7-TBCH, 6-TBCH, 3,3-DMTE, CHS	19–31
Onium salts: $R_3\overset{+}{O}-\bar{B}F_4$, $R_3\overset{+}{S}-\bar{B}F_4$	PS, TE, DMTE, 7-TBCH, 6-TBCH	23, 25, 26.
Metals, their oxides, and hydroxides (M = Na, K, Mg, Al, Ca, Fe, Co, Ni, Sr, Pb etc.)	ES, PS, BS	16, 22, 32, 33
Alkoxides (M = Na, K, Al, Fe, Zn)	PS, SS, ES	22, 34–37
Mercaptides (M = Na, K, Fe, Co, Cu, etc.)	ES, PS, SS	32, 35, 36, 38–48
MR, MRX	PS, ES, OS, TE, IBS	19, 22, 23, 32, 35, 36, 42, 43, 49–57
MR_2 + modifier (M = Zn, Cd, Mg)	ES, PS, BS, CHS, SS, TE	19, 42, 58–68
AlR_3 + mercaptides (Zn, Cu, Co, Ni, Fe); chelates	PS PS	35 69
Mineral salts of Cd, Zn, Mg, Hg	PS, ES, BS, SS, CHS	9–11, 70–76
Amines, polyamines, pyridine, carbazole, guanidine, hydroxylamine, *o*-aminophenol	CHS, PS, ES	77, 78
$NaNH_2$ and other amides	ES, PS	22, 79, 80
Xanthates, dithiocarbonates, thiocarboxylates of metals	ES, PS, BS	67, 81
$LiAlH_4$	1-OS	82
Charge transfer complexes	PS	83–85

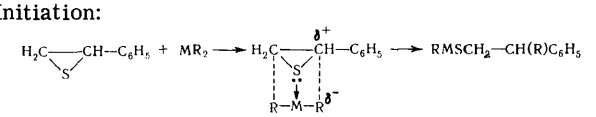
Symbols: ES ethylene sulphide [thiiran or epithioethane], PS propene sulphide [1,2-epithiopropane], BS butene sulphide [1,2-epithiobutane], CHS cyclohexene sulphide [1,2-epithiocyclohexane], SS styrene sulphide [$\alpha\beta$-epithioethylbenzene], TECH thioepichlorhydrin [3-chloro-1,2-epithiopropane], 1-OS 1-octene sulphide [1,2-epithiooctane], IBS isobutene sulphide [1,2-epithio-2-methylpropane], TE thiethane, TBCH thiobicycloheptane, DMTE dimethylthiethane.

From these results it was concluded that the hydrolysis products of organoaluminium compounds are ineffective for the induction of the polymerisation of thio-oxides. In 1968 the same investigators re-examined their previous results and published an article in which they examined in

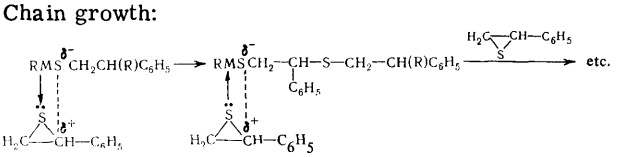
detail the $Al(C_2H_5)_3-H_2O$ system as an initiator of the polymerisation of PS. The results of this work will be considered in the appropriate section.

Nashay and Price[36] studied a large number of catalysts in the polymerisation of styrene sulphide [$\alpha\beta$-epithioethylbenzene], but only the use of triethylaluminium and chlorcadmiumbutylmercaptide at and below room temperature allowed poly(styrene sulphide) with rather high molecular weight to be obtained. It is assumed that chain initiation and growth is neither radical nor ionic in nature and a coordination mechanism is suggested:

Initiation:



Chain growth:



In considering the anionic polymerisation of the PS mention must be made of Kabayashi[70], who first observed that salts of elements of Group IIB, and especially cadmium compounds, give an excellent catalytic effect. CdS, CdO, $Cd(OH)_2$, $CdCO_3$, and $CdSiO_3$ were most active. Whereas zinc catalysts lead to the formation of amorphous, mainly atactic poly(propene sulphide), cadmium sulphides form crystalline polymers which are evidently isotactic ($T_f = 40-45°C$, $Tg = -52.5°C$) with a high value of the characteristic viscosity (up to 10). When cadmium silicates are used, addition of water is needed to increase its activity, which leads to an increase in the molecular weight of the polymer and the rate of the process. Addition of NaOH (up to pH 8) leads to a similar effect. Spectroscopic investigations confirmed the presence in the polymer of the metal used as catalyst. The investigators did not examine the mechanism of the catalytic action of water and sodium hydroxide, but suggested that the polymerisation was stepwise anionic for all types of cadmium salts.

In the presence of the $CdCl_2 + NH_4Cl + K_2S$ [71] or of cadmium or zinc carbonates[72] PS is also polymerised and copolymerised with the formation of high-molecular-weight and oligomeric polymers[73,92].

The studies of Cooper, Morgan, and Wragg[38-41,74] show the special effectiveness of cadmium compounds in the polymerisation of episulphides. The investigators studied the polymerisation of alkene sulphides in the presence of mercaptides, which model the active centres of the process, which is completely reproducible. However, the study of the mechanism and kinetics of the process is hindered by the restricted solubility of mercaptides[36] or by the presence in homogeneous systems of traces of mercaptides which are extremely active chain transfer agents[35].

Wragg and coworkers[38-40] obtained poly(propene sulphide) and poly(ethylene sulphide) of practically any molecular weight by using soluble heavy metal (Zn, Cd, Cu, Ni, Co, Pb, etc.) mercaptides as catalysts. Having studied the initiating capability, of mercaptides of various structures, they showed that the most effective inducers of polymerisation are cadmium and zinc thiolates; the mercaptides $M(SCH_2CH{=}CH_2)_2$ obtained from unsaturated thiols have good solubility, and the dialkayldiaminoalkylthiolates

$$M[SCH(CH_3)CH_2S-CHCH_2N(n\text{-}C_4H_9)_2]_2$$

dissolve almost instantaneously. They associate the increased solubility of the heavy metal mercaptides with their tetragonal structure, due to the presence in the initial thiol in the β-position of a substituent capable of coordination with a metal. All these compounds are stable in air and the presence of moisture does not affect their activity. Wragg and coworkers arranged the most active cadmium mercaptides in the following series:

$$Cd(SCH_2CH{=}CH_2)_2 \simeq Cd(SCH(CH_3)CH_2NR_2)_2 \simeq$$
$$\simeq Cd(SCH_2CH_2SBu)_2 > Cd(SCH_2CH_2OBu)_2.$$

By carrying out a detailed kinetic investigation, Wragg and coworkers[38-40] showed that polymerisation under the influence of heavy mercaptides proceeds by a "living" chain mechanism with an induction period, the length of which depends on the nature and solubility of the inducer. On the stationary part

$$v_p = k_p\,[\text{alkene sulphide}][\text{catalyst}].$$

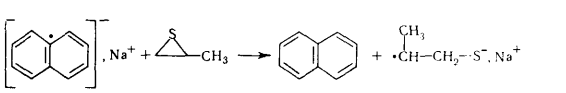
The first order of the reaction with respect to the monomer and the similarity in the growth rate constants in using cadmium mercaptides of various structures show that the coordination of the monomer with a metal does not play a decisive part. However, the latter is supported by the stereospecificity of the inducers used, leading to the formation of a crystalline poly(propene sulphide), and the suppression of polymerisation or a decrease in the rate of the process in the introduction of strong electron-donating additions (amines). As regards the use of aminothiols as polymerisation inducers they did not exclude the possibility of inter-chain interactions, leading to the cross-linking of polymers. The part played by thiols as chain carriers in the polymerisation of thio-oxides was proved convincingly in these studies.

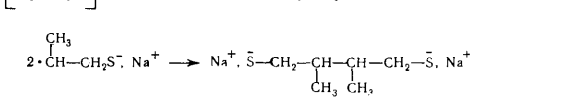
Over a long period there was systematic investigation of the anionic polymerisation of propene sulphide by French scientists led by Sigwalt[22,42,49-55,79].

In the first papers[22,79], which were qualitative, they showed that poly(propene sulphide) of high molecular weight can be obtained by using an anionic type of catalyst—sodium naphthalene in tetrahydrofuran (THF), sodium amide, sodium films. Subsequently, by studying the polymerisation of PS under the influence of the sodium–naphthalene complex in dilute THF solutions[49] they found that the process takes place by a "living" chain mechanism, not complicated by chain breaking or transfer reactions and the mean degree of polymerisation of the polymer formed at any stage of the transformation strictly calculated by the formula:

$$\overline{DP}_n = \frac{\Delta M}{{}^1/_2\,[\text{cat.}]} \quad \left(\text{in which } \frac{\bar{M}_w}{\bar{M}_n} \to 1\right)$$

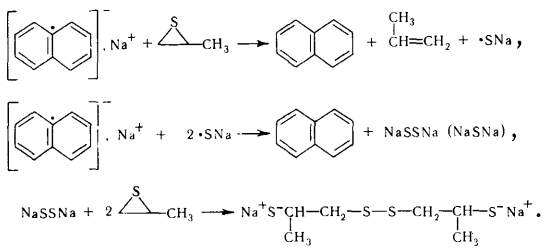
It was suggested[54,55] that the initiation of the polymerisation of PS in the presence of the sodium naphthalene complex takes place by a mechanism according to which, by analogy with vinyl compounds[93], there is transfer of an electron to the monomer with subsequent dimerisation of the anion-radical by the scheme:





Confirmation of this bifunctional mechanism was provided by the almost complete regeneration of the naphthalene (up to 98%). Although the instantaneous disappearance of the naphthalene anion-radical was observed at −78°C, chain growth was noted only above 0°C, which was attributed to the low reactivity of the primary active centre—sodium dimercaptide.

Subsequent kinetic, conductimetric, and spectrophotometric studies of the polymerisation of PS under the influence of the sodium naphthalene complex showed that the initiation is more complex and polymerisation can be effected below 0°C. In later studies[50-52,54] it was observed that the polymerisation of PS in this system is accompanied by the release of propene and the existence of an induction period which is most pronounced at low temperature (−30°C), and which can be avoided by the use of "seed" "living" polymers obtained in the presence of any anionic inducer (sodium naphthalene, sodium mercaptide, sodium carbazyl, or potassium carbazyl)[54]. The characteristic conductometric curves also confirm the slow initiation. On the basis of these results the act of primary interaction of the monomer with sodium naphthalene and the subsequent stages are formulated as follows:



The intermediate active compounds were not identified.

In the range of catalyst concentrations up to 1×10^{-3} M an expression was obtained for the overall rate of the process,

$$v_p = k_p[M][\text{cat.}]^{1/2},$$

where k_p is the overall growth rate constant, and [M] and [cat.] are the monomer and catalyst concentrations respectively. The variation of the rate of the process with the catalyst concentration is linked with the possibility of parallel growth of the polymeric chain into ion-pairs and free ions, present in equilibrium. By use of the Szwarc method[94,95] the individual rate constants of the reactions at free ions and ion-pairs with sodium counter-ions in THF and tetrahydropyran (THP) solution were calculated[54].

The change in the electrical conductivity of the system during the polymerisation of PS in THF [51] and THP [54] solution gave the dissociation constant K_d for the ion-pair S^-, M^+ with counter-ions Na^+, K^+, Li^+, and NR_4^+.[96] The sequence of activities of the counter-ions was found to be opposite to that observed for a carbanion[95], owing to the reduced contribution of the solvating effects. In studying the polymerisation of PS in THF it was found that with an initiator concentration above 1×10^{-3} M the rate of the process is not described by the above equation. This phenomenon is connected with the existence in the system of a series of equilibria involving ion-pairs and free ions:

$$(S_2Na)^- + Na^+ \overset{k_3}{\rightleftharpoons} (S,Na)_2 \overset{k_2}{\rightleftharpoons} 2\,S,Na \overset{k_1}{\rightleftharpoons} 2S^- + 2Na^+$$

where (S,Na) is a thiolate active centre in the form of an ion-pair, $(S_2Na)^-$ an associate of the ion-pair with a free ion, and $(S,Na)_2$ an associate including two ion-pairs.

The existence of associates under these conditions agrees with the departure of the electrical conductivity of the system from linearity in the same concentration region and this was proved by viscosimetric measurements by Morton's method[97] involving comparison of the time of flow of solutions of the reaction mixtures before and after disturbance of the active centres $\sim S^-, M^+$ by the terminating agent (ethyl bromide).

It has been shown[52] that in working with a monofunctional excitant (sodium triphenylmethyl) the regularity of the process is analogous to that in working with sodium naphthalene. It was assumed that bifunctional compounds of the SNa_2 or S_2Na_2 type or their mixtures are also polymer chain initiation agents. The use of sodium and potassium carbazyls as initiators of PS polymerisation[98] allowed a truly monofunctional polymer to be obtained, the formation of which obeys all the kinetic rules established for bifunctional poly(propene sulphide).

Another type of anionic inducer of polymerisation, butyllithium, has been investigated[23,32,43,99]. Under block polymerisation conditions in solution in non-polar solvents the polymerisation of PS under the influence of butyllithium proceeds at a low rate. The introduction of 10 to 70 mole % THF causes a marked increase in the rate of the process. In the temperature range from −25° to +20°C over a wide range of monomer and initiator concentrations the homogeneous process of polymerisation proceeds without an induction period up to complete disappearance of the monomer and is described as a quasi-stationary process with a constantly acting number of active centres and a total activation energy of 11.8 kcal mole^{-1}. The nature of the dependence of the molecular weight on the polymerisation conditions (temperature, concentrations of the initial reactants, degree of conversion) shows that the process takes place with participation of "live" polymeric chains with complete use of the initiator introduced and allows the formula for calculating the degree of polymerisation found for the uninterrupted processes to be used.

However, the investigation of the variation of the molecular-weight distribution (MWD) of poly(propene sulphide) with the extent of conversion and temperature of the reaction, made at various monomer and initiator concentrations and in the absence of a solvent showed the complexity of the process. In every instance the MWD curves were unimodal with an inflexion in the high molecular weight range (Fig. 1) and polydispersity coefficients of $\bar{M}_w/\bar{M}_n \to 1.5$ and $\bar{M}_z/\bar{M}_w \to 1.33$. In the absence of reaction the limit of the polymeric chain growth of the type of distribution of poly(propene sulphide) according to molecular weight was thought to be linked with the presence in the system of "pseudo-rupture" phenomena consisting of the occurrence throughout the entire process of a spontaneous deactivation of the $\sim S^-, Li^+$ active centres, due to the ability of the organolithium compounds to be associated and subsequently reactivated when they react with the monomer. Hence at every moment in the acts of polymeric chain growth only some of the active centres that are formed, and not all the initiator, participate. On the other hand, the fact that irrespective of the conditions under which the polymerisation is carried out the distribution of the macromolecules by size obeys the relation

$$q_w(M) = \frac{(\alpha M^2)e^{-\alpha M}}{\bar{M}_n},$$

where M is the molecular weight of a polymer fraction, $\bar{M}_n$ the number mean molecular weight, and α is either

proportional to M or is a constant ($2/\bar{M}_n$), and the polydispersity coefficients $\bar{M}_w/\bar{M}_n$ and $\bar{M}_z/\bar{M}_n$ are 1.5 and 1.33 respectively, is thought to show that under the chosen conditions each polymer chain is constructed from two statistically independent polymeric chains growing on a bifunctional active centre, which agrees with the observed values of the number mean molecular weights. Chromatographic analysis of the gaseous products formed showed the identity of the mechanism of interaction of butyl-lithium and sodium naphthalene with PS in THF medium and in the absence of the latter through the sulphur-elimination stage.

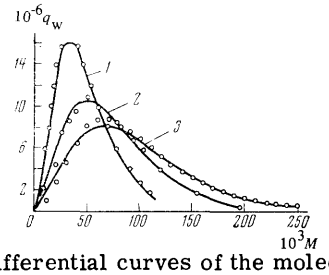


Figure 1. Differential curves of the molecular weight distribution of polypropene sulphide obtained at $[C_4H_9Li] = 4.8 \times 10^{-3}$ M; [PS] = 2.46 M, $t° = -25°C$, in a tetrahydrofuran medium. The experimental points are plotted along curves calculated by the formula

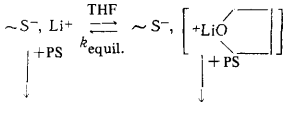
$$q_w(M) = \frac{(\alpha \cdot M)^2 \cdot e^{-\alpha M}}{\bar{M}_n}:$$

Conversion, %: *1*) 46.0; *2*) 71.5; *3*) 100.

The main kinetic parameters of the polymerisation of PS were studied at 0°C. In the range of butyl-lithium concentrations from 1×10^{-3} to 1.8×10^{-2} M the order of reaction with respect to the excitant was varied from 1 to 0. The dependence of the rate of polymerisation of PS on its concentration in THF is shown in Fig. 2. The total rate of the process is

$$v_p = k_p[M]^2[\mathrm{THF}]^2[\mathrm{cat.}].$$

It was assumed that the nature of the relation between the polymerisation rate and the concentrations of the initial reagents is determined by the fact that butyl-lithium is present in a medium of two strongly electron-donating agents, of which PS is the more polar ($\epsilon_{PS} = 10.2$, $\epsilon_{THF} = 7.6$), but THF is the stronger complexing agent[100,101], due to the presence in the polymerising system of the equilibrium:



A study of the electrical conductivity of the PS–butyl-lithium + THF system[99] enabled us to draw conclusions about the decisive part played by ion-pairs in polymer chain growth and to find that THF participates in the specific solvation of the low-reactivity contact ion-pair $\sim S^-, Li^+$, converting it into a "loose" (separated by the solvent) ion pair $\sim S^-, [Li^+, THF]$ the reactivity of which is 50–80 times greater than the reactivity of the contact pair.

A study of the copolymerisation of PS with α-, β-, and γ-thio-oxides: ethylene sulphide, thiethane, and thiophan, which are distinguished by the basicity of the heteroatom and the strain of the ring enabled us to answer the problem which is crucial in the growth stage: coordination of the sulphide with the counter-ion or the introduction of complex-bound monomer at the S–Li bond (ring opening, thermal effect). The results of infrared spectroscopy and elemental analysis show that the copolymers are enriched with the component with the more highly strained ring, which is also the determining factor in ring opening under the action of a nucleophilic reagent. However, the retardation of polymerisation on the addition of small amounts of the compounds of greater basicity (thiophan, thiethane) suggests that a significant part is also played by the coordination of sulphide with the counter-ion, which modifies the active centre and shows the kinetics of the process but does not alter the direction of the chain formation. On the basis of the results obtained a coordination-anionic mechanism of polymerisation of the PS under the influence of butyl-lithium is proposed, including stages of initiation, growth, "pseudo-breaking", reactivation, and the corresponding kinetic calculations are given[99].

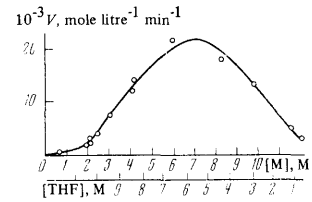


Figure 2. Variation of the rate of polymerisation of propene sulphide with the concentrations of the monomer and tetrahydrofuran at 0°C and $[C_4H_9Li]_0 = 3 \times 10^{-3}$ M.

Some regularities in the polymerisation of PS initiated by $Al(C_4H_9^i)_2Cl$ in benzene and diethyl ether solution have been studied by gas–liquid chromatography[44]. It was shown that polymerisation can be effected at temperatures from −20° to +20°C with an overall activation energy of 11.4 kcal mole^{-1}. Thermogravimetric analysis of the poly(propene sulphide) *in vacuo* and in air showed that the decomposition of the polymer takes place almost entirely in the range 225–320°C, to give propene, ethane, and isopropylthiol and is accompanied by appreciable endothermic effects. No suggestions were made as to the mechanism of the initiation, growth, or breaking of the polymeric chain.

Hence in the opinion of most authors, in the anionic polymerisation of alkene sulphides irrespective of the initial initiator the growth of the polymeric chains is effected by the thiolate anion S^-, M^+. When growth precedes the coordination of the active centre with the monomer, the polymerisation is effected by a coordination-anionic mechanism.

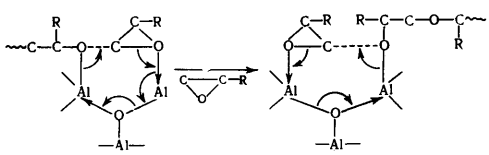
2. Polymerisation of Alkene Sulphides under the Influence of Modified Organometallic Compounds

Catalytic systems based on organozinc and organoaluminium compounds in the presence of cocatalysts are

widely used for the preparation of high-molecular-weight polyoxyethylenes with a high degree of tacticity[58-62,102-113].

Despite the prolonged and serious study of the polymerisation and copolymerisation of alkene oxides under the influence of modified organometallic compounds, the mechanism of their action is far from being explained completely. Whereas in the first studies of Furukawa and Saegusa[102] catalytic activity was attributed to the O–M–O bond, at which coordination of the monomer took place, Colclough and Wilkinson[103] and Vandenberg[104] thought that the growth of the polymeric chain takes place by a cationic mechanism with participation of stable onium ions formed during the interaction of the monomer with the hydrated form of the organoaluminium compound. Many investigators drew conclusions about the "onium" nature of the polymerisation of oxygen-containing heterocycles at AlR_3 + H_2O and $Zn(C_2H_5)_2$ + H_2O systems on the basis of a study of the constants of the copolymerisation of the various oxides and their comparison with results on copolymerisation under the influence of catalysts of typically cationic nature [$BF_3.(C_2H_5)_2O$, $SnCl_4$].[105-108]

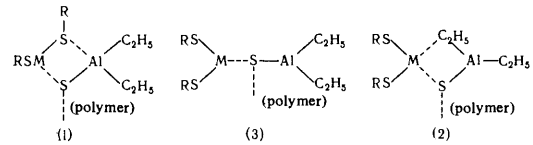
Recently a series of papers by Vandenberg[114,115] and Price[116,117] has reported that the polymerisation of oxides, which leads to the production of regularly constructed crystalline polymers, is due to the coordination of the monomer at an active centre having more than one metal atom:



This was proved convincingly by Osgan and coworkers[118,119] in investigating bimetallic μ-oxoalkoxides as catalysts of the polymerisation of epoxides by an injection mechanism. The part played by electronic and structural factors and also by other cooperative effects in the mechanism of coordinated polymerisation under the influence of the catalysts employed was examined and the possibility of bridging oxygen participating in the monomer addition stage was demonstrated. Some new aspects of the catalysis of the polymerisation of heterocycles by organometallic compounds were examined in a paper published recently by Furukawa[120].

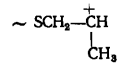
As recent studies have shown, in the presence of various modifying additions the $Al(C_2H_5)_3$ and $Zn(C_2H_5)_2$ systems are active for the induction of directed polymerisation of α-thio-oxides, but we have found only a few publications and these contain extremely limited material[35,63,67,68,70,121-125]. Nevertheless, the results of these studies allow our ideas about the nature of the active centres and the mechanism of polymerisation of the heterocyclic compounds in using organozinc and organoaluminium compounds to be extended.

Coordination leading to a regular structure of the chain and the production of a crystalline polymer were observed by Ishii and coworkers[35] in the polymerisation of PS under the influence of AlR_3, modified with water and various metal mercaptides. They showed that whereas Na, Co, Zn, Ni, and Cu mercaptides form low-molecular-weight amorphous polymers but triethylaluminium both in the absence of additions and in the presence of water is of little effect on the induction of polymerisation, a combination of trialkylaluminium with mercaptides leads to the formation of a high-molecular-weight crystalline polymer. The greatest activity is observed in using iron and cobalt mercaptides. It was found, by the example of $Al(C_2H_5)_3$ + $Co(SBu^n)_n$ and $Al(C_2H_5)_3$ + $Fe(SBu^n)_3$, that on varying the Al/M ratio from 0.5 to 2 the degree of conversion is increased, but the maximal value of the molecular weight ($[\eta] = 2.0$) is reached at the ratio Al/Co = 1.0. This was attributed to the phenomenon of chain transfer from the excess of $Al(C_2H_5)_3$ but the mechanism of this process was not examined. It was assumed that in the initial stage of the polymerisation takes place under the action of $Al(C_2H_5)_3$ but subsequently the polymeric ions coordinate with the metal mercaptide, acquiring form (1), (2), or (3), and polymerisation takes place at the $S^- - M^+$ bond, which ensures stereoregular growth of the chain. Growth of the polymeric chain at complexes of structure (1) and (2) is preferred by the investigators.



The non-stereospecificity of the $Al(C_2H_5)_3$ + $Ni(SR)_2$ system is attributed to the monomeric structure of nickel mercaptides in which the sulphur atoms are arranged non-regularly[126]. Some conclusions drawn in this study concerning the reactivity of the O–M bond were disproved by the French investigators Machon and Sigwalt[121,122] and also subsequently by Ishii[124]. In a later paper, Ishii and coworkers[124] showed that under strict control of the water content the $Al(C_2H_5)_3$ + H_2O system is active for the polymerisation and copolymerisation of alkene sulphides in toluene at 0–50°C. The influence of the ratio of the components in the initial mixture, the polarity of the medium, and the concentrations of the monomer and catalyst on the rate of the process and the molecular weight of the polymer were investigated. It was found that in comparison with pure $Al(C_2H_5)_3$ the $Al(C_2H_5)_3$ + H_2O system is more active for polymerisation over a wide range of component ratios, and maximal activity is observed at the ratio $Al/H_2O = 1$.

On the basis of various kinetic regularities the polymerisation of PS in the presence of the $Al(C_2H_5)_3$ + H_2O system and its copolymerisation with other α-thio-oxides, conclusions were drawn about the cationic nature of the polymeric chain growth at active centres of the



type and about the presence of intensively developing chain transfer reactions at the monomer or sulphur atoms of the polymeric chain but we do not think that the proposed scheme for these reactions is sufficiently clear.

From the standpoint of the stereospecificity of the catalyst used, the diethylzinc–water system proposed in 1958 by Furukawa and coworkers[111,127] for the polymerisation of cyclic oxides is interesting. This system attracted the attention of many investigators and is now being studied intensively. Many papers have been published about the use of various modifiers with the aim of increasing the effectiveness of this system[58-63,67,115,128].

It is stated in several patents[60-63,67] that $Zn(C_2H_5)_2$ and other organometallic compounds of Group II, modified with compounds which contain atoms with an unshared electron pair or proton-donating additions, are effective in the polymerisation of α-oxides and episulphides and their copolymerisation.

Recently Shozo and Teiji[86] thoroughly investigated the $Zn(C_2H_5)_2 + H_2O$ system for the polymerisation of α-oxides and found that the mechanism of its action (cationic or anionic) is connected with the change in the molar ratio of the components, which is reflected in the structure of the hydrolysis products formed, leading to polymerisation. According to recent results[110], obtained by infrared spectroscopy, gas–liquid chromatography, and X-ray diffraction, $C_2H_5(ZnO)_n.Zn(C_2H_5)$ (I), $C_2H_5(ZnO)_nH$ (II), and $HO(ZnO)_nH$ (III), which have a disordered würtzite structure containing a Zn–O–Zn bond, are excitants of the polymerisation of propene oxide, depending on the degree of hydrolysis. Their relative acidity increases in the order: (III) < $Zn(C_2H_5)_2$ < (I) < $Al(C_2H_5)_3$.

The possibility of the use of this catalytic system for the polymerisation of episulphides was first shown in 1963 by Kabayashi and Ishii[70]. The French investigators Machon and Sigwalt[121,122] made a more detailed investigation of the effect of the addition of water on the extent of the conversion and the properties of the polymer obtained in the polymerisation of PS in benzene solution—the catalytic $Zn(C_2H_5)_2/H_2O$ system. It was shown that the system is effective for the excitation of polymerisation over a wide range of ratios $\rho = H_2O/Zn(C_2H_5)_2$ but the crystallinity of poly(propene sulphide), which was estimated from the solubility of the polymer in ethyl methyl ketone, reaches a maximum at $\rho = 1$. On the basis of extremely few experimental results it is difficult to draw any conclusions about the actual mechanism of the system being studied, but a preference was expressed for the anionic nature of the initiation and growth of the polymeric chain independently of the value of ρ.

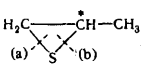
The poly(propene sulphide) obtained is an elastomer with increased rigidity and breaking resistance, its crystallinity is connected with the ratio of the components in the initiating system.

Interesting information about the nature of the active centres in the polymerisation of α-oxides and α-thio-oxides was obtained by Lal[123]. The new systems $Zn(C_2H_5)_2$ + sulphur and $Zn(C_2H_5)_2 + H_2O_2$ were investigated and their action was compared with that of the $Zn(C_2H_5)_2 + H_2O$ system. It was found that sulphur emerges as a cocatalyst and the $Zn(C_2H_5)_2$ + S system effects the heterogeneous polymerisation of α-oxides and α-thio-oxides over a wide range of ratios of the components. During the course of the investigation an effect by the polarity of the medium was not observed and it was shown that all the three systems have similar stereospecificity but the sulphides were polymerised more rapidly than the oxides and had a lower molecular weight. The results obtained led Lal to assume that the effectiveness of the $Zn(C_2H_5)_2$ + S system is associated with the presence of polysulphide bonds. This assumption was confirmed in studying the polymerisation of propene oxide in the presence of model mercaptides of the type: RSZnR, RSZnSR, RS_XZnS_YR, RS_XZnR, and RS_XZnSR (where $x + y = 2-8$). It was shown that the compounds which contain monosulphide bonds of the RSZnR type and the mercaptides obtained *in situ* in the $Zn(C_2H_5)_2$ + S system are ineffective for exciting the polymerisation of α-oxides and thio-oxides. Prolonged ageing of the catalyst $Zn(C_2H_5)_2$ + S (0.5–19 h) facilitates the formation of active polysulphide bonds RS_XZnS_YR, in which the R–S structure also plays a significant part. It is thought that polymerisation proceeds by a coordination mechanism but this problem was not discussed.

To understand and identify the mechanism of polymerisation of α-thio-oxides under the action of various excitants there was great interest in studying the synthesis of optically active polymers from monomers containing asymmetric carbon atoms. It is known that an optically active polymer can be prepared when the polymerisation of the optically active form of the monomer (enantiomer) is carried out, or by using the racemate of an optically active excitant to initiate the polymerisation. Spassky and coworkers[68,75,87,88] used both these possibilities to obtain optically active poly(propene sulphide).

As Machon and Sigwalt showed[121,122], the stereospecific polymerisation of racemic PS allows a high-molecular-weight polymer with up to 50% crystalline phase to be obtained. Spassky[88] thought that the crystallinity of this polymer could be due either to the simultaneous presence of two types of polymer, obtained on the basis of each of the enantiomers, or to the existence of a single polymeric chain consisting of successions of each enantiomer of various lengths. Therefore the preparation of polymers of each antipode should give valuable information about the mechanism of the stereospecific polymerisation of episulphides.

On the other hand, a comparison of the optical activity of the polymers obtained with various catalytic systems allows the presence of an irregularity in the macrochain, due to opening of the ring at the C–S bond at the primary or secondary carbon atom, to be observed. Actually, under the influence of various agents the ring of the optically active PS



can be opened to form a polymer of type (a) (anionic polymerisation) with retention of the configuration at C* and consequently with increase in optical activity, or of type (b) (cationic polymerisation), or of a mixture of types (a) and (b) with loss of or decrease in the optical activity of the polymer. As follows from Spassky's results[68,87], in the polymerisation of *d*- and *l*-propene sulphide under the influence of anionic excitants (sodium, KOH, cadmium tartrate) polymers with increased-optical activity are formed, but under the influence of boron trifluoride–diethyl ether, polymers with reduced optical activity are formed. In this connection there is considerable interest in studying the nature of the action of the $Zn(C_2H_5)_2 + H_2O$ system at various ratios of the initial components. For $Zn(C_2H_5)_2/H_2O = 1:1$ the optical activity is close to that obtained in an anionic system. A reduction in the proportion of water decreases the optical activity, which could be linked with the appearance of a cationic nature in the active centre formed. The system with $Zn(C_2H_5)_2/H_2O = 1:0.5$ is similar in its action to the $Al(C_2H_5)_3/H_2O = 1:0.7$ system and is a cationic excitant[105], but $Zn(C_2H_5)_2/CH_3OH = \frac{1}{2}$ and $Zn(C_2H_5)_2$ + glycol[68] is anionic, which agrees with the results of Inoue and coworkers[128]. It was noted[68,75,87-89] that in the polymerisation of episulphides there is not a complete analogy in the behaviour of the $Zn(C_2H_5)_2/MOH = \frac{1}{2}$ and $Zn(C_2H_5)_2/H_2O = \frac{1}{1}$ systems, since the latter shows a tendency to a cationic nature.

The polymerisation of the racemic *d,l*-propene sulphide in the presence of organolithium and organozinc compounds modified with optically active additions [LiC_4H_9 + LiOR*, $Zn(C_2H_5)_2$ + 2ROH*] was studied by Aliev and Krentsel'.[129,130] In an investigation of the lithium system low-molecular-weight polymers exhibiting a comparatively high optical activity (up to −63.7 deg) were obtained. The polymerisation was accompanied by the release of propene and under certain conditions there was almost complete decomposition of the poly(propene sulphide) into propene and

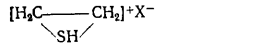
elemental sulphur. The process could also be directed to the production of a polymer with S–S bonds. It was suggested[129] that under the action of a strongly nucleophilic agent polymerisation takes place in three successive directions: (a) desulphidation of the PS and polymerisation, (b) decomposition of the polymer chains with release of propene and formation of oligomeric products with ~S–Li groups at both ends of the chain, (c) oxidation of the oligomers either by elemental sulphur or by lithium polysulphide with the formation of polymers with disulphide bonds.

Another probable mechanism of initiation and chain growth with formation of disulphide bonds has been suggested[130]. The formation of propene and polysulphide bonds in a macromolecule was also observed in a study[41] of the polymerisation of PS in the presence of zinc and cadmium mercaptides, which the investigators attributed to the act of elimination of sulphur in the coordination of S–Zn–S bonds of a polymeric chain with a monomer.

3. Cationic Polymerisation of Alkene Sulphides

The ability of alkene sulphides to polymerise in the presence of excitants of cationic type has been noted repeatedly[8,24,43,49,50]. In 1920 Délépin[8], who had been the first to synthesise episulphides, drew attention to the fact that they are readily polymerised under the influence of dilute mineral acids and acetic acid. In 1960 Dermer showed[24] that boron trifluoride and tetramethylammonium chloride bring about the polymerisation of episulphides in bulk with great velocity, and Boileau[49,50] polymerised PS in the presence of boron trifluoride–diethyl ether and of titanium and aluminium chlorides. However, in these studies only the fact of the formation of a low-molecular-weight polymer was noted and the mechanism of polymerisation under the influence of electrophilic agents was not taken into account.

In 1951 Tarbell and Harnish[131] examined the polymerisation of episulphides in the presence of acidic agents and first suggested the formation of an intermediate sulphonium ion of the type

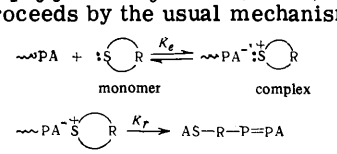


The "onium" mechanism lies at the basis of modern views on the mechanism of cationic polymerisation of heterocycles[132–137]. In the general instance, the initiation of polymerisation is regarded as the interaction of the electron-withdrawing part of the catalyst (Lewis acid) with the unshared electron pair of the heteroatom of the monomer with the formation of a stable onium pair, which is also an active centre of polymerisation:

The capability of the reacting substances to form onium (or sulphonium) ion is linked with the strain and basicity of the heterocycle, and also with the acidity of the catalyst, which ensures that the ionic complex is of sufficient stability.

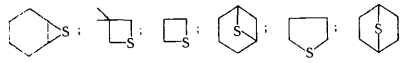
Oddon[138] made a detailed study of the reactivity of three-membered sulphur-containing heterocycles in relation to electrophilic agents; Stille and Empen[25,26] attempted to correlate between the physicochemical parameters of various cyclic sulphides and their capability for polymerisation.

In the first publication[25] the possibility of polymerisation of alkene sulphides with rings of various sizes in the presence of $Al(C_2H_5)_3$ and PF_5 was reported; it was suggested that it proceeds by the usual mechanism:



where PA is the growing polymer and A the electron acceptor.

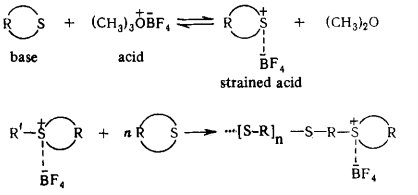
Subsequently[26], by assuming that the polymerisation, at the start of which coordination or complex formation occurs, should be determined both by the basicity of the cyclic sulphide and by its tendency to ring opening, Stille and Empen determined the basicity of six cyclic sulphides:



and investigated their capability for polymerisation under the influence of the systems: (1) $AlR_3 + H_2O$ + epichlorhydrin, (2) PF_5, (3) $BF_3:O(C_2H_5)_2$ + epichlorhydrin, (4) $R_3O:BF_4$.

The basicity was estimated from the shift of the absorption band of the OH group in the infrared spectra of solutions of phenol and sulphides in CCl_4 and also from the heat of complex formation with iodine. The order of basicity found for alkene sulphides with various ring sizes ($5 > 6 > 4 > 3$) differs from that for oxides ($4 > 5 > 6 > 3$) and agrees with other results[100,139–143]. The basicity series for the oxides and thio-oxides are connected with the difference in size of the heteroatoms, the strain of the ring, and the polarisability of the bonds. On comparing the heats of formation of the complex and the heats of polymerisation it was concluded that the conversion of a cyclic sulphide into a polymer is determined not so much by its basicity as by the ring strain.

On considering the mechanism of polymerisation of alkene sulphides under the influence of trialkyloxonium salts we have suggested that, by analogy with the reactions studied by Meerwein[144,145], leading to the formation of trialkylsulphonium salts from trialkyloxonium salts and dialkyl sulphide—in this instance a stable trialkylsulphonium salt is formed, brought about by polymerisation:

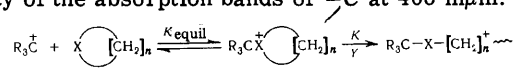


Extremely interesting results dealing with the reactivity of thio-oxides and the stability of sulphonium ions were given by Japanese scientists[146]. They measured the constants of the equilibrium

$$\text{carbonium} \underset{}{\overset{K_{equil}}{\rightleftharpoons}} \text{oxonium and}$$

$$\text{carbonium} \underset{}{\overset{K'_{equil}}{\rightleftharpoons}} \text{sulphonium}$$

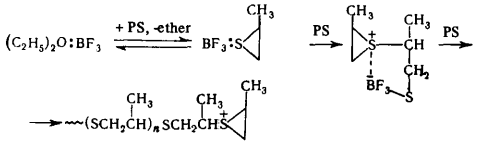
for the reactions of trityl hexachloroantimonate with various cyclic oxides and thio-oxides from the decrease in the intensity of the absorption bands of $\rangle\overset{+}{C}\langle$ at 408 mμm:



where X = S, O; Y = nucleophile.

It was shown that in every instance the equilibrium of the reaction is shifted to the right and the equilibrium constants (K_{equil}) for the thio-oxides considerably exceed those for the oxides. Sakai and coworkers associate these results with the greater stability of the sulphonium salts. They used K_{equil} and K'_{equil} to calculate the apparent rate constant for the opening of the heterocycle (k) and found that according to reactivity the sulphides can be arranged in the order 4 > 5 > 3, which agrees with the results on their basicity but not with those on their ability to polymerise (3 > 4 > 5). The stability of the sulphonium salts, which depends on their structure and the nature of the counter-ion, determines the temperature range in which they can be used for the excitation of the polymerisation of PS. It has been shown[23] that despite the similar values for the activation energy of the polymerisation of PS in the presence of boron trifluoride–diethyl ether, and of its trialkyloxonium and trialkylsulphonium salts (E_{act} = 18 ± 2, 16 ± 0.5, and 20 ± 0.5 kcal mole^{-1} respectively) in the last instance the polymerisation is effected only above 50°C whereas for the first two inducers polymerisation proceeds effectively from 0° to 20°C.

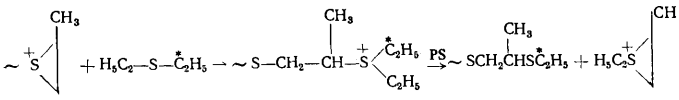
The polymerisation of PS under the influence of a typically cationic inducer, boron trifluoride–diethyl ether, has been studied repeatedly[99,147,148]. In ethyl chloride, nitroethane, or diethyl ether solution at 20°C and monomer concentrations of 3.5–6.4 M and inducer concentrations of 1.5×10^{-3}–9.0×10^{-3} M the polymerisation develops with participation of "living" polymeric chains without an induction period, irreversibly until complete depletion of the monomer, with the formation of a polymer which exhibits relatively broad MWD. The total activation energy of the process in 18 ± 1.5 kcal mole^{-1}. By initiating the polymerisation with seed "living" polymers the investigators showed that the high value of E_{act} is determined mainly by the limiting stage of the opening of the episulphide ring. The overall expression for the initial rate is $v_p = k_p[PS][cat]$, where k_p = 3.35 litre mole^{-1} min^{-1}. It is assumed that growth of the polymeric chain is effected by the stable sulphonium ion, formed according to the scheme:



It was shown[99,147,148] that the polymerisation of PS in the presence of boron trifluoride–diethyl ether is complicated by interchain exchange interaction the contribution of which increases with the degree of conversion. This is proved by the change in the nature of the MWD curves during the polymerisation and after its completion, the decrease in the molecular weight of the polymer during the polymerisation in the presence of dialkylsulphides and the possibility of the preparation of block-copolymers during the polymerisation of ethylene sulphide in a solution of "dead" poly(propene sulphide).

Enikolopyan and coworkers[149,150] developed the theory of interchain exchange interaction by the example of oxygen-containing heterocycles. A similar conversion of macromolecules is now known as a chain transfer reaction with chain breaking (CTB).

By making certain assumptions, a quantitative estimation of the contribution of the CTB in the polymerisation of PS under the influence of boron trifluoride–diethyl ether in the presence of diethyl sulphide (DES) labelled with ^{14}C was made[23,99]. The great stability of the sulphonium ions and the specific structure of the polymeric chain in which the basicity of the heteroatom is close to the interaction of the active centre not only with the monomer but also with the DES modelling the polymeric chain:



The polymerisation was studied at various stages of the conversion and characterised by the ^{14}C content in the polymeric chain. E_{act}CTB was calculated from the change in the rate of reaction of CTB in the temperature range 20–50°C and found to be 15 ± 2 kcal mole^{-1}, which corresponds to published results on the activation energy of thioether exchange[151]. By considering the polymerisation of PS under the action of boron trifluoride–diethyl ether as a "pseudocopolymerisation", in which $k_{DES-DES} = 0$, the relative value of the constant of the CTB reaction as

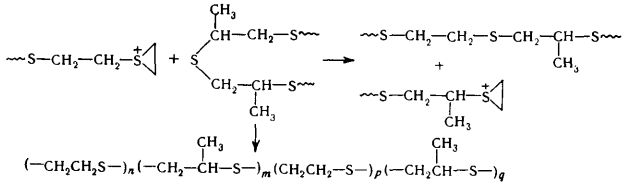
$$\frac{k_{CTB}}{k_{growth}} = [M]/[DES]\frac{\Delta DES}{\Delta M},$$

where [M] and [DES] are the concentrations of the monomer and DES in the initial mixture, and ΔM and ΔDES are the mole fractions of PS and DES in the polymer respectively.

By calculations from the radioactivity of the polymer, obtained at various compositions of the initial mixture,

$$k'_{CTB} = \frac{k_{CTB}}{k_{growth}} = 2 \cdot 10^{-3},$$

which shows the insignificant contribution to the CTB reaction at the stages which do not exceed 10% conversion. The CTB reaction develops more intensively on replacing DES by the already polymerised chain, that is, when there is a considerable increase in the concentration of thioacetal groups[99,147,148,152]. The polymerisation of ES under the influence of a cationic-type inducer in a solution of "dead" poly(propene sulphide) leads to the formation of statistical block-copolymers and was used for the direct proof of the existence of CTB reactions.



The phase composition of the fractions isolated by the method of fractional precipitation and selective extraction was controlled by elemental analysis and calorimetrically. The individual fractions of block-copolymers were investigated by physicochemical methods. The different proportions of crystalline poly(ethylene sulphide) links in the chain of the amorphous poly(propene sulphide) are readily

fixed by X-ray diffraction and are shown by the melting point of the fraction, determined from the thermomechanical curve.

4. Polymerisation of Propene Sulphide under the Influence of Complexes with Charge Transfer Complexes (CTC)

The presence of a lone pair of electrons localised at the sulphur atom in the thiirans suggested that compounds of this class can act as electron-donating partner in interaction with various electron-acceptors, by forming donor–acceptor CTC with development of polymerisation [83-85].

Stotskaya and coworkers showed, by the example of PS, that when it reacts with organic acceptors coloured CTC of the p–π type are formed with a specific absorption band maximum in the ultraviolet range which brings about the polymerisation of PS without the introduction of additional initiating agents. The principal kinetic parameters of the polymerisation of PS in the presence of a weak acceptor of electrons—maleic anhydride (MA) (E_a = 0.5 eV)—and of a strong acceptor—tetranitromethane (TNM) (E_a = 1.2 eV) in polar and non-polar solvents were studied. The polymerisation of PS had specific features which distinguish it from the polymerisation of the thiirans so far studied in the presence of cationic and anionic excitants. Independently of the nature of the acceptor and the polarity of the solvent, the kinetic curves were S-shaped, which the investigators associated with retardation of the initiation. The polymerisation was accompanied by intensively developing chain transfer and breaking reactions. The consumption of the acceptor not only in the formation of CTC but also in other side-processes was also found to be specific. The nature of the acceptor and the polarity of the medium determined the composition of the CTC which appear in the orders of the reaction with respect to the monomer and to the acceptor. Thus in the PS–MA system in a non-polar solvent and in the bulk

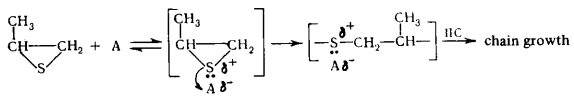
$$v_p = k_1 [PS]^2[MA];$$

in a polar solvent

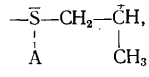
$$v_p = k_p [PS]^2[MA]^2,$$

and when the strong acceptor TNM was used the reaction was of variable order with respect to the acceptor (from 0.5 to 0) and of first order in relation to the monomer. The composition of the donor–acceptor complexes of PS with MA and THM was studied spectrophotometrically and the equilibrium constants for their formation in polar and non-polar media were calculated.

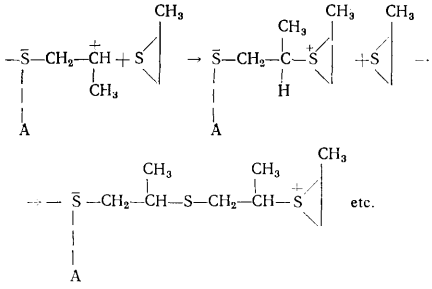
Sitnikova and coworkers [83] first supported a purely coordination mechanism for polymeric chain growth at an active centre formed during the opening of the thiiran ring in the CTC:



Subsequently [85] they concluded that the initiation of polymerisation is effected through a CTC stage, ring opening, and formation of an active centre:



and subsequently the chain growth proceeds by a cationic mechanism with participation of stable sulphonium ions which include the stages of chain transfer and breaking:



Sitnikova and coworkers did not give any experimental facts which confirm the correctness of the proposed mechanism of polymer chain growth.

III. COPOLYMERISATION OF ALKENE SULPHIDES

There is considerable theoretical and practical interest in the rules of copolymerisation of α-thio-oxides with derivatives of the same homological series and with other compounds, and in the properties of the copolymers obtained. The very few papers and patents have shown that the introduction of monosulphide bonds into the main chain of a polymer of another type gives a series of specific valuable properties [153-157]. Two- and three-component copolymers of α-thio-oxides in which one of the monomers has a C=C bond to ensure the possibility of their vulcanisation are of definite practical interest.

Kabayashi and Morivaki [76] obtained such a rubber on the basis of PS and allyloxypropene sulphide in the presence of various cadmium compounds. Thanks to the presence of thioether groups the rubber had good acid resistance and antioxidants were not needed in the vulcanisation usual for rubber.

Adamek and coworkers [72] used a three-component system of ethylene sulphide, PS, and allyloxymethylthiiran, and by employing zinc and cadmium carbonates as catalysts also obtained a vulcanising rubber. In comparison with the rubbers obtained by Kabayashi, the three-component copolymer had increased mechanical strength associated with the presence of a crystalline phase due to the ethylene sulphide links. The copolymer is stable to ozonation, certain chemical reagents, and over a wide range of temperatures it exhibits physicomechanical properties close to standard butadiene–styrene rubber. One of the features of the ternary copolymer is the rapidity of the vulcanisation (thrice as rapid as for the copolymer based on propene oxide). The capability of thiirans to give "living" polymeric chains has been used by many investigators for the production of block-copolymers. Thus Pstrosky [158] obtained block copolymers of ethylene sulphide with styrene and 4-vinylpyridine but Robert and Pearce [159] prepared block-copolymers of ethylene and propene sulphides with methyl methacrylate, styrene, and α-methylstyrene. French scientists obtained block copolymers of dienes with episulphides [153,154].

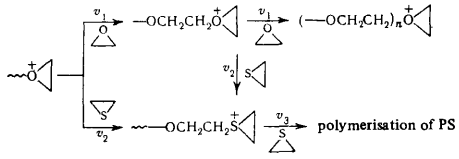
In every instance for the preparation of block copolymers in the initiation of polymerisation of episulphides by "living" polymers obtained in the anionic polymerisation of vinyl monomers or of dienes the quantitative conversion of the $-C^-$ active centre into $-S^-$ was used.

The relative reactivity of thiirans in anionic and cationic copolymerisation was studied by Bualo [190] and

Spassky[27]. It was found that the basicity of thiiran does not affect its activity during anionic copolymerisation[160]. On the basis of a comparison of the constants for the copolymerisation of PS and cyclohexene sulphide—initiating systems of boron trifluoride–diethyl ether and of $Zn(C_2H_5)_2 + H_2O$ at a component ratio of 1 : 1—Spassky drew conclusions about the common mechanism of action of these catalytic systems and the basicity of the monomers determined their relative reactivity[27].

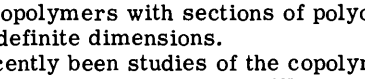
Copolymers of α-oxides with α-thio-oxides have been described in the patent literature[61,62,155-157,161]. Copolymerisation is effected under the influence of alkali metal hydroxides or of modified organometallic compounds at 25–175°C. The polymers formed exhibit high resistance to oxidation and are recommended for practical use as dielectrics and additions to lubricating oils and consistent lubricants. Copolymers of trioxan with a small quantity of thiiran obtained from boron trifluoride–diethyl ether[56,162] exhibit a thermal stability greater than that of homopolymers or other copolymers of trioxan.

The possibility of the copolymerisation of thiirans with their oxygen analogues under the influence of inducers of the cationic type has been studied[163,164]. It was shown that in the presence of boron trifluoride–diethyl ether and trialkyloxonium salts over a wide range of PS and propene oxide, or epichlorhydrin concentrations polymers enriched in thiiran are formed. Having studied certain kinetic regularities of the process and the composition of the polymers formed, the investigators showed that the irreversible and quantitative conversion of the oxonium ion into the stable sulphonium ion rules out the possibility of the formation of a statistical copolymer of thiiran with oxiran, and in this instance only block copolymers or their mixtures with a homopolymer of thio-oxide could be obtained. The composition and structure of the polymer are determined by the ratio of the rates v_1, v_2, and v_3 of the processes which occur:



The irreversible change oxonium → sulphonium was used to prepare block-copolymers in the initiation of the polymerisation of thio-oxides by "living" polymers of polyoxides. On taking into account the intensely developing interchain exchange reactions which are characteristic of cationic polymerisation of heterocyclic compounds, we thought it possible to obtain[163] block-copolymers of a specified composition, but it was difficult to calculate for the formation of copolymers with sections of polyoxide and polythio-oxide of definite dimensions.

There have recently been studies of the copolymerisation of thio-oxides with carbon disulphide[165] and isothiocyanates[166]. Under the action of tertiary amines first an oligomeric ethylene trithiocarbonate is obtained, then low-molecular-weight crystalline copolymers with the structure:

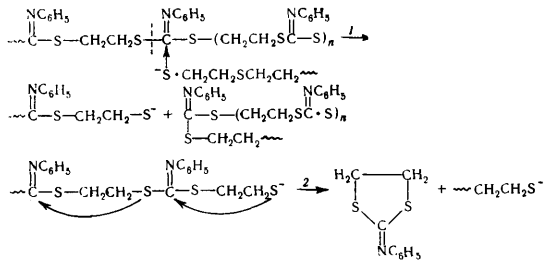


These investigations have progressed considerably[23,167-172]. In studying the copolymerisation of thio-oxides with isothiocyanates under the influence of butyllithium or the sodium–naphthalene complex in THF solution it was found that the process proceeds by a "living" chain mechanism with the formation of high-molecular-weight products exhibiting increased resistance to radiation. Some of the rules for the process were investigated by the example of the copolymerisation of ethylene sulphide with phenyl isothiocyanate. The isothiocyanate, which is active in relation to the inducer and to the $-CH_2CH_2S^-$ anion, reacts at a high rate with butyllithium, forming the anion of low activity $-C(=NR)S^-$, which is incapable of breaking the C=S bond of the isothiocyanate, but breaks the α-thio-oxide ring. Such selective interaction of the monomer with anions of different activity leads to the preparation of a copolymer of strictly alternating structure. In this process the relative reactivity of the phenyl isothiocyanate is considerably greater than that for alkyl isothiocyanates[170].

At equimolecular ratios of the reactants or with an excess of isothiocyanate a copolymer is formed in quantitative yield. An excess of ethylene sulphide (which is capable of homopolymerisation) does not lead to the production of the block-copolymer

$$[-SCH_2CH_2SC(=NR)S-]_n \cdot [-SCH_2CH_2]_m,$$

of calculated composition; the process is complicated by secondary phenomena arising after the disappearance of isothiocyanate from the system. The active polymeric anion $\sim CH_2CH_2SCH_2CH_2S^-$, by acting on the chain of the copolymer, brings about its breakdown to cyclic 2-phenylimino-1,3-dithiolane:



Finally, in the excess of ethylene sulphide there is complete breakdown of the copolymer that has been formed into cyclic dithiolane and the quantitative formation of the homopolymer of ES. In the copolymerisation of equimolecular quantities of phenyl isothiocyanate and PS it was shown that at 20°C even at different stages of the conversion the growth of the chain of the copolymer is accompanied by the formation of 2-phenylimino-4-methyl-1,3-dithiolan and above 65°C the process is shifted completely to the side of formation of the less strained cyclic dimer. Carrying out the copolymerisation under milder conditions in the presence of hexamethylphosphortriamide leads to a minimum in the decomposition of the copolymer[171].

From the published results discussed above the polymerisation and copolymerisation of thio-oxides under the influence of various catalytic systems has attracted great attention. In the most recent publications special sections are devoted to these problems[57,90]. There have been communications dealing with the possibility of the practical application of polymeric materials based on poly(alkene sulphides).[174-176] This all provides a basis for suggesting the wide use of polymers based on alkene sulphides in the not too distant future.

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Tautomerism of Aromatic Azo-compounds

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Recent results on the tautomeric properties of aromatic azo-compounds in neutral and acid solutions are reviewed. The tautomerism of the conjugate acids of azo-compounds (the *trans*-azonium cations) is discussed, and also the tautomeric equilibria between azo-forms and quinone hydrazones in acid solutions of *p*-aminoazo-compounds and in neutral solutions of hydroxyazo- and aminoazo-compounds. Available qualitative and quantitative results on the effects of substituents and of the properties of the medium on the position of tautomeric equilibrium are compared. The problem of applying correlation analysis to tautomeric systems is analysed. A list of 179 references is included.

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I. INTRODUCTION

Azo-compounds constitute an extraordinarily interesting and important class of compounds from both practical and theoretical points of view. The ready availability, cheapness, and versatility of properties have guaranteed to azo-compounds a high proportion of the range of organic dyes manufactured by industry[1]. Azo-compounds have found wide application in the laboratory as acid–base, redox, metallochrome, and other indicators, stains for bacteriological and histological investigations, standard materials in adsorption chromatography, etc.

The study of azo-compounds has been of great value for the development of theoretical organic chemistry. Together with triphenylmethane, keto–enolic, and certain other classes of compounds, azo-compounds have been widely used in developing and testing theories of colour and constitution, indicator action, and acid–base and tautomeric transformations.

The tautomeric properties of certain aromatic azo-compounds were detected as early as the beginning of the twentieth century. Hantzsch and several other investigators (see list of references[2]) studied the tautomerism of the conjugate acids of *p*-aminoazo-compounds. Somewhat later[3] tautomerism was confirmed between azoid and quinone hydrazone forms in neutral solutions of hydroxyazo-derivatives of naphthalene. Finally, the tautomerism of the conjugate acids of *trans*-azo-compounds was studied as early as the 1960s.[4]

It can be stated without exaggeration that almost all known methods of investigating tautomeric equilibrium have been used for the quantitative and qualitative study of tautomeric relations in various classes of azo-compounds. Many of these methods were in fact first developed in connection with azo-compounds.

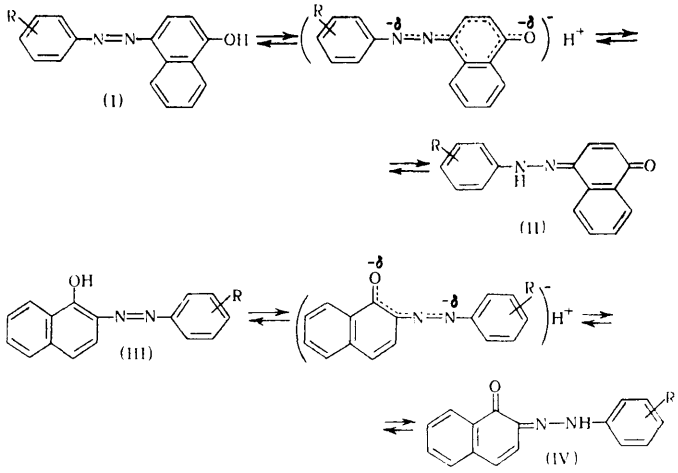
The total number of papers on the tautomerism of aromatic azo-compounds can hardly be fewer than those on classical keto–enol tautomerism. However, no

reviews are available on the present state of this problem. The present survey deals mainly with papers dating from 1955 (up to the beginning of 1970 inclusive). Bibliographies of earlier investigations will be found in the monographs by Venkataraman[1] and by Zollinger[5] and also in reviews[2,6].

II. TAUTOMERISM OF HYDROXYAZO-COMPOUNDS

1. Hydroxyazo-compounds of the Naphthalene Series

A wide circle of investigators became interested in the tautomerism of hydroxyazo-compounds after Zincke and Bindewald[7] had shown that the same product is obtained by coupling the benzenediazonium ion with 1-naphthol and by condensing phenylhydrazine with naphtha-1,4-quinone. The structure of this product, which could be represented by either formula (I) or (II) (both with R = H) became a matter of controversy (lists of references will be found in papers[8,9] and in monographs[1,5]).



Zincke had already suggested[7] that a mobile equilibrium between the two forms might be established in solution. A similar suggestion was made for the product of the condensation of phenylhydrazine with naphtha-1,2-quinone, which proved to be identical with 2-phenylazo-1-naphthol (III: R = H). The concept of tautomerism between azo-forms (I and III) and quinone hydrazone forms (II and IV) in solutions of *p*- and *o*-hydroxyazo-compounds of the naphthalene series has since been put forward several times, but it became generally accepted after the classic work of Kuhn and Bär[3].

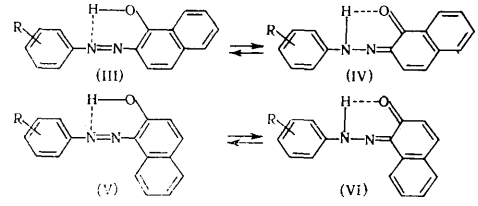
These workers suggested that the absorption spectrum of (I) should be analogous to that of its *O*-methyl ether, and the spectrum of (II) to that of its *N*-methyl derivative. On comparing the spectra of 4-phenylazo-1-naphthol in various solvents with the spectra of its *O*- and *N*-methyl derivatives, they concluded that the tautomeric equilibrium (I) $\rightleftharpoons$ (II) was established in all the solutions studied. The position of this equilibrium (according to modern views it should involve a common ion) depends in considerable measure on the nature of the solvent: e.g. it is displaced towards (I) in pyridine, but towards (II) in glacial acetic acid. In the case of *o*-hydroxyazo-compounds of the naphthalene series, according to these workers[3], the tautomeric equilibrium (III) $\rightleftharpoons$ (IV) is displaced in favour of the quinone hydrazone form (IV) in the majority of solvents.

The concept of tautomerism was developed in a large number of studies on the absorption spectra of *o*- and *p*-hydroxyazo-compounds of the naphthalene series[10-22]. The spectra of derivatives of 4-phenylazo-1-naphthol exhibit two maxima at 390–420 and 470–510 nm, due to the presence respectively of azoid and quinone hydrazone forms in solution. Variation in the polarity and also the solvating power of the solvent leads to a shift in the tautomeric equilibrium: the optical density at the absorption maximum of one form increases, while that at the maximum of the other form decreases. In some cases an isosbestic point is observed in the spectra with variation in the solvents (mixtures of alcohols with water[15,19]). Frequently, however, such a point cannot be distinguished, owing to the effect of the solvent on the spectra of the tautomers[3,14].

Increase in the polarity of the solvent displaces the equilibrium (I) $\rightleftharpoons$ (II) towards the more polar quinone hydrazone form. At the same time, the formation of hydrogen bonds with the solvent stabilises the azo-form. The overall sequence of solvents, producing an increasing proportion of the quinone hydrazone form according to Burawoy and Thompson[14], is—hexane < alcohol < benzene < chloroform < 50% aqueous alcohol < acetic acid. Increase in the alkalinity of the medium leads to a shift in the equilibrium towards the azo-form[21].

Solvation stabilisation of the quinone hydrazone form is prevented by substituents *ortho* to the azo-bond. Hence solvents have opposite effects on *o*- and *p*-hydroxyazo-compounds: in aprotic solvents the quinone hydrazone is preferred, but in alcohols the azo-form[14].

The influence of substituents on the equilibrium (I) $\rightleftharpoons$ (II) has been assessed from the relative intensities of the absorption maxima due to the two tautomeric forms[10,13,14,17,23]. Electron-donating *meta*- and *para*-substituents in the benzene ring of (I) increase the proportion of the azo-form; but electron-accepting substituents shift the equilibrium towards the quinone hydrazone form (II)

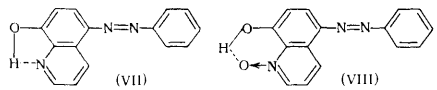


With *o*-hydroxyazo-compounds of the naphthalene series—notably with derivatives of 2-phenylazo-1-naphthol (III) and 1-phenylazo-2-naphthol (V)—the influence of solvents on the equilibria (III) $\rightleftharpoons$ (IV) and (V) $\rightleftharpoons$ (VI), and hence on the spectra of solutions of these compounds, is considerably smaller than in the case of *p*-hydroxyazo-compounds[3,13]. The explanation is that the tautomeric equilibrium of *o*-hydroxyazo-compounds is displaced to a considerable extent towards the quinone hydrazone forms[3,10,13,20].

The shift in equilibrium towards forms (IV) and (VI) of *o*-hydroxyazo-compounds is explained by the presence of a strong intramolecular hydrogen bond, first suggested by Oddo and Puxeddu[24]. This hypothesis has since been confirmed by a study of the infrared spectra[20,25-28]. An intramolecular hydrogen bond stabilises the quinone

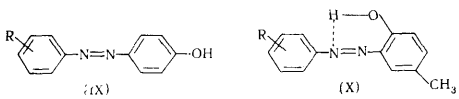
hydrazone form† and leads to a sharp decrease in the overall basic strength of the *o*-hydroxyazo-compound [30,31], together with the appearance of chelating properties. These are particularly strongly developed in *oo'*-dihydroxyazo-compounds, which are often used as analytical reagents for metals.

The intramolecular hydrogen bond in compounds of the type (III) and (V) forms part of a quasi-aromatic six-membered ring [32,33], the energy of formation of which may reach 16 kcal mole^{-1}. [33] This explains the absence of frequencies due to the hydroxy-group from the infrared spectra of *o*-hydroxyazo-compounds of the naphthalene series [27,34], the bathochromic shift in the ultraviolet spectra of *o*-hydroxyazo-compounds compared with the *para*-isomers [35], and also the difficulty of exchanging the hydroxyl hydrogen for deuterium by boiling in heavy water [36].



(VII) (VIII)

8-Hydroxy-5-phenylazoquinoline (VII) and especially its *N*-oxide (VIII) provide examples of intramolecular hydrogen bonds which stabilise azo-forms [16].



(IX) (X)

The influence of substituents on the strength of the hydrogen bond, and also the effect of the bond on the basic strength, have been assessed from the difference in basicity between the substituted *p*- and *o*-hydroxyazobenzenes (IX) and (X). [31,37] If the hydroxy-group has the same electronic effect in *para*- and *ortho*-positions, and the presence of an unchanged substituent—the 5-methyl group in (X)—can be neglected, the hydrogen bond in (X) can be characterised by the difference $pK_{(X)} - pK_{(IX)} = pK_H$.

Electron-acceptor substituents R produce a decrease in pK_H by diminishing the electron density on the nitrogen atom [31,37]. The correlation of pK_H with the σ-constants of the substituents is characterised by the parameter $\rho = -0.531$ [37] or -0.489 [31], while the relation $pK_{(X)} = f(\sigma)$ has $\rho = -1.21$ [37]. Comparison of these values confirms that the influence of substituents on the basicity of *o*-hydroxyazo-compounds is largely transmitted through the nitrogen atom and the hydrogen bond.

A similar conclusion was reached by Korolev and Stepanov [38], who used a two-parameter correlation of the pK_a of derivatives (X) with the σ^-- and σ-constants of the substituents. Here the σ^--constants represented the effects of substituents transmitted through the azo-group and the oxygen atom; while the σ-constants represented effects transmitted through one of the nitrogen atoms and the hydrogen bond. The values obtained for ρ_1 and ρ_2 were respectively -0.396 ± 0.108 and -0.757 ± 0.180.

Spectrophotometric data indicate [13] that the influence of the nature of substituents on the position of the (III) ⇌ (IV) equilibrium is similar to that found for the (I) ⇌ (II) equilibrium. Quantitative results have been obtained by means of ^{14}N-nuclear magnetic resonance spectroscopy (Table 1). Azobenzene and 10-*p*-methoxyphenylazo-9-phenanthrol were used as model compounds having an azoid and a quinone hydrazone structure. The presence of a mobile proton in the latter form impedes accurate determination of the signal to a greater extent the higher the concentration of this form. Therefore the values in Table 1 are insufficiently accurate for the application of correlation analysis to investigate the relation between the position of tautomeric equilibrium and the nature of the substituent.

Table 1. Content of quinone hydrazone form in solutions of 1-phenylazo-2-naphthol derivatives in deuterochloroform [39].

Substituent	Quinone hydrazone, %	Substituent	Quinone hydrazone, %
4'-CN	97	H	79
3'-CN	91	4'-Cl	78
3'-Cl	81	4'-Me	69
3'-Me	80	4'-OMe	52
3'-OMe	81	H (in hexane)	38

The proton magnetic resonance spectra could not be used for accurate determination of the position of tautomeric equilibrium [40,41], owing to rapid proton exchange between the two forms (lifetime of each form ~ 0.2 ms [39]).

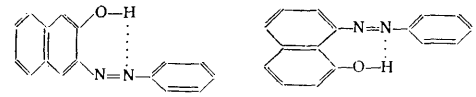
Studies have been made also of the polarographic behaviour [42,43], the surface tension of solutions [44], and the semiconductor characteristics of solid hydroxyazo-compounds [45,46]. These properties show little correlation with the tautomeric equilibrium position.

The ^{15}N-nuclear magnetic resonance spectra have been used to investigate the temperature dependence of the tautomeric equilibrium of 1-phenylazo-2-naphthol [47,48]. In dichloromethane the equilibrium shifts towards the quinone hydrazone form as the temperature falls ($\Delta H = 1.38$ kcal mole^{-1}). A similar conclusion was reached from a study of the absorption spectra at low temperatures [18,49]. With 4-phenylazo-1-naphthol cooling displaces the equilibrium towards the azo-form in ethanol, but towards the quinone hydrazone in methylcyclohexane ($\Delta H = 2 \pm 0.2$ kcal mole^{-1}) [18,50].

The basicity of derivatives of (V) has been studied in 50% aqueous ethanol [51], when the correlation

$$pK_a = 12.53 - 1.44\sigma^0 \quad (r = 0.99) \qquad (1)$$

was obtained. The dependence of the exponents of the effective basicity constants of a tautomeric mixture on the σ-constants of the substituents will be discussed in Section IV. Here we note merely that the linear relation (1) is due to a considerable shift in the equilibrium towards one of the tautomeric forms (cf. Table 1).



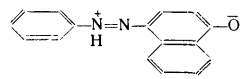
(XI) (XII)

3-Phenylazo-2-naphthol (XI) constitutes a special case among *o*-hydroxyazo-compounds of the naphthalene series.

† Quantum-chemical calculations by the Hückel molecular-orbital method, disregarding the effect of the hydrogen bond, predict for (III) that energy considerations will greatly favour the azo-form. With 4-phenylazo-1-naphthol the conjugation energy is similar for the two forms [29].

The diminished order of the 2–3 bond in naphthalene is responsible for the existence of (XI) only in the azo-form[52,53]. The presence of a hydrogen bond in (XI) has been proved by means of the infrared spectra[53] and is apparent in the lower activation energy of *cis–trans* isomerisation of (XI) in comparison with its *O*-methyl ether[54]. A similar phenomenon—the presence of a hydrogen bond in the absence of azo-quinone hydrazone tautomerism—has been shown also with *peri*-hydroxyazo-compounds of the naphthalene series (XII).[55]

Formulae (II), (IV), and (VI) probably do not represent accurately the structure of the quinone hydrazone forms of hydroxyazo-compounds. The lower frequency and intensity of vibrations of the CO group in the infrared spectra of (I) and (V)[26,53] indicate that zwitterionic structures of the type



(XIII)

which diminish considerably the order of the C=O bond, make a large contribution, a conclusion supported by measurements of the dipole moments of (I).[56] Since the hydroxy-group is a strong electron-donor substituent, there is no need to take into account the possible appearance of hydrazone tautomers with the proton on the α-nitrogen atom (Section IV).

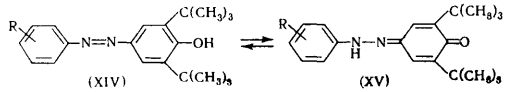
Infrared spectra indicate that hydroxyazo-compounds which are capable of tautomerism are present in the solid state as quinone hydrazones or as tautomeric mixtures[15].

2. Hydroxyazo-compounds of the Benzene and Anthracene Series

It has been concluded, from a comparative study of the ultraviolet spectra of hydroxyazobenzene, its derivatives, and their *O*-methyl ethers[10,11,22,57–59], proton magnetic resonance[40] and infrared[60] spectra, and polarographic investigation[42,43], together with a study of *cis–trans* isomerisation[61,62], that both *ortho*- and *para*-hydroxy-derivatives of azobenzene exist in the azo-form. The weak fluorescence observed with *o*- and *p*-hydroxyazobenzene[49] suggests that their solutions may contain very small quantities of the quinone hydrazone forms. True azo-compounds are incapable of fluorescence, which, on the other hand, is characteristic of all compounds having a hydrazone structure.

Dual reactivity is probably the explanation of published information on the reaction of 4-hydroxy-2′(or 4′)-nitroazobenzene derivatives with 2,4-dinitrophenylhydrazine[63] and also on their Diels–Alder reaction with cyclopentadiene[64].

The only known exception among hydroxyazo-compounds of the benzene series is provided by derivatives of 2,6-di-t-butyl-4-hydroxyazobenzene (XIV), for which the equilibrium

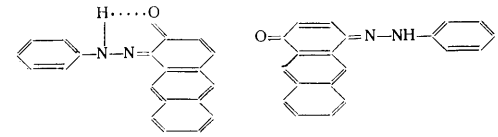


(XIV) (XV)

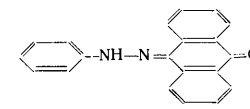
has been demonstrated (for all R other than $N(CH_3)_2$ and OCH_3)[65]. This exception is explained by the greater tendency of sterically hindered phenols to pass into quinoid forms[66]. The corresponding equilibrium constants, determined spectrophotometrically[67], show that the introduction of electron-acceptor substituents R increases the proportion of (XV), as with hydroxyazo-compounds of the naphthalene series.

Investigation of the basicity of *o*- and *p*-hydroxyazobenzene derivatives revealed in all cases a linear dependence of pK_a on the σ-constants of the substituents[31,37,68,69]. In 96–100% sulphuric acid doubly charged cations may be formed, probably by protonation not only of the azo-group but also of the hydroxyl[70].

When the absorption spectra of the products obtained by coupling 1-, 2-, and 9-anthrols with the benzenediazonium ion are compared with those of their *O*-acetyl derivatives, it is evident that *p*-hydroxyazo-compounds of the anthracene series exist predominantly in the quinone hydrazone form[11,71,72]. The tautomeric properties of (XVI) are confirmed by the strong fluorescence of its solutions, and also by the fact that the product (XVI) obtained by condensing phenylhydrazine with anthraquinone is identical with 10-phenylazo-9-anthrol prepared by azo-coupling[73].

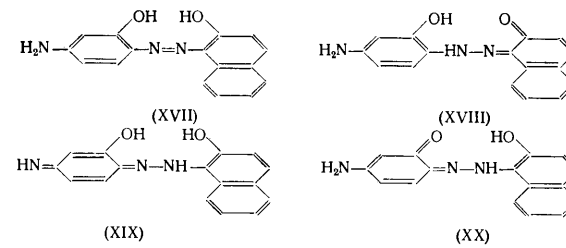


$\lambda_{max} = 511$ nm[11] $\lambda_{max} = 506$ nm[11]



(XVI)

The displacement of the tautomeric equilibrium towards the quinone hydrazone form on passing from hydroxyazo-derivatives of benzene to those of polyacenes was attributed by Ospensen[11] to a fall in the redox potential of the corresponding quinones on passing from *p*-benzoquinone (E_0 = 0.715 V, alcohol) to naphtha-1,4-quinone and anthra-1,4-quinone (0.484 and 0.401 V). This rule breaks down when we compare *p*- and *o*-hydroxyazo-derivatives of naphthalene with the redox potentials of the *o*-naphthaquinone (0.555 V, water) and *p*-naphthaquinone, which is explained by the presence of an intramolecular hydrogen bond in the *o*-hydroxyazo-compound. Similar results on a shift in the tautomeric equilibrium on passing from hydroxyazo-derivatives of benzene to those of naphthalene and anthracene were obtained[74] in a study of monolayers of azo-compounds having long alkyl groups.



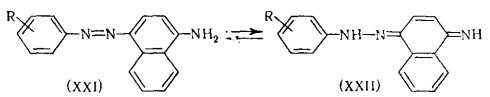
(XVII) (XVIII)

(XIX) (XX)

An interesting case of tautomerism has been described recently by Dedkov and Kotov[75] with 1-*p*-amino-*o*-hydroxyphenylazo-2-naphthol, for which the four tautomeric forms (XVII)–(XX) are possible. The ultraviolet spectra, supported by Hückel molecular-orbital calculations, indicate that three forms (XVII)–(XIX) are in equilibrium in the proportions 1 : 1.2 : 1.25.

III. TAUTOMERISM OF AMINOAZO-COMPOUNDS

The possibility of tautomerism between the azo-form (XXI) and the quinone hydrazone (XXII) in neutral solutions of *o*- and *p*-aminoazo-compounds of the naphthalene series has been investigated by many workers, mainly by comparing the absorption spectra of the compounds, their *N*-acetyl derivatives [35,71,76,77], and their *NN*-dimethyl derivatives [35] with those of the corresponding azo-compounds containing no auxochromic group [78,79]. Most authors have concluded that the quinone hydrazone form (XXII) is absent from solutions of *p*-aminoazo-derivatives of naphthalene.

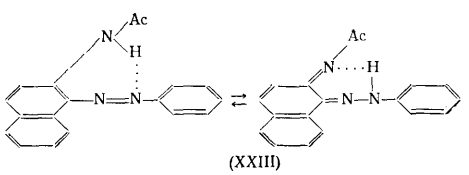


(XXI) (XXII)

No definite conclusion can yet be reached concerning *o*-aminoazo-compounds. There are results indicating that they exist in the quinone hydrazone form containing an intramolecular hydrogen bond [35], and also that tautomerism is absent in this case [78,80]. The presence of a strong intramolecular hydrogen bond in the naphthalene derivatives is confirmed by infrared spectroscopy [81,82].

The existence of aminoazo-compounds in the azo-form is confirmed by comparing their dipole moments with those of the corresponding aniline derivatives [83] and also by polarographic investigations [84]. Filippychev [85] reported that the solid hydrazone forms (XXII) could be obtained by heating the compounds in concentrated hydrochloric acid. The products could not be diazotised. However, no elementary analysis or other evidence of structure was given [85].

The *N*-acyl derivatives cannot be regarded as model compounds having an undoubted azo-structure. By diminishing the basic strength of the amino-group and thereby levelling out those of the two reaction centres [86] the acyl group makes azo–quinone hydrazone tautomerism more probable. Skulski and Urbanski [77] have mentioned the possibility of such tautomerism with 2-acetamido-1-phenylazonaphthalene

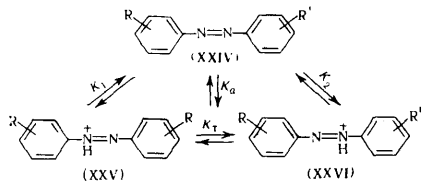


(XXIII)

Spectroscopic results indicate that aminoazo-derivatives of anthracene are probably capable of tautomerism with quinone hydrazone forms [71,72], but this equilibrium has not been examined in detail.

IV. TAUTOMERISM OF CONJUGATE ACIDS OF AZO-COMPOUNDS

Salt formation by azo-compounds in concentrated mineral acids has been known for a long time [87–89], but the structure of the products has only recently become a matter of controversy. If it is postulated that an azo-group contains two potentially basic centres, monosubstituted and unsymmetrically disubstituted azobenzenes (XXIV) may be expected to form two tautomeric conjugate acids (XXV) and (XXVI):



(XXIV) (XXV) (XXVI)

The effective basicity constant K_a and the tautomeric equilibrium constant K_T will then be related to K_1 and K_2 by the formulae [90]

$$K_a = \frac{K_1 \cdot K_2}{K_1 + K_2} \tag{2}$$

$$K_T = \frac{[XXV]}{[XXVI]} = \frac{K_2}{K_1} \tag{3}$$

Jaffé and his coworkers used correlation analysis to examine the possibility of the tautomerism (XXV) ⇌ (XXVI) in the cases of monosubstituted [91] and disubstituted [68] azobenzenes. If the influence of the substituents on the acid–base properties of these tautomers is described by Hammett's equation

$$pK_1 = (pK_1)_0 - \rho_1\sigma \tag{4}$$

$$pK_2 = (pK_2)_0 - \rho_2\sigma \tag{5}$$

and (4) and (5) are expressed as powers of 10, on substituting for K_1 and K_2 in Eqn. (2), we obtain

$$K_a = \frac{(K_1)_0 (K_2)_0 \cdot 10^{(\rho_1+\rho_2)\sigma}}{(K_1)_0 10^{\rho_1\sigma} + (K_2)_0 10^{\rho_2\sigma}} \tag{6}$$

or, taking logarithms,

$$pK_a = (pK_1)_0 + (pK_2)_0 - (\rho_1 + \rho_2)\sigma + \lg[(K_1)_0 10^{\rho_1\sigma} + (K_2)_0 10^{\rho_2\sigma}] \tag{7}$$

Equation (7) shows that the dependence of the exponents of the effective basicity constants of the tautomeric system on the σ-constants of the substituents is represented by a curve having the straight lines (4) and (5) as asymptotes. Analysis of Eqn. (7) by Kabachnik [92,93] and by Jaffé [91,94] indicates that this generally non-linear relation becomes linear when

$$\rho_1 = \rho_2 \tag{8}$$

i.e. when the substituents do not affect the position of the tautomeric equilibrium. Furthermore, the curvature of the pK_a–σ relation becomes slight with closely similar values of ρ_1 and ρ_2, with a considerable shift in the equilibrium towards one of the tautomers

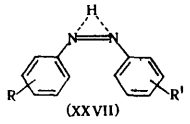
$$K_1 \gg K_2 \quad \text{or} \quad K_1 \ll K_2 \tag{9}$$

and finally with large absolute values of ρ_1 and ρ_2. [95] In all these cases the dependence of pK_a on σ for the tautomeric systems can be represented approximately by a straight line with a high correlation coefficient‡.

Jaffé and his coworkers [68,91] showed that values of pK_a for salt formation by a large number of azobenzene derivatives vary linearly with the σ^+-constants of the substituents (in the case of disubstituted derivatives the sum of

‡ By plotting model curves of Eqn. (7) we have shown that, if the experimental error is taken into account, the curvature becomes significant when very narrow boundary conditions, $|\rho_1 - \rho_2| \geq 2$ and ρ_1 or $\rho_2 < 3$, are satisfied simultaneously. For the compounds studied K_T varies between 0.3 and 3.

the σ^+-constants was taken) (Fig. 1). Since in this case it could not be predicted *a priori* that condition (8) or (9) would be satisfied, these workers concluded that the azo-group acts as a single reactive centre in salt formation. The structure of the conjugate acids of azobenzene and its derivatives would then be represented by the formula



(XXVII)

in which the proton is attached to both nitrogen atoms.

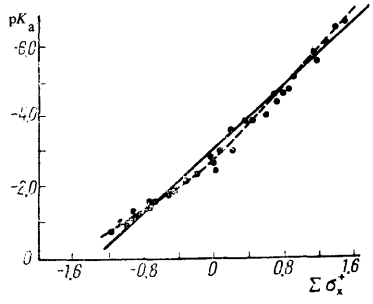
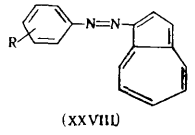


Figure 1. Dependence of pK_a for substituted azobenzenes on the σ^+-constants of the substituents[68] (sulphuric acid containing 20 vol.% of alcohol). The broken curve has been plotted from Eqn. (7) with $\rho_1 = 1.7$ and $\rho_2 = 3.0$ (see Section IV).

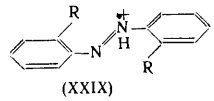
A linear dependence of pK_a on σ was found also by Gerson and Heilbronner[96] when studying the basicity of substituted phenylazoazulenes



(XXVIII)

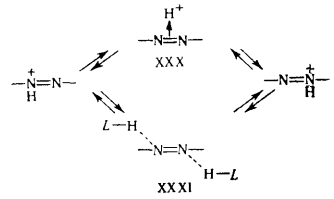
The azobenzene cation has subsequently been assumed to have a symmetrical structure in order to explain differences in the spectra of the conjugate acids of azobenzene and benzylideneaniline[97], and also in quantum-mechanical calculations of the spectra of azobenzene in concentrated sulphuric acid[98]. Simultaneous attachment of the proton to the lone pairs of both nitrogen atoms requires that the conjugate acid of azobenzene should have the *cis*-configuration, independently of the configuration of the original base. In 1960, however, Lewis[99] and Gerson et al.[100] showed simultaneously that *trans*- and *cis*-azobenzene form two conjugate acids differing in absorption spectra and in basic strength. Thus formula (XXVII) was proved to be incorrect, at least for conjugate acids of *trans*-azo-compounds.

A detailed investigation of the structure of *trans*-azonium cations has been made by Haselbach and Heilbronner[4,101], several aspects of the problem being examined. With unsymmetrical *N*-protonation the equivalence of the two identical substituents in the *ortho*- and *ortho'*-positions with respect to the azo-group in the compound



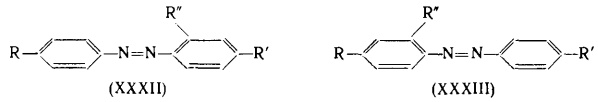
(XXIX)

should break down. Splitting of the signals due to protons in R should then be observed in the proton magnetic resonance spectra of (XXIX). Such splitting has been found with 2,2'-di- and 2,2',4,4'-tetra-methoxyazobenzenes in a mixture of trifluoroacetic and perchloric acids[4] and also with 2,2'-azoisobutane in 95% sulphuric and dideutero-sulphuric acids[101]. The absence of splitting with a large number of other methylated azobenzenes was explained[4] by rapid proton exchange between the tautomeric forms. The intermediate state is the π-complex (XXX) (intramolecular rearrangement) or a complex with two solvated protons of the solvent (XXXI) (intermolecular rearrangement)[101]:



XXX XXXI

As other evidence of unsymmetrical protonation of the azo-group Haselbach[4] examines the change in basicity on the introduction of substituents at position 2 or 2' in an unsymmetrically substituted azobenzene. If protonation of the azo-group is symmetrical, the compounds



(XXXII) (XXXIII)

should be similar in basicity. In fact (XXXII) and (XXXIII) differ in basic strength, to a greater extent the greater the difference between the properties of the substituents R and R'. With $\sigma_R - \sigma_{R'} = 1.56$, for example, the difference $pK_{(XXXII)} - pK_{(XXXIII)} = 1.90$.[4]

Finally, accepting the hypothetical unsymmetrical protonation of the azo-group, Haselbach attempted to estimate separately the effects of substituents on the nearer and on the more remote nitrogen atom by means of the arbitrary parameters R_α and R_β. He treated basicity data on 57 azobenzene derivatives by the method of least squares, and after several successive approximations he obtained values of R_α and R_β for the 4-substituents—methyl (−0.21 and −0.75), methoxyl (−0.31 and −1.85), and nitro (1.37 and 2.76).[4] This worker regards the statistically significant difference in the quantities R_α and R_β as confirmation of the starting hypothesis of unsymmetrical *N*-protonation.

On the assumption of a parallelism between the effects of substituents in the benzylideneaniline and azobenzene series Haselbach used data on the basic strengths of the former derivatives[101-103] to obtain the Hammett parameters $\rho_\alpha = 1.74$ and $\rho_\beta = 2.99$ for the effects of substituents on the basicities of the nearer and more remote nitrogen atom of the azo-group[4].

Since benzylideneaniline derivatives have a non-planar structure, in contrast to azo-compounds, the values obtained by Haselbach are extremely rough approximations. However, the following important conclusions can be reached on their basis. Thus if Eqn. (7) is plotted with $\rho_1 = 1.7$ and $\rho_2 = 3.0$ (broken curve in Fig. 1), it can be

concluded that Jaffé's results can be represented by this equation, and hence are consistent with the tautomerism (XXV) ⇌ (XXVI).

Since azobenzene itself is symmetrical, $(K_1)_0 = (K_2)_0$ in Eqns. (4) and (5). Substituting the values of ρ_α and ρ_β in these equations, we find that, when a substituent having $|\sigma| = 0.5$ is present in the azobenzene molecule, the content of one of the tautomeric forms is less than 20% ($K_T > 4.4$ or < 0.2). When the σ-constant of the substituent (or the difference between those of two substituents in different benzene rings) is unity, the position of tautomeric equilibrium will shift to 95% or more of one of the tautomers.

Unsymmetrical protonation of the azo-group is consistent with the proton magnetic resonance spectra of *p*-hydroxyazobenzene derivatives[104], the basic strengths and rates of oxidation of a series of azobenzene derivatives[105], and also the infrared spectra and the structure of complexes of azo-compounds with metal halides[106].

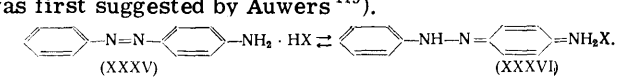
Thus it can be accepted as established that the protonation of *trans*-azo-compounds in concentrated acids is accompanied by the formation of a tautomeric mixture of the two cations (XXV) and (XXVI). This conclusion cannot be extended to the conjugate acids of *cis*-azo-compounds. Collins and Jaffé[107] showed that the basic strengths of *trans*-azo-compounds are correlated by the σ^+-constants, and those of the *cis*-isomers by the σ^--constants. The explanation of this difference is that the azo-group is an electron-acceptor reactive centre in *trans*-azo-compounds, but in *cis*-azo-compounds with their non-planar structure[108] the possibility of competing n,π-conjugation of the lone electron pairs of the nitrogen with the benzene rings confers an electron-donor character on the azo-group.

The extraordinarily deep colour of *pp'*-bisdimethylaminoazobenzene (XXXIV) in acid solution ($\lambda_{max} = 670$ nm) led Cilento[109] to attribute a π-complex structure to the conjugate acid of this aminoazo-compound. However, other results[110,111] indicate that the properties of (XXXIV) are entirely consistent with those of other azo-compounds. Thus there is no need to assume a special structure for the conjugate acid in the case of (XXXIV).

An interesting but hitherto uninvestigated fact is the change in the spectra of azobenzene (and its derivatives) in oleum[89], which is attributed to the formation of a doubly charged salt.

V. TAUTOMERISM OF CONJUGATE ACIDS OF *p*-AMINOAZO-COMPOUNDS

Derivatives of *p*-aminoazobenzene have been widely used as indicators for almost a century[112]. After Thiele[113] had shown, and Hantzsch and Hilscher[87] had confirmed, that two series of isomeric salts§—yellow and reddish violet—can be isolated in the solid form from acid solutions of *p*-aminoazo-compounds, the hypothesis was put forward that the acid solutions contain two tautomeric forms, in which the proton is attached to the amino-group (XXXV) or to the azo-group (XXXVI) (the latter formula was first suggested by Auwers[115]).

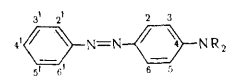


(XXXV) (XXXVI)

§ However, there is as yet no evidence that these salts differ in chemical structure. Their infrared spectra[114] suggest rather that the two series of salts of *p*-aminoazo-compounds are merely crystalline modifications.

This hypothesis is supported by spectroscopic investigations. The spectra of *p*-aminoazo-compounds in dilute acids exhibit two absorption maxima—in the region of 320 and 520 nm—in the range 300–600 nm[2] (Table 2). By analogy with azobenzene and its *p*-trimethylammonium derivative, whose spectra in neutral and weakly acid solutions have a maximum at 320 nm, the corresponding maximum in the spectra of *p*-aminoazo-compounds was assigned to the ammonium tautomer (XXXV). On the basis of a comparison with the spectra of azoanisole ($\lambda_{max} = 500$ nm[116]) and *p*-methylthioazobenzene (532 nm[117]) in concentrated acids, the maximum in the region of 520 nm was ascribed to the quinone hydrazone tautomer.

Table 2. Absorption spectra of some *p*-aminoazo-compounds in 50% alcoholic hydrochloric acid.



No.	4-Dimethylaminoazobenzene derivative	*C* line λ_{max} ($10^{-3}\varepsilon_C$)	*A* line λ_{max} ($10^{-3}\varepsilon_A$)	$\varepsilon_C/\varepsilon_A$	Ref.
1	(Aminoazobenzene)	500 (12.2)	320 (16.8)	0.73	131
2	(Dimethylaminoazobenzene)	20 (34.0)	320 (10.1)	3.4	131
3	(4-Ethylmethylaminoazobenzene)	516 (21.5)	318 (15.2)	1.4	131
4	(Diethylaminoazobenzene)	518 (9.50)	318 (19.5)	0.49	131
5	3-Methyl	508 (2.6)	a	—	148
6	3-Ethyl	490 (1.0)	a	—	148
7	3-Isopropyl	460 (0.6)	a	—	148
8	2-Methyl	512 (47.6)	330 (3.0)	15.9	118
9	2,6-Dimethyl	496 (53.2)	328 (2.0)	26.8	118
10	2'-Methyl	515 (5.10)	325 (17.6)	0.29	131
11	2'-Ethyl	510 (2.60)	332 (18.1)	0.14	131
12	2'-Carboxylic acid	518 (43.4)	325 (3.3)	13.1	131
13	3'-Ethoxy	522 (36.6)	318 (8.2)	4.5	131
14	3'-Nitro	500 (37.8)	312 (10.5)	3.6	131
15	4'-Methoxy	548 (18.5)	352 (18.2)	1.0	131
16	4'-Nitro	512 (61.6)	332 (7.10)	8.7	131

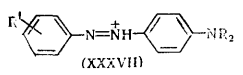
[a] Values not given in Ref. 148.

The absorption spectra of acid solutions of *p*-aminoazo-compounds were analysed in papers by Hantzsch (bibliography in Ref. 2), and the results have since been confirmed by many workers on a large number of compounds (see review[6]). This work demonstrated that the two maxima relate to different compounds. Thus Hantzsch noted long ago that increase in the acid concentration was accompanied by an increase in optical density at the 520-nm maximum but a decrease at the 320-nm maximum[2]. He interpreted this as due to a shift in the equilibrium in favour of the tautomer (XXXVI). A study of a series of methylated[118] and sulphonated[119] derivatives of *p*-dimethylaminoazobenzene showed that, if the introduction of a substituent into the molecule increases the molar extinction coefficient at 520 nm, the coefficient at 320 nm decreases. Conversely, if substitution produces a decrease in the coefficient at 520 nm, the extinction coefficient at 320 nm increases. This agrees well with the view that the solution contains two compounds, whose concentrations are interrelated.

It is now generally accepted that tautomerism occurs in acid solutions of *p*-aminoazo-compounds. Isolated papers in which salt formation by these compounds was regarded as involving addition of a proton solely to the amino-group[120–123] or solely to the azo-group[89,124,125] were

based on incomplete data or erroneous concepts. They have all been subjected to soundly based criticism[6,117,126,127].

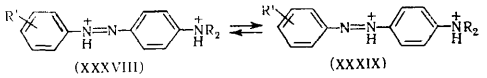
The possibility that the equilibrium may involve a tautomer with a proton attached to the α-nitrogen of the azo-group



(XXXVII)

can be assessed on the basis of the above analysis of the tautomerism of azonium cations (Section IV). Since the amino-group is a strongly electron-donating substituent (values of σ^+ for NH_2, $N(CH_3)_2$, and $N(C_2H_5)_2$ are respectively −1.3, −1.7, and −1.42[128]), it may be supposed that the proportion of the cation (XXXVII) in the tautomeric equilibrium of the conjugate acids of *p*-aminoazo-compounds should in most cases be insignificant. This conclusion is confirmed by quantum-mechanical calculations by the Hückel molecular-orbital method, which have shown that cation (XXXVII) is considerably less favoured energetically than are cations of the types (XXXV) and (XXXVI)[129].

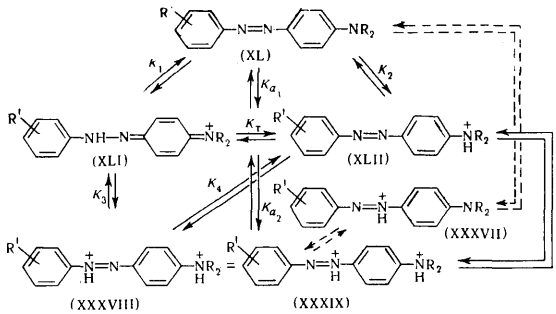
In concentrated mineral acids *p*-aminoazo-compounds add a second proton to form a doubly charged cation, whose structure is usually represented by the formula (XXXVIII). In view of the above discussion on the tautomerism of azonium cations, however, it must be assumed that a tautomeric equilibrium between the doubly charged cations (XXXVIII) and (XXXIX) is established in concentrated acids:



(XXXVIII) (XXXIX)

Whereas conversion of a *p*-aminoazo-compound into a monocationic salt will lead to a deepening of the colour of the solution from yellow to red-violet, addition of a second proton will [also] heighten its colour. The absorption maximum of the doubly charged cation usually lies in the range 410–440 nm,[130] which is approximately where the conjugate acid of azobenzene absorbs (435 nm).

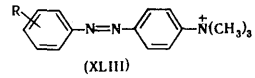
Thus the acid–base and tautomeric transformations of *p*-aminoazo-compounds (XL) can be represented over a wide range of acidities by the scheme



(XXXVIII) (XXXIX)

Values of pK_{a_1} for *p*-aminoazo-compounds vary in the range 1.8–2.5 (in 50% alcohol)[116,120,125,126,131,132]; those of pK_{a_2} lie either between −2.1 and −6.7 (aqueous sulphuric acid)[116,120,125] or between −2.3 and −8.5 (sulphuric acid containing 20 vol.% of alcohol)[95,133]. The acid–base properties of derivatives of *p*-aminoazobenzene have also been studied in aprotic solvents[134,135].

After completion of the first salt formation, changes occur in the solvation sheath of molecules of *p*-aminoazo-compounds in the acidity range $0 \geqslant H_0 \geqslant -1$. These changes are evident in the intensities of the absorption bands in the spectra of these compounds and also of *p*-phenylazophenyltrimethylammonium derivatives



(XLIII)

which are analogues of the ammonium tautomers (XLII)[130,133].

Pal'm and Khaldna[136,137] have studied similar changes with many organic bases in the same acidity range. The processes consist essentially in hydrogen bonding between the *p*-aminoazo-molecules and hydrated protons of the medium, which may be regarded as the initial stage of the second protonation.

Further increase in the acid concentration of the solution is accompanied by a shift in the equilibrium in favour of the tautomer (XLI)[68,126,131,138,139], which continues as far as the second salt formation (Fig. 2).

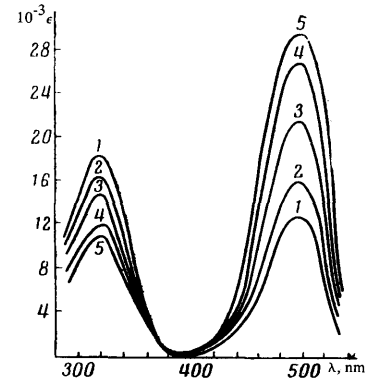


Figure 2. Absorption spectra of *p*-aminoazobenzene in different concentrations (N) of sulphuric acid: *1*) 3.2; *2*) 4.9; *3*) 6.5; *4*) 9.8; *5*) 10.7[160].

Most papers on tautomerism in acid solutions of *p*-aminoazo-compounds published during the past fifteen years had the aim of assessing quantitatively the position of the (XLI) ⇌ (XLII) equilibrium and the influence of substituents on this equilibrium. Since salt formation by *p*-aminoazo-compounds takes place almost instantaneously even at low temperatures[140], attention has been concentrated on physicochemical methods, mainly spectrophotometry. A substantial obstacle was the impossibility of obtaining a solution containing only one of the tautomers¶. It was therefore impossible to determine the molar extinction coefficients of the tautomers and to apply the usual methods of quantitative spectrophotometric analysis to the equilibrium.

¶ As Milliaresi and Izmail'skii assume[141], only the cation (XLI) is present in dichloromethane to which trifluoroacetic acid has been added, but its spectrum undoubtedly differs from the spectrum in aqueous solutions.

One attempt to avoid this difficulty was the method, used by several authors [142-146] and most consistently by Sawicki [117,127,131,147], of characterising the position of the tautomeric equilibrium by the intensity ratio of the absorption maxima corresponding to the two tautomers. The ratio ϵ_C/ϵ_A was employed, where ϵ_C and ϵ_A are the molar extinction coefficients of the solution at the absorption maxima of the quinone hydrazone and the ammonium tautomers respectively. It is easy to show that, if neither tautomer absorbs at the wavelength of maximum absorption by the other,

$$\frac{\varepsilon_C}{\varepsilon_A} = \frac{[XLI]}{[XLII]} \cdot \frac{\varepsilon_{XLI}}{\varepsilon_{XLII}} = K_T \frac{\varepsilon_{XLI}}{\varepsilon_{XLII}} \qquad (10)$$

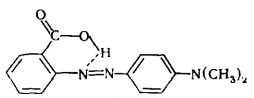
where $\epsilon_{(XLI)}$ and $\epsilon_{(XLII)}$ are the molar extinction coefficients of the tautomers at their maxima. The use of ϵ_C/ϵ_A instead of K_T is based on the postulate that the ratio $\epsilon_{(XLI)}/\epsilon_{(XLII)}$ is either constant or almost constant for all the compounds investigated.

Although such a postulate is admittedly inaccurate, it has helped to reveal several qualitative features of the effect of substituents in different positions in the molecule on the (XLI) ⇌ (XLII) equilibrium. Table 2 shows that replacing the hydrogen atoms of the amino-group by methyl groups creates a decrease in the proportion of the ammonium tautomer, probably owing to a diminution in its stabilisation by solvation energy [118]. Substitution of ethyl for methyl groups lowers ϵ_C/ϵ_A as a consequence of the larger positive inductive effect of ethyl groups, and perhaps partial emergence of the diethylamino-group from the plane of the molecule.

Substituents at position 3 or 5 in dimethylaminoazobenzene deflect the dimethylamino-group out of the plane of the benzene ring, thereby destroying its conjugation with the general π-system. Therefore the proportion of the quinone hydrazone tautomer falls with increase in the bulk of the substituent (compounds 5–7 in Table 2). This effect is present, although somewhat weaker, in aminoazobenzene derivatives [145]†.

Methyl groups at positions 2 and 6 greatly increase azo-protonation, which is explained by an increase in electron density on the β-nitrogen atom of the azo-group due to the $+I$-effect and hyperconjugation of the methyl groups [131]. In contrast, 2′-substitution sharply diminishes the proportion of the quinone hydrazone tautomer (compounds 10 and 11 in Table 2), which is interpreted by all authors as due to steric hindrance to attack by protons on the β-nitrogen atom, and also as indirect evidence of addition of the proton to the β- and not to the α-nitrogen atom. Furthermore, 2′-methyl groups somewhat disrupt the coplanarity of the molecule [104].

An exception among 2′-substituted derivatives is Methyl Red (No. 12 in Table 2). The sharp increase in ϵ_C/ϵ_A in this case is explained by the presence of an intramolecular hydrogen bond [142]



(XLIV)

Kipriyanov and Zhmurova [148] noted that even the 3-alkylation of (XLIV) does not appreciably diminish the proportion of the quinone hydrazone tautomer.

† It is interesting that 4-dimethylamino-3,5-dimethylazobenzene, which adds a proton only at the amino-group, does not possess the carcinogenic properties characteristic of most *p*-aminoazo-compounds [145].

The variation in ϵ_C/ϵ_A could not be used to indicate the effect of 3′-substituents, since the range of observable changes was narrow (compounds 13 and 14 in Table 2). Although this range is quite wide with 4′-substituted compounds, the conclusions reached by different workers [118,119,131,143] on the nature of the effect of 4′-substituents are often contradictory. The probable reason is that the constancy of the ratio $\epsilon_{(XLI)}/\epsilon_{(XLII)}$ originally postulated does not hold for these compounds. The most reliable conclusion is that the equilibrium (XLI) ⇌ (XLII) is displaced by electron-donor substituents in favour of the ammonium tautomer, and by electron-acceptor substituents towards the quinone hydrazone tautomer (compounds 15 and 16 in Table 2).

In a series of papers Jaffé and his coworkers [126,133,149-152] suggested two methods of using model compounds to determine K_T for the equilibrium (XLI) ⇌ (XLII). The compounds chosen as models were *p*-trimethylammonioazobenzene derivatives (XLIII), which are closely analogous to the ammonium tautomers (XLII). In the first of these methods, since used by Reeves [153], the molar extinction coefficients of the cations (XLII) and (XLIII) were equated:

$$\varepsilon_{(XLII)} = \varepsilon_{(XLIII)} \qquad (11)$$

The concentration of the ammonium tautomer was then calculated from the optical density of the solution of the *p*-aminoazo-compound at the wavelength of maximum absorption by the cation (XLII) (the total concentration of the tautomers was taken to be equal to the initial concentration of the base). This involved the assumption that the tautomer (XLI) did not absorb at this wavelength. Results [133] obtained by this method for a series of derivatives of dimethylaminoazobenzene in aqueous sulphuric acid containing 20 vol.% of alcohol are listed in column A of Table 3. An attempt was also made to allow for possible absorption by the tautomer (XLI) at the wavelength of maximum absorption by the tautomer (XLII). This absorption was assumed to be 2000 $mole^{-1}$ cm^{-1} (from data for 4-amino-3,5-di-t-butylazobenzene, which was considered [126] to add a proton only at the azo-group). These results are listed in column B.

Table 3. Values of K_T for dimethylaminoazobenzene derivatives (aqueous sulphuric acid containing 20 vol.% of alcohol) [133].

Substituent (4′-)	A	B	C
CH_3O	0.53	0.60	2.39
CH_3	1.44	1.88	4.13
H	2.10	3.10	7.15
Cl	1.80	2.40	5.02
Br	2.61	3.86	6.05
CF_3	3.57	5.62	16.8
NO_2	4.36	7.00	57.9

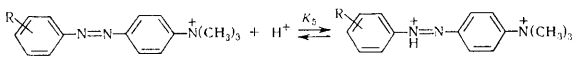
The second method proposed by Jaffé et al. utilised the pK_{a_2} values. Examining the formation of a dicationic salt of the *p*-aminoazo-compound (disregarding the presence of the tautomer XXXIX), Jaffé showed that

$$K_T = \frac{K_{a_2}}{K_4} - 1 \qquad (12)$$

(for notation see above scheme). Since K_4 was unknown, he assumed that

$$K_4 = K_5 \qquad (13)$$

where K_5 is the experimental equilibrium constant for



Values obtained for K_T by this method are given in column C of Table 3. They exceeded the spectrophotometric values by factors of 3–4. On comparing the results obtained, these workers were inclined to prefer the constants in column C.

A further defect of this work, in addition to the admitted inaccuracy of Jaffé's assumptions (Eqns. 11 and 13), is his neglect of the dependence of the position of tautomeric equilibrium on the concentration of acid in the solution. Nevertheless, the actual fact that the tautomeric equilibrium shifts with change in the acid concentration has enabled a method to be developed for determining K_T without the use of model compounds[154–156]. If the total concentration of tautomers in the solutions whose absorption spectra are illustrated in Fig. 2 is constant,

$$C_{XLI} + C_{XLII} = C_0 \qquad (14)$$

where C_0 is the initial concentration of the base, and Beer's law holds for both tautomers, the optical densities of these solutions are connected by a linear relation[67]. With the absorption maxima of the tautomers as analytical wavelengths (λ_{XLI} and λ_{XLII}), and provided that neither tautomer absorbs at the wavelength of maximum absorption by the other, the equation expressing this relation will be

$$\frac{D^{\lambda_{XLI}}}{\varepsilon^{\lambda_{XLI}}_{XLI}} + \frac{D^{\lambda_{XLII}}}{\varepsilon^{\lambda_{XLII}}_{XLII}} = C_0 d \qquad (15)$$

where the D are the optical densities of these solutions at λ_{XLI} and λ_{XLII}, the ϵ are the molar extinction coefficients of the tautomers (XLI) and (XLII) at these wavelengths, and d is the thickness of the cuvette. The validity of the assumption that one tautomer does not absorb at the wavelength of maximum absorption by the other can be checked by the method suggested in Ref. 67. Equation (15) enables us to find (either analytically or graphically) the quantities

$$D^{\lambda_{XLI}}_{max} = \varepsilon^{\lambda_{XLII}}_{XLI} C_0 d \qquad (16)$$

$$D^{\lambda_{XLII}}_{max} = \varepsilon^{\lambda_{XLII}}_{XLII} C_0 d \qquad (17)$$

which give the optical density of the solution at ϵ_{XLI} and ϵ_{XLII} if the equilibrium is completely displaced towards tautomer (XLI) (i.e. when $C_{XLI} = C_0$) or tautomer (XLII) (when $C_{XLII} = C_0$). After (16) and (17) have been evaluated, determining the molar extinction coefficients of the tautomers and calculating K_T in all the solutions investigated present no difficulty.

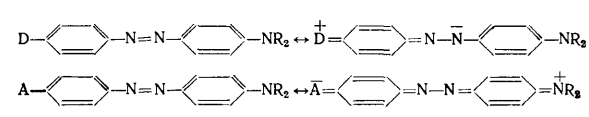
This method has been used to study the tautomeric equilibrium of several 3′- and 4′-substituted derivatives of aminoazobenzene, dimethylaminoazobenzene, and diethylaminoazobenzene[95,156,157]. Table 4 shows that 3′-substituents have little effect on the position of tautomeric equilibrium. In conformity with the discussion in Section IV, therefore, the dependence of pK_{a_1} on σ is linear for 3′-substituted dimethylaminoazobenzene[156]. The small changes in K_T with variation in the 3′-substitution from the nitro- to the methoxy-group suggests that the equilibrium (XLI) ⇌ (XLII) is insensitive to the inductive effect of the substituent.

This conclusion is supported by the correlations of $\lg K_T$ with the difference $\sigma^+ - \sigma_I$ or $\sigma^- - \sigma_I$ for +C and –C substituents respectively, which are found with 4′-substituted derivatives of dimethylaminoazobenzene and diethylaminoazobenzene[95,156] (Fig. 3). The dominant role of conjugation in the effect of substituents on the position of the tautomeric equilibrium of conjugate acids of *p*-aminoazo-compounds is consistent with the correlation found by Isaacs and Jaffé[133] between $\lg K_T$ and the σ^+- or σ^--constants ($r = 0.968$) for the approximate values of K_T determined by them for 4′-substituted dimethylaminoazobenzenes (Table 3, column C).

Table 4. Values of K_T with $H_0 = -1.20$ and parameters of Eqn. (18) for certain *p*-aminoazo-compounds[95] (values of H_0 from Ref. 159).

Substituent	*a*	*b*	*r*	K_T
p-Aminoazobenzene derivatives				
H	—0.620	0.217	0.995	0.44
3′-NO_2	—0.673	0.209	0.995	0.38
p-Dimethylaminoazobenzene derivatives				
H	0.241	0.104	0.994	2.3
4′-CH_3	0.078	0.102	0.993	1.6
4′-OCH_3	—0.066	0.091	0.974	1.1
4′-Br	0.127	0.114	0.998	1.8
4′-F	—0.305	0.090	0.976	0.65
4′-SO_3Na	0.457	0.080	0.983	3.7
3′-OCH_3	0.195	0.100	0.997	2.1
3′-Cl	0.273	0.114	0.976	2.7
3′-F	0.193	0.102	0.998	2.1
3′-COOH	0.149	0.106	0.999	1.9
3′-SO_3Na	0.136	0.100	0.991	1.8
3′-NO_2	0.159	0.075	0.995	1.8
Diethylaminoazobenzene derivatives				
H	—0.532	0.104	0.995	0.39
4′-CH_3	—0.715	0.128	0.997	0.27
4′-OCH_3	—	—	—	0.04
4′-F	—0.982	0.125	0.998	0.15
4′-Br	—0.724	0.100	0.995	0.25
4′-SO_2NH_2	—0.129	0.090	0.996	0.95
4′-CN	—0.006	0.099	0.992	1.30
4′-NO_2	+0.019	0.076	0.999	1.29
4′-$COCH_3$	—0.287	0.089	0.997	0.66
3′-OCH_3	—0.670	0.116	0.994	0.29
3′-Cl	—0.673	0.123	0.999	0.30
3′NO_2	—0.703	0.097	0.996	0.26

The simultaneous use in the correlation of values of σ^+ for electron-donor substituents and of σ^- for electron-acceptor substituents is explained by the presence of two reactive centres of opposite character—+C (amino-group) and –C (azo-group)—in the molecules of *p*-aminoazo-compounds. Electron-donor substituents (D) may undergo conjugation with the azo-group, and electron-acceptor substituents (A) with the amino-group:



This hypothesis explains several peculiarities of the behaviour of *p*-aminoazo-compounds containing strong –C substituents at position 4′[125,133,146]. Such compounds also exhibit an enhanced tendency to association both in solution[132,146] and in the gas phase[158].

The above effects of substituents on the (XLI) ⇌ (XLII) tautomeric equilibrium are consistent with calculations by the Hückel molecular-orbital method. Pullman and Baudel[161,162] showed that the proportion of a tautomer in the mixture varies directly with the electron density on the corresponding reactive centre. An attempt to assess separately conjugation and inductive effects on the tautomeric equilibrium has shown[129] that the π-electron densities on the reactive centres, and also the differences in delocalisation energies of the tautomers, are relatively insensitive to the inductive effect of the substituents, and also to the presence of substituents in the 3′ position.

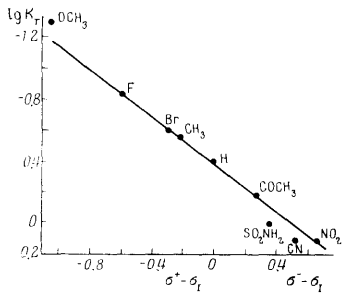


Figure 3. Dependence of $\lg K_T$ of 4′-substituted diethylaminoazobenzenes on $\sigma^+ - \sigma_I$ for electron-donor substituents and $\sigma^- - \sigma_I$ for electron-acceptor substituents[160].

The tautomeric equilibrium in acid solutions of *p*-aminoazo-compounds has been investigated quantitatively also by means of the proton magnetic resonance spectra[163]. The model compound used was 4-dimethylamino-3-methyl-3′-nitroazobenzene, which was assumed to add a proton solely at the amino-group. The calculation was based on the chemical shifts of the 2,6- and 3,5-protons and also on the position of the signal due to the *N*-methyl group. The results agree qualitatively with the above spectrophotometric data. This method could not be extended to a wide range of compounds owing to the relative inaccuracy (10–20%) of the constants obtained from the proton magnetic resonance spectra and to the inadequate solubility of the compounds.

Determination of the tautomeric equilibrium constants from the absorption spectra of solutions of *p*-aminoazo-compounds in different acid concentrations[154-156] has shown that $\lg K_T$ for the (XLI) ⇌ (XLII) equilibrium varies linearly[95,156,157] with the acidity function of the solution:

$$\lg K_T = a + b \cdot H_0 \qquad (18)$$

Parameters in Eqn. (18) are given in Table 4 for several *p*-aminoazo-compounds.

The dependence of the position of tautomeric equilibrium on the acid concentration of the solution is explained by the fact that the tautomers (XLI) and (XLII) belong to different chemical classes. Therefore their activity coefficients $f_{(XLI)}$ and $f_{(XLII)}$ vary differently with change in the properties of the medium, which in turn leads to a change in the concentration constant found for the tautomeric equilibrium:

$$K_T = K_T^* \frac{f_{XLII}}{f_{XLI}} = \frac{K_2^*}{K_1^*} \frac{f_{XLII}}{f_{XLI}} \qquad (19)$$

in which K_T* is the thermodynamic tautomeric equilibrium constant. Since K_T* is related to the thermodynamic constants K_1* and K_2* of the equilibria (XL) + H^+ ⇌ (XLI) and (XL) + H^+ ⇌ (XLII), we can express K_1* and K_2* in terms of the concentrations and the activity coefficients of the species involved in the equilibrium, substitute in Eqn. (19), take logarithms, and rearrange to obtain

$$\lg K_T^* = \lg \frac{[XLI]}{[XLII]} + \lg \frac{[H^+] \cdot f_{H^+} \cdot f_{(XL)}}{f_{XLII}} - \lg \frac{[H^+] \cdot f_{H^+} \cdot f_{XL}}{f_{XLI}} \qquad (20)$$

As

$$f_{H^+} \cdot [H^+] = a_{H^+} \qquad (21)$$

we can write from the definition of acidity function[164]

$$-\lg \left(a_{H^+} \cdot \frac{f_{XL}}{f_{XLII}} \right) = H_0' \qquad (22)$$

$$-\lg \left(a_{H^+} \cdot \frac{f_{XL}}{f_{XLI}} \right) = H_0 \qquad (23)$$

where H_0 and H_0' are acidity functions based on indicators which are respectively azo-compounds and aniline derivatives. Substituting (22) and (23) in (20) and rearranging, we obtain

$$\lg K_T = \lg K_T^* + (H_0 - H_0') \qquad (24)$$

Most acidity functions vary linearly with the normality of the acid in the range employed (3–20 *N*). Therefore Eqn. (18) follows directly from (24). Furthermore, $\lg K_T$ is a linear function of the acid normality[165].

The dependence of the position of tautomeric equilibrium on the acid concentration of the solution established for *p*-aminoazo-compounds, and also the linear relation between $\lg K_T$ and the normality and acidity function of the solution, should apply generally to any prototropic (or other) equilibria involving reactive centres of different chemical types. The slope of the relation (18) will then depend on the difference $H_0 - H_0'$ in Eqn. (24). This conclusion is not, of course, valid for the equilibrium (XXV) ⇌ (XXVI), for the reactive centres in these species are of different types.

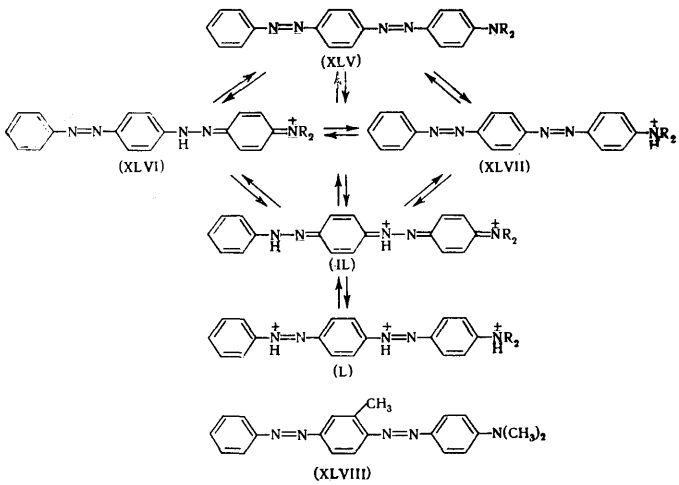
Since the basic strengths of primary and tertiary aromatic amines are described by different acidity functions[166], different values of the coefficient *b* in Eqn. (18) apply to aminoazobenzene and its derivatives and to derivatives of dimethyl- and diethyl-aminoazobenzenes (Table 4). The mean value for the latter is[95] $b = 0.103$: i.e. increase in the acidity function of the solution by unity on the H_0 scale is accompanied by an average increase of about 30% in the value of K_T for dimethyl- and diethyl-aminoazobenzene derivatives. This is probably the reason for the difference in the values obtained for K_T (Table 3) spectrophotometrically by Jaffé and from pK_{a_2} values determined at higher acid concentrations. The close similarity in the coefficients *b* in Eqn. (18) for derivatives of dimethyl- and diethyl-aminoazobenzene is apparent also in their conforming to Kabachnik's formula[167]

$$pK_{T_1} = pK_{T_2} + \text{const} \qquad (25)$$

relating the positions of tautomeric equilibrium in different solvents[156,157]. In this case K_{T_1} and K_{T_2} pertain to solutions of different acid concentrations.

The position of tautomeric equilibrium in the conjugate acids of *p*-aminoazo-compounds is influenced by additions of various salts and also by the ionic strength of the solution[146,168]. This effect has been explained by variation in the strength of hydrogen bonds between the azo-compounds and water molecules[168], and also by association phenomena[146]. However, a more probable reason is variation in the acidity of the medium on addition of the salts[169].

The electron density of the azo-group in *p*-aminoazo-compounds is increased in an excited state[170], so that the tautomeric equilibrium should be completely displaced to the quinone hydrazone tautomer ($K_T \simeq 10^{26}$).[171]



Amino-derivatives of bisphenylazobenzene (XLV), which contain five potential centres of basicity, form a special class of *p*-aminoazo-compounds. Spectrophotometric investigations[172,173] show that addition of the first proton to (XLV) yields a mixture of tautomeric cations (XLVI) and (XLVII) (λ_{max} = 540 and 355 nm). Addition of the proton to the β-nitrogen of the azo-group is proved by the marked displacement of the tautomeric equilibrium towards the ammonium tautomer on passing to 2′-methyl-4′-phenylazo-4-dimethylaminoazobenzene (XLVIII), in which the β-nitrogen atom is shielded by the methyl group.

Addition of a second proton (in 11–22 *N* sulphuric acid) is accompanied by a considerable deepening of the colour of the solution (λ_{max} = 630 nm), owing to formation of a doubly charged cation (XLIX). No other tautomeric forms are detected in these solutions. Finally, a triply charged cation (L) (λ_{max} = 500 nm) is formed in concentrated sulphuric acid. All the above characteristics of *p*-aminoazobenzene derivatives apply to the equilibrium (XLVI) ⇌ (XLVII)[173].

Aminoazo-compounds form complexes with Lewis acids[106,174-177], whose absorption spectra are completely analogous to those of acid solutions of *p*-aminoazo-compounds. From this Gutmann and Steininger concluded[106] that a mixture of two tautomeric forms is also formed on interaction with Lewis acids.

Prototropic tautomeric transitions involving the azo-group have been reported for *p*-aminoazo-compounds of the naphthalene series[131], various *N*-substituted aminoazobenzenes[111,142,178], and also amino-derivatives of phenylazoazulene[179].

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Cyclocarbosiloxanes

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Cyclocarbosiloxanes are a comparatively new class of heterocyclic silicon compounds[1,2] the cyclic skeleton of which consists of alternating siloxane and carbon groups. During the last decade, considerable advances have been made in the chemistry of cyclocarbosiloxanes.
The present review considers the methods of preparative synthesis of cyclocarbosiloxanes and certain reactions leading to the formation of carbosiloxane rings (including reactions in complex polycondensation and polymerisation systems), their physical properties and structure, and also chemical properties. The latter have been divided into reactions involving the cleavage of the heterocyclic skeleton and the reactions of groups and atoms functioning as substituents in the carbosiloxane ring. The polymerisation of cyclocarbosiloxanes, thermal reactions in the gas phase, and dissociations on electron impact have been considered separately.
The bibliography includes 135 references.

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I. INTRODUCTION

Cyclocarbosiloxanes (CCS) are compounds whose cyclic skeleton consists of Si–O, Si–C, and sometimes C–C bonds, i.e. the main structural elements of these compounds are siloxane and carbosilane groups.

Owing to the presence of the cyclic siloxane groups, cyclocarbosiloxanes are capable of polymerisation with ring opening, forming polymers, the main chains of which are made up of siloxane and carbosilane units. According to the data of a number of patents and publications, the characteristic features of these polymers are high thermal[3-11] and chemical[3] stabilities, resistance to a thermal oxidation[9,10,12], resistance to radiation[6], and also improved physicomechanical properties[6,10] compared with polysiloxanes. Carbosiloxane polymers can be used as brake fluids[5,13], moulding materials[13,14], rubbers[13,14], films[8,13,14], oriented fibres[14], and binding resins in the manufacture of fibreglass[15].

In addition, the study of the structure, the nature of the bonds, and the properties of this new class of heterocyclic silicon compounds with a mixed organic–inorganic skeleton is of considerable interest.

The study of the processes involving the formation of cyclocarbosiloxanes makes it possible to estimate in turn the effect of factors such as the number of carbon atoms and silicon functional groups in the initial molecule, their distribution, the inductive and steric effects of the substituents, etc. on the capacity of the molecule for cyclisation. The knowledge of these factors is extremely important in the choice of the optimal monomers for the preparation of polycondensation polymeric materials based on polyfunctional bridge-type silanes, which are of practical value, and makes it possible to assess the structure of the products formed.

The first mention of the synthesis of cyclocarbosiloxanes was made in 1947,[16] but neither the constants of the compounds obtained nor the reaction conditions were quoted. Soon after this an eight-membered heterocycle, 1,1,3,3,5,5,7,7-octamethyl-2,6-dioxa-1,3,5,7-tetrasilacyclo-octane, was obtained; this was the first characterised representative of the class of cyclocarbosiloxanes[3,17].

Among the cyclocarbosiloxanes known at the present time, compounds containing five and more atoms in the heterocycle have been described. The simplest representatives of cyclocarbosiloxanes with the four-membered 2-oxa-1,3-disilacyclobutane ring are probably chemically and thermally unstable, as a result of which all attempts at their synthesis have so far resulted in the formation of cyclic dimers or more rarely polymeric products.

This paper is a first attempt at an exhaustive review and a systematic account of data concerning compounds of the above type published in journal articles or patents.

II. METHODS OF SYNTHESIS

The most common methods for the formation of carbosiloxane rings are based on the hydrolytic and joint hydrolytic condensation of bridge compounds containing hydrolysable silicon functional groups Si–X (X = Cl, F, H, OH, OCH_3, or OC_2H_5), heterofunctional condensation of bridge-type silanes with other silanes or siloxanes, organometallic synthesis based on siloxanes containing halogen–carbon and halogen–silicon bonds, reaction of acetylenic compounds with dihydrodisiloxanes (cycloaddition), synthesis via malonic ester derivatives, and thermal and thermocatalytic rearrangement of linear carbosiloxanes. In addition, a number of reactions of cyclocarbosiloxanes are known, which, although resulting in the formation of new compounds of this class, do not involve the formation or rearrangement of the cyclic skeleton of the molecule. These reactions are considered in Section IV dealing with the chemical properties of cyclocarbosiloxanes.

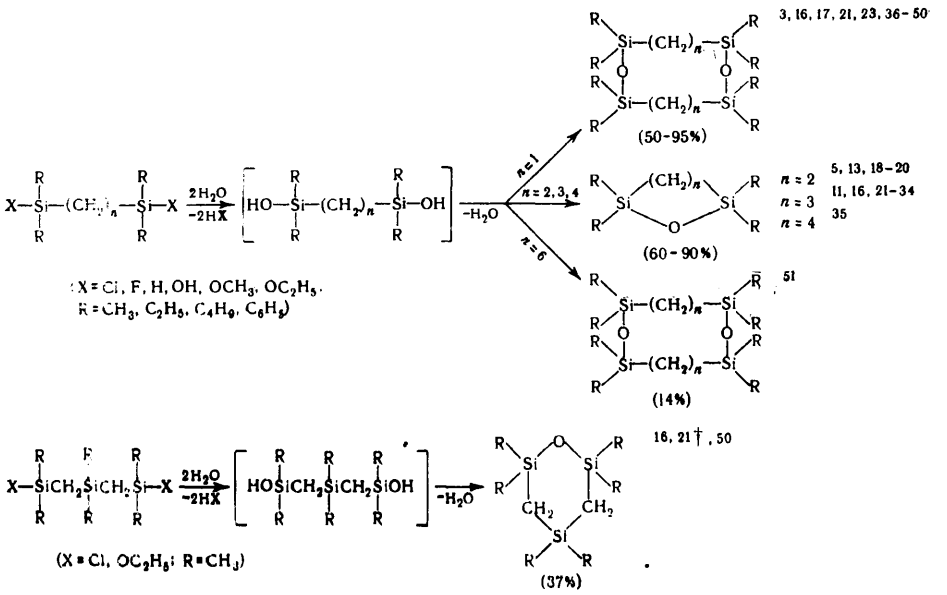
1. HYDROLYTIC CONDENSATION OF POLYFUNCTIONAL ORGANOSILICON COMPOUNDS WITH A CARBON BRIDGE BETWEEN SILICON ATOMS°

The hydrolytic condensation of polyfunctional organosilicon compounds $X_nR_{3-n}Si-A-SiR_{3-n}X_n$ [where A is a

carbon bridge of the type $(CH_2)_n$, $-(\langle\rangle)$, etc.] has been used to synthesise a large number of five-,[5,13,18-20] six-,[11,16,21-34] seven-,[35] and eight-membered[3,16,17,21,23,36-50] cyclocarbosiloxanes, cyclocarbosiloxanes with a large number of units[51], and polycyclic cyclocarbosiloxanes[11,30-32,45,46,52-55].

a. Difunctional Compounds

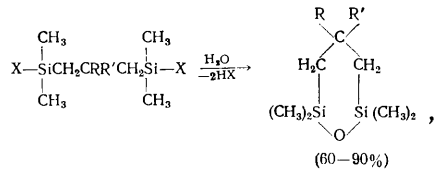
The hydrolysis of difunctional bridge-type di- or trisilanes leads to the formation of cyclocarbosiloxanes according to the following mechanism:



The condensation reaction is carried out at moderate temperatures in the bulk phase of the reactant or in solvents, frequently in the presence of an acceptor of the hydrogen halide evolved; intermolecular condensation of the $\alpha\omega$-silanediol, leading to the formation of linear carbosiloxane oligomers, is a competing reaction.

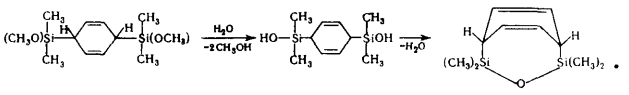
The yield of cyclocarbosiloxane depends on the concentration of the difunctional compound in the reaction mixture: on dilution, intermolecular condensation of the intermediate silanediols is facilitated. For example, the yield of 1,1,3,3-tetramethyl-2-oxa-1,3-disilacycloheptane[35] increases by a factor of two, from 43 to 85%, on dilution of the reaction mixture. In the hydrolysis of 1,3-bis-(chlorodimethylsilyl)propane in ether, the yield of the cyclic product is 60–70%;[11] in similar reactions of 1,2-bis(chlorodimethylsilyl)ethane[18], but in the absence of solvent, the oligomer is mainly formed. The latter may be converted into a cyclocarbosiloxane by thermal catalytic rearrangement (see p. 116).

The hydrolysis of bridge-type compounds with a substituted carbon atom results in the formation of the corresponding C-substituted cyclocarbosiloxanes[24-27]:

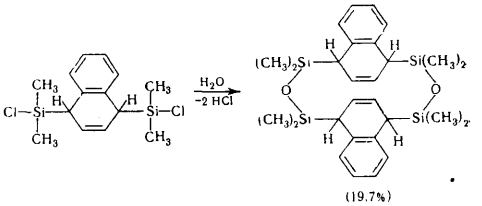


where X = Cl or OC_2H_5, R = CN or H, and R′ = COOH, COOK, $COOCH_3$, or $COOC_2H_5$.

If there is a cyclic group between the silicon atoms, the cyclisation process takes place with greater difficulty—the yield of the products of the intramolecular cyclisation of silanediols diminishes. Thus in the hydrolysis and condensation of 3,6-bis(methoxydimethylsilyl)-hexa-1,4-diene the yield of 2,2,4,4-tetramethyl-3-oxa-2,4-bicyclo-[3,2,2]nona-6,8-diene is only 20%:[56]



When the cyclohexene ring is condensed with an aromatic ring [for example, when the starting material is 1,4-bis(chlorodimethylsilyl)-1,4-dihydronaphthalene], bimolecular condensation products are formed[57]:

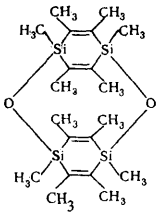


In this case the intramolecular condensation product was not detected.

If the silicon atoms in the difunctional compound are part of a cyclohexadiene ring, cyclocarbosiloxanes with a single siloxane group are not detected even when the reaction is carried out in a highly dilute solution and the corresponding cyclic dimer is formed in a yield of 1–5%.

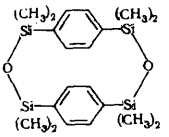
† The formula of a twelve-membered cyclocarbosiloxane $\{[Si(CH_3)_2CH_2]_2Si(CH_3)_2O\}_2$ is attributed to the product, but is probably erroneous since the physical constants of this compound are identical with those of the six-membered heterocycle[50].

Thus, when 1,4-dichlorohexamethyl-1,4-disilacyclohexa-2,5-diene is treated with anhydrous hydrazine, a certain amount of a [1,1]paracyclophane analogue is formed together with the polymer[58]:



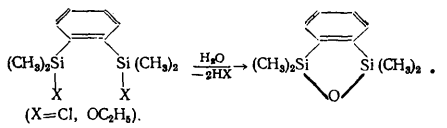
The same compound was synthesised by the reaction of equimolar amounts of 1,4-dichlorohexamethyl-1,4-disilacyclohexa-2,5-diene and 1,4-dihydroxyhexamethyl-1,4-disilacyclohexa-2,5-diene.

It has been shown[14,59] that in the hydrolysis of difunctional compounds with a *para*-substituted aromatic bridge, for example 1,4-bis(chlorodimethylsilyl)benzene, cyclic compounds are not formed at all; the main reaction product is the corresponding silanediol which forms a polymer on dehydration. However, McKay[60], who carried out this reaction in the presence of trifluoroacetic acid and in dilute benzene solution, succeeded in isolating a cyclic product of the intermolecular condensation of *p*-phenylenebis(dimethylsilanol):



It is noteworthy that later attempts to obtain this compound[61] by hydrolysing *p*-phenylenebis(dimethylsilane) or by the condensation of *p*-phenylenebis(dimethylsilanol) were unsuccessful even in dilute solution; the main reaction products were linear polymers with a molecular weight of $(2-7)\times 10^3$, the thermal-catalytic rearrangement of which results in the formation of the cyclic dimer mentioned above (see p. 116).

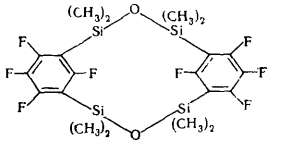
In contrast to *p*-disilyl-substituted benzene, in the hydrolysis of *o*-substituted compounds, for example *o*-bis(chloroethoxydimethylsilyl)benzene[62,63], a certain amount of an intramolecular cyclisation product is formed:



(X=Cl, OC_2H_5).

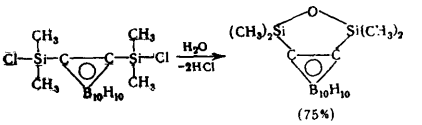
A similar compound with a perfluorophenylene ring was obtained by the hydrolysis of *o*-tetrafluorophenylenebis-(dimethylsilane).[64]

When hydrochloric acid is allowed to react with *m*-tetrafluorophenylenebis(dimethylsilanol), or on hydrolytic condensation of *m*-chlorotetrafluorophenylenedimethylsilane, or on intramolecular condensation of 1,1,3,3-tetramethyl-1,3-bis(tetrafluorophenylenedimethylsilane)disiloxane, a dimeric cyclocarbosiloxane is formed[64,65]:



(1-10%)

A cyclic oxadisilacarborane was also obtained by hydrolytic condensation[66]:

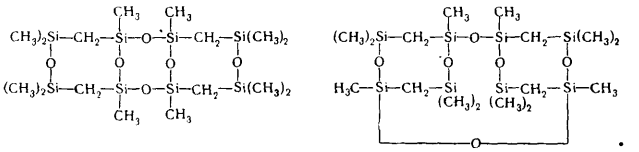


(75%)

When a benzene solution of 1-[*m*-(ethoxydimethylsilyl)-phenyl]-3-[*p*-(ethoxydimethylsilyl)phenyl]hexafluoropropane is refluxed[67,68] in 50% of sulphuric acid, a polymer is formed, which can be converted into the corresponding cyclocarbosiloxane (see p. 116).

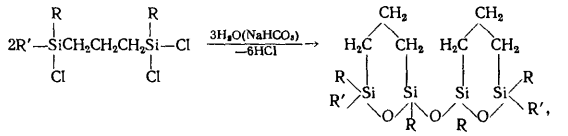
b. Trifunctional Compounds

Hydrolytic condensation of compounds with carbon bridges between silicon atoms and with more than two hydrolysable groups leads as a rule to the formation of polycyclic cyclocarbosiloxanes[11,30-32,45,46,52-55]. Thus hydrolysis of (ethoxydimethylsilyl)(diethoxymethylsilyl)-methane in ethereal solution leads to the formation of a compound in 20% yield, to which the following possible formulae have been ascribed:



According to the authors[45,46], the first structure is more likely.

Hydrolysis of trichlorodisilanes with a trimethylene bridge in ethereal solution results in the formation of bicyclic carbosiloxanes[11,30-32]:

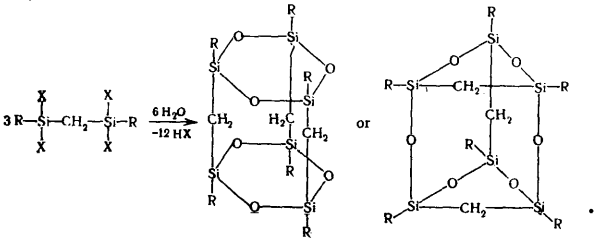


where R = R′ = CH_3 (62.5%) or R = CH_3 and R′ = C_6H_5.

Hydrolysis of an analogous compound with a phenylene bridge—1-chloromethylphenylsilyl-4-dichlorophenylsilylbenzene—in an acid medium does not result in the formation of a bicyclic compound of the above type, an oligomer being formed instead[55].

c. Tetrafunctional Compounds

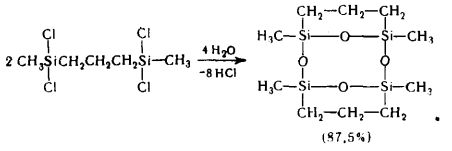
Hydrolytic condensation of symmetrical tetrafunctional disilylmethanes[45,46,52,53,69] yields cyclocarbosiloxanes with a "cage" structure:



Although the authors[45,46,52] give preference to the first structure, the second formula is probably more likely,

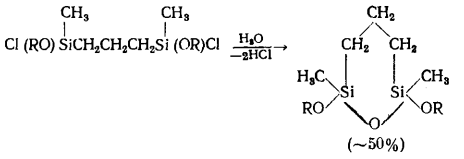
since the ^1H NMR spectra of this compound show two signals due to nonequivalent methylene protons[53,69]: in the first structure all the methylene protons should be equivalent.

A tricyclic cyclocarbosiloxane has been obtained in a high yield by the hydrolytic condensation in a neutral medium of a tetrafunctional disilane with a trimethylene bridge:



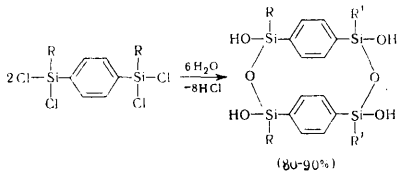
In alkaline and acid media, the yields of this compound were reduced to 60.5 and 45% respectively[11,31,32].

Hydrolysis of 1,3-bis(alkoxychloromethylsilyl)propanes in the presence of a hydrogen chloride acceptor (triethylamine or its mixture with urea) yields 2,6-dialkoxy-2,6-dimethyl-1-oxa-2,6-disilacyclohexanes[11,31,32], i.e. in this case the compound behaves like difunctional disilanes:



In the presence of sodium bicarbonate, the above tricyclic compound is mainly formed.

Hydrolytic condensation of silicon compounds with *p*-phenylene bridges [for example 1,4-bis(dichloromethylsilyl)benzene] leads to an insoluble polymer; individual cyclocarbosiloxanes were not isolated[10]. However, a more detailed study of this process[54,55] showed that the intermediates in the reaction are cyclocarbosiloxanes containing hydroxy-groups:



(R = R′ = CH_3 or C_6H_5; R = CH_3, R′ = C_6H_5), which give rise to di- and poly-cyclic compounds on prolonged standing in solution.

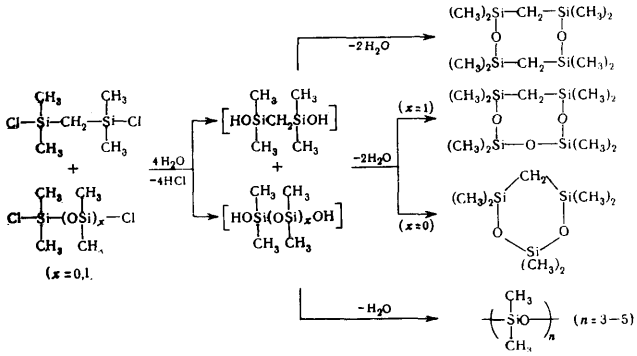
If the hydrolysis of 1,4-bis(dichloromethylsilyl)benzene is carried out in the presence of chlorotrimethylsilane, the halogen is partly replaced by the trimethylsiloxy-group; complete substitution of the chlorine can be achieved by treatment with an excess of hydroxytrimethylsilane in the presence of ammonia[70].

d. Pentafunctional Compounds

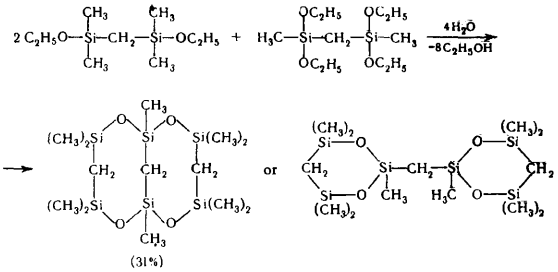
Hydrolysis of (diethoxymethylsilyl)(triethoxysilyl)-methane yielded an infusible and insoluble polymers in a yield of 96%, the structure of which could not be established[45,46]. It has been suggested that it contains cyclocarbosiloxane units of the "cage" type built into a three-dimensional network.

2. JOINT HYDROLYTIC AND HETEROFUNCTIONAL CONDENSATION

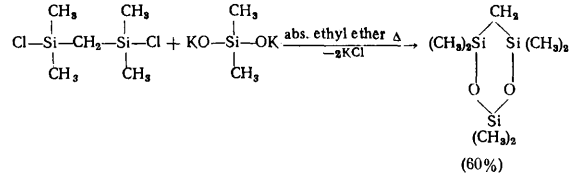
The possibility of obtaining cyclocarbosiloxanes by the joint hydrolytic condensation of bis(chlorodimethylsilyl)-methane with dichlorodimethylsilane or 1,3-dichloro-1,1,3,3-tetramethyldisiloxane had been investigated[50,71]. The composition of the joint hydrolysis product depends on the component ratio and the amount of hydrolysing agent. The optimal conditions for the preparation of 1,1,3,3,5,5-hexamethyl-2,4-dioxa-1,3,5-trisilacyclohexane (yield 64.5%) are equimolar proportions of the dichlorides and an excess of water; the maximum yield of 1,1,3,3,5,5,7,7-oxamethyl-2,4,6-trioxa-1,3,5,7-tetrasilacyclo-octane (about 40%) is also attained for equimolar proportions of the initial compounds and a stoichiometric amount of the hydrolysing agent. The principal reactions occurring on joint hydrolysis are shown below:



The joint hydrolysis of tetrafunctional compounds with di- and tri-functional silicon derivatives has been described. For example, the following possible structures have been attributed to the crystalline products obtained by the joint hydrolytic condensation of bis(ethoxydimethylsilyl)methane with bis(diethoxymethylsilyl)-methane[45,46]:

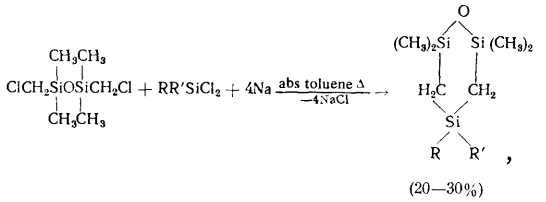


According to the authors[45,46], the first formula is more likely. Heterofunctional condensation has been hardly used for the synthesis of cyclocarbosiloxanes. Only one example of this type of synthesis is known. When bis-(chlorodimethylsilyl)methane was allowed to react with potassium dimethylsilanediolate, the main product was 1,1,3,3,5,5-hexamethyl-2,4-dioxa-1,3,5-trisilacyclo-hexane[50,71]:



3. ORGANOMETALLIC SYNTHESIS

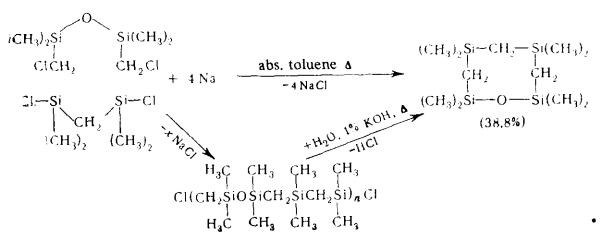
When symmetrical bis(chloromethyl)tetramethyldisiloxane and aryl(alkyl)dichlorosilanes reacted with metallic sodium, a number of six-membered cyclocarbosiloxanes were obtained[72]:



where R = R′ = CH_3 or C_2H_5 and R = CH_3 and R′ = C_6H_5. In addition, considerable amounts of oligomers are formed, which can be converted into six-membered cyclocarbosiloxane by hydrolysis and subsequent thermal catalytic rearrangement of the hydrolysate; in this case the overall yield of cyclocarbosiloxanes may be increased approximately to 70%.[50,73]

A condensation reaction with magnesium similar to that described above yielded a cyclocarbosiloxane (R = R′ = CH_3) in a yield of about 45%.[50]

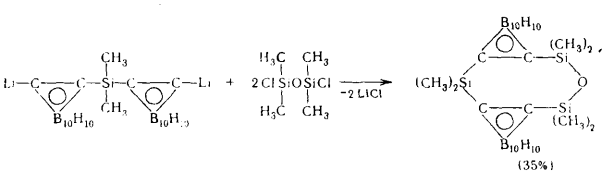
If instead of dichlorodimethylsilane one employs bis(chlorodimethylsilyl)methane, the main reaction product is 1,1,3,5,5,7,7-octamethyl-4-oxa-1,3,5,7-tetrasilacyclooctane[49,50,73]:



On condensation of 1,5-bis(chloromethyl)-1,1,3,3,5,5-hexamethyltrisiloxane and dichlorodimethylsilane in the presence of metallic sodium or magnesium, 1,1,3,3,5,5,7,7-octamethyl-2,4-dioxa-1,3,5,7-tetrasilacyclo-octane is hardly formed[50]. It was found that in both cases the main reaction products are six-membered cyclocarbosiloxanes. Their formation can probably be accounted for by rearrangements of the siloxane bonds under the reaction conditions.

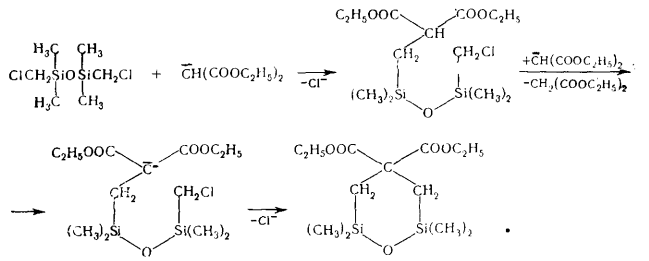
The possibility of the cyclisation of chloromethyldisiloxanes containing a halogen or an alkoxy-group at the silicon atom [$ClCH_2Si(CH_3)_2OSi(CH_3)_2X$; X = Cl or OC_2H_5] with metallic magnesium has been investigated[50]. The formation of an intramolecular cyclisation product of the initial compound—1,1,3,3-tetramethyl-2-oxa-1,3-disilacyclobutane—was not observed. The main reaction products were 6- and 8-membered methylenesiloxane cyclocarbosiloxanes.

A cyclocarbosiloxane with two carborane rings[74] was obtained via a dilithium derivative by the following reaction:

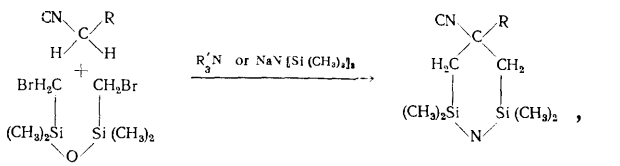


4. SYNTHESIS OF CYCLOCARBOSILOXANES BY THE CONDENSATION OF BIS(HALOGENOMETHYL)DISILOXANES WITH COMPOUNDS CONTAINING ACTIVE HYDROGEN ATOMS

The reaction of *sym*-bis(iodomethyl)tetramethyldisiloxane with sodiomalonic ester yielded a cyclic diester—1,1-diethoxycarbonyl-3,3,5,5-tetramethyl-4-oxa-3,5-disilacyclohexane[75] (yield 61%). The use of the less reactive *sym*-bis(chloromethyl)tetramethyldisiloxane reduced the yield of this heterocycle to 28%. The following reaction mechanism has been proposed:



C-substituted six-membered cyclocarbosiloxanes are formed also on condensation of *sym*-bis(bromomethyl)-tetramethyldisiloxane with cyanoacetic esters[26] (in the presence of tertiary amines) or with nitriles[27] [in the presence of sodium bis(trimethylsilyl)amide]:



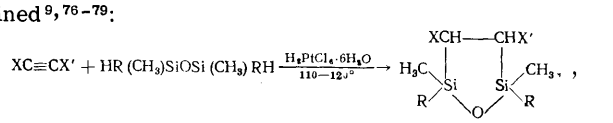
where R = H, CH_3, CN, $COOCH_3$, or $COOC_2H_5$.

In the presence of triethylamine, the condensation with cyanoacetic ester taking place with a yield of about 60%, monoalkylated products being virtually absent from the reaction mixture.

When acetonitrile and sodium bis(trimethylsilyl)amide are employed, the yield of 4-cyano-2,2,6,6-tetramethyl-1-oxa-2,6-disilacyclohexane is 60—70%. It is interesting that a reagent such as sodium bis(trimethylsilyl)amide gives rise to hardly any side reactions (cleavage of the Si—C bond in $Si-CH_2Br$, cleavage of the Si—O bond, substitution of the bromomethyl group with formation of $Si-CH_2-N$, etc.). The acetonitrile monoalkylation product is detected only in a small amount. If other compounds with active C—H bonds are introduced into this reaction, the yield of cyclocarbosiloxane diminishes[27]. For example, in the presence of diethyl malonate and ethyl cyanoacetate, the yield is about 20%. When an acetate ester is employed, only traces of cyclocarbosiloxanes are formed.

5. INTERACTION OF SUBSTITUTED ACETYLENES WITH DIHYDROSILOXANES (CYCLOADDITION)

When substituted acetylenes reacted with dihydrodisiloxanes in the presence of chloroplatinic acid as a catalyst, a number of five-membered cyclocarbosiloxanes with different substituents at the carbon atom were obtained[9,76-79]:

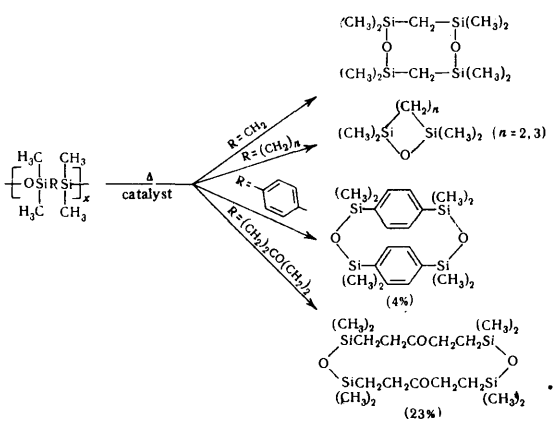


where X = H, C_6H_5, C_4H_9, or α-$C_{10}H_7$, X' = H, CH_3, or C_6H_5, and R = CH_3, C_2H_5, or C_6H_5.

The yield of cyclocarbosiloxanes varies between 5 and 75% depending on the structure of the initial reagents and the reaction conditions. It was established that the tendency towards the formation of a cyclic compound is greatly influenced by the nature of the substituents at the carbon atoms in acetylene and at the silicon atoms in dihydrodisiloxane. The substituents at the carbon atoms in acetylene can be arranged in the following sequence in terms of their effect on the formation of cyclic compounds: aryl > alkyl > hydrogen; the corresponding sequence of substituents at the silicon atoms is ethyl > phenyl > methyl.

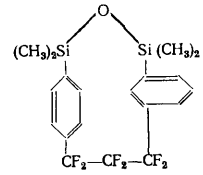
6. THERMAL CATALYTIC AND THERMAL REARRANGEMENT OF LINEAR CARBOXILOXANES

The thermal catalytic rearrangement of oligomeric products containing siloxane and silicon–carbon residues can be employed as a preparative method for the synthesis of many cyclocarbosiloxanes. Such oligomers are usually formed as side products in the synthesis of cyclocarbosiloxanes. They are obtained as the main products, for example, in the reaction involving the polyaddition of $\alpha\omega$-dihydrodisiloxanes to dienes and acetylene[9,76–85], in the copolymerisation of cyclosiloxanes with 1,3-disilacyclobutanes[50], and of course in the polymerisation of cyclocarbosiloxanes. At fairly high temperatures (up to 300°C) in the presence of catalytic amounts of alkalis or acids, the siloxane bond dissociates in linear carbosiloxane oligomers with formation of cyclocarbosiloxanes ("siloxy–siloxy" rearrangement). In particular, this method has proved convenient for the preparation of five-membered[5,13,18–20], six-membered[28,29,50,71,73], eight-membered[48,50,71,73], and sixteen-membered[86] compounds and also cyclocarbosiloxanes with *p*-phenylene bridges[61]:



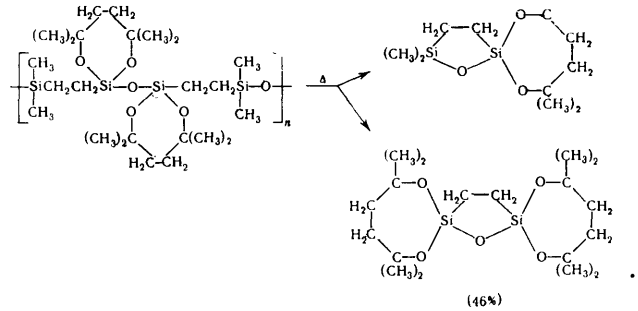
In the thermal decomposition of a polymer with the composition $[-SiCH_2CH_2CH_2SiO-]_n$, the main product was a six-membered heterocycle—1-oxa-2,6-disilacyclohexane[11].

Oxadisila-[3,3]-metaparacyclophane

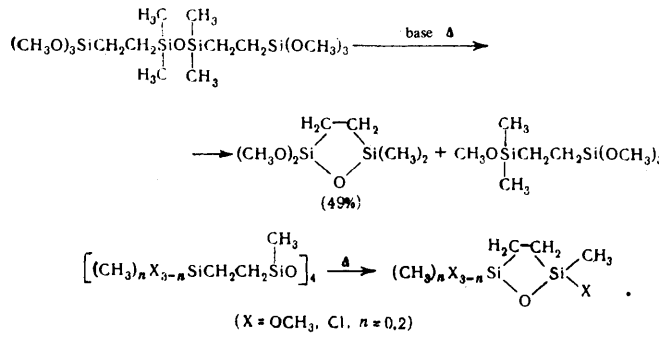


was obtained by heating *in vacuo* a linear polymer with the corresponding structure[67,68].

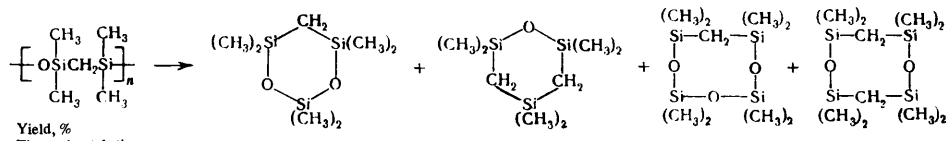
Thermal rearrangement of organosilicon oligomers also yielded oxadisilacyclopentane heterocycles[87]:



Thermal and thermalcatalytic "alkoxy–siloxy" and "chloro–siloxy" rearrangements of the corresponding compounds are varieties of the above method for the preparation of cyclocarbosiloxanes[87]:



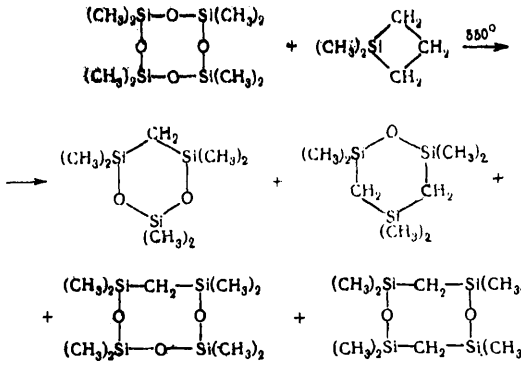
Examples of thermal and thermalcatalytic rearrangements of oligomeric carbosiloxanes involving the dissociation not only of Si–O but also of Si–C bonds in the chain are given below[50]:



Yield, %				
Thermal catalytic rearrangement (1% KOH; <300°)	43.1	32.2	10.6	7.5
Thermal rearrangement (>500°)	48.	24.8	9.6	3.1

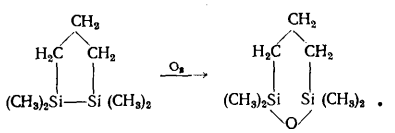
7. OTHER METHODS

Apart from the reactions discussed above, there are others leading to the formation of carbosiloxane rings, but these are without preparative value. Thus it has been shown that cyclocarbosiloxanes can be formed, in principle, on joint pyrolysis of cyclosiloxanes and cyclocarbosilanes[50,88]:

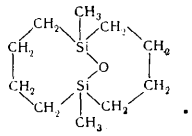


The formation of the same cyclocarbosiloxanes was observed on thermolysis of 1,1,3,3-tetramethyl-1,3-disilacyclobutane in the presence of water vapour at 550°C.[50,88] However, in both cases the yield of cyclocarbosiloxanes does not exceed several per cent.

Like 1,2-digermacyclopentanes[89], 1,2-disilacyclopentane can be oxidised with formation of the corresponding oxadisilacyclohexanes[135]. Thus 1,1,2,2-tetramethyl-1,2-disilacyclopentane is converted on prolonged standing into 2,2,6,6-tetramethyl-1-oxa-2,6-disilacyclohexane:

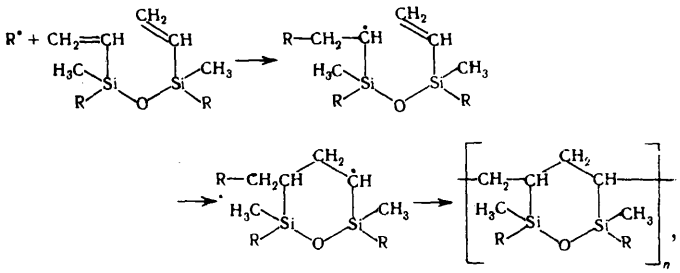


1,2-Disilacyclohexanes (*cis*- and *trans*-) are converted into the corresponding seven-membered *cis*- and *trans*-cyclocarbosiloxanes on interaction with perbenzoic acid. The reaction is distinguished by high stereospecificity[90]. A bicyclic compound with a similar structure is also readily oxidised by perbenzoic acid, yielding 1,6-dimethyl-11-oxa-1,6-disilabicyclo[4,4,1]undecane[91]:



It is interesting to note that, regardless of which (*cis*- or *trans*-) initial isomeric compound was oxidised, the reaction products always had the *cis*-configuration. Construction of molecular models for *cis*- and *trans*-isomers shows that, in contrast to the *cis*-isomer, the *trans*-siloxane isomer has a strained structure giving rise to steric hindrance. Oxidation with trimethylsilyl peroxide proceeds similarly, but the yield of the oxidation product is only 22% in the case of the *trans*-isomer.

The formation of cyclocarbosiloxane structures in the polymer chain has been noted in the free-radical and radiation-induced polymerisation of certain polyfunctional vinylsiloxanes[28,29,92]:



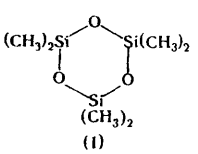
where R = CH_3 or C_6H_5.

Thermal rearrangements of cyclocarbosiloxanes with a change in the skeleton may be of definite interest for the synthesis of other cyclocarbosiloxanes (see p. 125).

III. PHYSICAL PROPERTIES

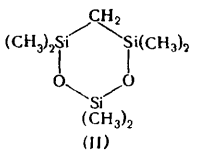
Cyclocarbosiloxanes are liquid or crystalline substances (Tables 1–2). The boiling points, refractive indices, and specific gravities of cyclocarbosiloxanes vary steadily as siloxane oxygen is replaced by methylene groups. Thus in the series of six- and eight-membered heterocycles the boiling points and refractive indices increase linearly and the specific gravity decreases with increase in the number of methylene groups[49,50,73].

Cyclosiloxanes

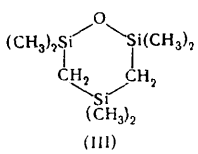


(I)

Cyclocarbosiloxanes

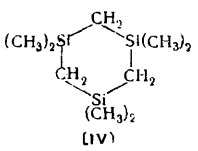


(II)

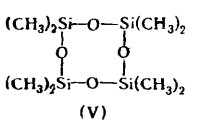


(III)

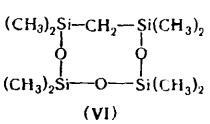
Cyclocarbosilanes



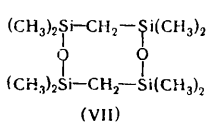
(IV)



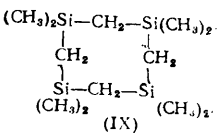
(V)



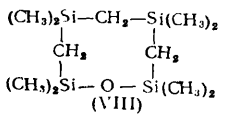
(VI)



(VII)

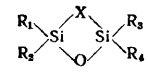


(IX)



(VIII)

Table 1. Physical properties of cyclocarbosiloxanes of the type

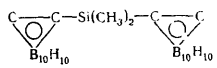
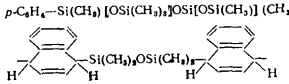
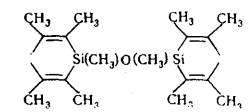


No.	X	R_1	R_2	R_3	R_4	Empirical formula	Mol. wt.	B.p., °C/mmHg	M.p., °C	n_D^{20}	d_4^{20}	Yield, %	References
1	$(CH_2)_2$	CH_3	CH_3	CH_3	CH_3	$Si_2C_6H_{16}O_1$	160.4	124/735	—	1.4142*	0.8550*	68.0	18
								125/734	—	1.4155*	0.8616*	68.0	5, 20, 100
2	$(CH_2)_2$	CH_3	CH_3	CH_3	C_6H_5	$Si_2C_{11}H_{18}O_1$	222.4	146/50	—	1.4962*	0.9740*	87.0	18
								144/50	—	1.4962*	0.9742*	90.8	5, 20
3	$(CH_2)_2$	CH_3	C_6H_5	CH_3	C_6H_5	$Si_2C_{16}H_{20}O_1$	284.5	182/10	—	1.5492*	1.047*	69.0	18
								158—160/3	—	1.5502*	1.0378*	5.0	9
4	$(CH_2)_2$	CH_3	CH_2	C_6H_5	C_6H_5	$Si_2C_{16}H_{20}O_1$	284.5	181/11	—	1.5492	1.044	75.0	18
5	$(CH_2)_2$	CH_3	C_6H_5	C_6H_5	C_6H_5	$Si_2C_{21}H_{22}O_1$	346.6	241/11	—	1.5860	1.092	86.0	18
6	$(CH_2)_2$	C_6H_5	C_6H_5	C_6H_5	C_6H_5	$Si_2C_{31}H_{28}O_1$	408.7	—	80—81	—	—	78.0	5, 18
7	$(CH_2)_2$	CH_3	CH_3	CH_3	C_6H_{11}	$Si_2C_{16}H_{32}O_1$	216.5	—	—	—	—	—	5
8	$(CH_2)_2$	CH_3	CH_3	CH_3	$C_{12}H_{23}$	$Si_2C_{17}H_{34}O_1$	314.7	—	—	—	—	—	5
9	$(CH_2)_2$	CH_3	C_6H_5	CH_3	C_6H_5	$Si_2C_{17}H_{20}O_1$	188.4	27.5—30/1	—	1.4360	0.8797	3.2	9, 79
10	$(CH_2)_2$	CH_3	CH_3	CH_3	OCH_3	$Si_2C_6H_{14}O_2$	176.2	30/5.5	—	—	—	48.0	87
11	$(CH_2)_2$	CH_3	CH_3	OCH_3	OCH_3	$Si_2C_6H_{14}O_3$	192.2	52/15	—	—	—	49.0	87
12	$(CH_2)_2$	CH_3	OCH_3	OCH_3	OCH_3	$Si_2C_6H_{14}O_4$	208.2	61/4.5	—	—	—	36.0	87
13	$(CH_2)_2$	CH_3	CH_3	CH_3	Cl	$Si_2C_6H_{13}O_2Cl_1$	180.7	~120	—	—	—	82.0	87
14	$(CH_2)_2$	CH_3	Cl	Cl	Cl	$Si_2C_6H_{12}O_2Cl_2$	221.5	50—60/4—5	—	—	—	39.0	87
15	$(CH_2)_2$	OC_4H_9	OC_4H_9	OC_4H_9	OC_4H_9	$Si_2C_{14}H_{40}O_4$	392.3	119/0.01	—	—	—	43.0	87
16	$(CH_2)_2$	CH_3	CH_3	$OC(CH_3)_2(CH_2)_2C(CH_3)_2O$		$Si_2C_{12}H_{22}O_3$	274.3	55/0.2	—	—	—	—	87
17	$(CH_2)_2$	$OC(CH_3)_2(CH_2)_2C(CH_3)_2O$		$OC(CH_3)_2(CH_2)_2C(CH_3)_2O$		$Si_2C_{18}H_{34}O_5$	388.3	97/0.05	78—80	—	—	46.0	87
18	$CH(C_6H_5)CH_2$	CH_3	CH_3	CH_3	CH_3	$Si_2C_{12}H_{20}O_1$	236	82—83/3	—	1.5038	0.9680	16.0	9, 77, 79
19	$CH(C_6H_5)CH_2$	CH_3	C_6H_5	CH_3	C_6H_5	$Si_2C_{17}H_{24}O_1$	264	119—120/3	—	1.5050	0.9689	40.5	9, 77, 79
20	$CH(C_6H_5)CH_2$	CH_3	C_6H_5	CH_3	C_6H_5	$Si_2C_{22}H_{24}O_1$	360.5	178—180/3	—	1.5858	1.0784	28.0	9, 79
21	$CH(C_6H_5)CH(CH_3)$	CH_3	C_6H_5	CH_2	C_6H_5	$Si_2C_{17}H_{22}O_1$	278	110/2	—	1.5003	0.9602	10.0	9, 79
22	$CH(C_6H_5)CH_2$	CH_3	C_6H_5	CH_3	C_6H_5	$Si_2C_{18}H_{20}O_1$	244	70/1	—	1.4470	0.8701	14.6	9, 79
23	$CH(\alpha\text{-}C_{10}H_7)CH_2$	CH_3	C_6H_5	CH_3	C_6H_5	$Si_2C_{21}H_{22}O_1$	314	156—159/2	—	1.5580	1.0302	40.0	9, 79
24	$[CH(C_6H_5)]_2$	CH_3	CH_3	CH_3	CH_3	$Si_2C_{17}H_{22}O_1$	312.5	133—134/2	76—77	—	—	51.0	9, 79
25	$[CH(C_6H_5)]_2$	CH_3	C_6H_5	CH_2	C_6H_5	$Si_2C_{20}H_{28}O_1$	340.0	154—156/3	~0	1.5668	1.0232	74.5	9, 77, 79
26	$(CH_2)_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_7H_{18}O_1$	174.4	146/760	—	1.4240	0.8679	—	23, 24
								146/761	—	1.4263	0.8735	79.4	2, 30, 31, 101
27	$(CH_2)_3$	CH_3	CH_3	CH_3	C_2H_5	$Si_2C_7H_{16}O_1$	188.4	48—49/10	—	1.4324	0.8796	37.8	11, 103
28	$(CH_2)_3$	CH_3	CH_3	CH_3	$n\text{-}C_3H_7$	$Si_2C_8H_{18}O_1$	202	61/2	—	1.4368	0.8791	68.0	2, 11, 31
29	$(CH_2)_3$	CH_3	CH_3	CH_3	C_4H_9	$Si_2C_{10}H_{24}O_1$	212	75/2	—	1.4394	0.8776	69.4	2, 11, 31
30	$(CH_2)_3$	CH_3	CH_3	CH_3	C_5H_{11}	$Si_2C_{11}H_{26}O_1$	230.0	116—117/25	—	1.4385	0.8726	28.0	11, 103
31	$(CH_2)_3$	CH_3	CH_3	CH_3	C_6H_5	$Si_2C_{12}H_{20}O_1$	236.4	98/2	—	1.4990	0.9758	—	2, 11, 31
								128—129/25	—	1.4969	0.9747	64.6	28, 29
32	$(CH_2)_3$	CH_3	CH_3	CH_3	C_6H_4Cl	$Si_2C_{12}H_{19}Cl_1O_1$	270.5	115—116/3	—	1.5100	1.0612	57.2	11, 103
33	$(CH_2)_3$	CH_3	CH_3	CH_3	OCH_3	$Si_2C_7H_{18}O_2$	190	49—50/10	—	1.4254	0.9378	66.0	11, 33
34	$(CH_2)_3$	CH_3	CH_3	CH_3	OC_2H_5	$Si_2C_8H_{20}O_2$	204	59—62/10	—	1.4264	0.9295	81.6	11, 33
35	$(CH_2)_3$	CH_3	CH_3	CH_3	$n\text{-}OC_3H_7$	$Si_2C_9H_{22}O_2$	218	71—73/17	—	1.4253	0.9177	56	11, 33
36	$(CH_2)_3$	CH_3	CH_3	CH_3	$iso\text{-}OC_4H_9$	$Si_2C_{10}H_{24}O_2$	232	86—87/10	—	1.4322	0.9178	60.5	11, 33
37	$(CH_2)_3$	CH_3	CH_3	CH_3	$iso\text{-}OC_5H_{11}$	$Si_2C_{11}H_{26}O_2$	242	98—99/7	—	1.4338	0.9125	67.5	11, 33
38	$(CH_2)_3$	CH_3	CH_3	CH_3	OC_6H_5	$Si_2C_{12}H_{20}O_2$	252	115—116/7	—	1.4888	1.0145	60.7	11, 33
								134.5/16		1.4810	1.0071		11
39	$(CH_2)_3$	CH_3	CH_3	CH_3	CH_3COO	$Si_2C_7H_{14}O_3$	218	79—80/14	—	1.4343	0.9922	60.2	11, 33
								74—75/10	—	1.4316	0 9976	91.0	11, 33
40	$(CH_2)_3$	CH_3	CH_3	CH_3	$(C_2H_5)_2N$	$Si_2C_{10}H_{23}O_1N_1$	231	98—100/7	—	1.4438	0.9047	62.0	11, 33
41	$(CH_2)_3$	CH_3	CH_3	CH_3	$C_6H_4CH_2O$	$Si_2C_{13}H_{20}O_2$	266.4	130—132/10	—	1.4848	1.0080	64.5	33
42	$(CH_2)_3$	CH_3	CH_3	CH_3	Cl	$Si_2C_7H_{15}O_1Cl_1$	194.8	50—52/7	—	1.4412	1.014	68.0	2, 11, 38
								50—52/11	—	1.4419	—	74.0	11
								67/25	—	—	—	58.4	30, 31

Table 1 (continued).

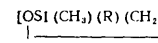
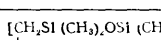
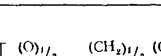
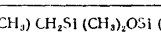
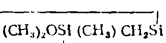
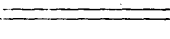
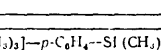
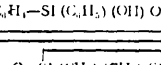
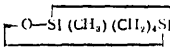
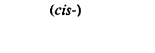
No.	X	R_1	R_2	R_3	R_4	Empirical formula	Mol. wt.	B.p., °C/mmHg	M.p., °C	n_D^{20}	d_4^{20}	Yield, %	References
43	$(CH_3)_2$	CH_3	Cl	CH_3	Cl	$Si_2C_6H_{12}O_1Cl_2$	230.0	64—66/7	—	1.4570	1.1655	77.0	11, 33
								90—91/15	—	1.4592	1.1680	27.0	11, 33
44	$(CH_3)_2$	CH_3	OC_6H_5	CH_3	OCH_3	$Si_2C_{15}H_{20}O_2$	252.4	92—95/1	—	1.5130	1.044	16.8	32
45	$(CH_3)_2$	CH_3	C_6H_5	CH_3	C_6H_5	$Si_2C_{17}H_{20}O_1$	298.4	142.5—143/1	—	1.5495	1.0509	31.1	31, 32
								135—137/1	—	1.5545	1.0500	—	11
46	$(CH_3)_2$	CH_3	$C_6H_4CH_2O$	CH_3	OC_2H_7	$Si_2C_{10}H_{22}O_2$	310.4	90—93/1	—	1.4825	1.022	32.0	31, 32
47	$(CH_3)_2$	CH_3	OCH_3	CH_3	OCH_3	$Si_2C_7H_{14}O_2$	206.4	59—61/7	—	1.4250	1.001	57.4	11, 31, 32
48	$(CH_3)_2$	CH_3	OCH_3	CH_3	C_6H_5	$Si_2C_{13}H_{20}O_2$	252.3	94—95/1	—	1.4592	1.168	16.8	11
49	$(CH_3)_2$	CH_3	OC_2H_5	CH_3	OC_2H_5	$Si_2C_8H_{20}O_2$	234.5	32—34/2	—	1.4250	0.9655	51.7	11, 22, 31, 32
50	$(CH_3)_2$	CH_3	iso-OC_3H_7	CH_3	iso-OC_3H_7	$Si_2C_{12}H_{28}O_2$	262.4	53—54/1	—	1.4240	0.9371	39.8	11, 31, 32
51	$(CH_3)_2$	CH_3	iso-OC_4H_7	CH_3	$OC_6H_5CH_2$	$Si_2C_{16}H_{30}O_2$	310.5	90—92/1	—	1.4825	1.022	—	11
52	$(CH_3)_2$	CH_3	n-OC_4H_9	CH_3	n-OC_4H_9	$Si_2C_{12}H_{30}O_2$	290.2	122—123/4	—	1.4345	0.9477	38.6	11, 31, 32
53	$(CH_3)_2$	CH_3	iso-OC_4H_9	CH_3	iso-OC_4H_9	$Si_2C_{12}H_{30}O_2$	290.2	68—69/1	—	1.4300	0.9286	49.5	11, 31, 32
54	$(CH_3)_2$	CH_3	n-OC_5H_{11}	CH_3	n-OC_5H_{11}	$Si_2C_{14}H_{34}O_2$	318.6	91—93/1	—	1.4380	0.9346	38.5	11, 31, 32
								105—107/2	—	1.4378	0.9311	—	11
55	$(CH_3)_2$	CH_3	iso-OC_5H_{11}	CH_3	iso-OC_5H_{11}	$Si_2C_{14}H_{34}O_2$	318.6	97—98/1	—	1.4360	0.9306	43.1	11, 31, 32
56	$(CH_3)_2$	CH_3	OC_6H_5	CH_3	OC_6H_5	$Si_2C_{17}H_{22}O_2$	330	139—140/1	—	1.5285	1.100	42.0	11, 31, 32
57	$(CH_3)_2$	CH_3	$C_6H_5CH_2O$	CH_3	$C_6H_5CH_2O$	$Si_2C_{19}H_{26}O_2$	358.5	173—174/1	—	1.5220	1.083	74.5	11, 31, 32
58	$(CH_3)_2$	CH_3	$OSi(C_6H_5)_3$	CH_3	$OSi(C_6H_5)_3$	$Si_4C_{37}H_{42}O_3$	406.9	137—139/2	—	1.4430	0.9340	70.5	11, 31, 32
								168—173/8	—	1.4433	0.9345	85.0	11, 33
59	$CH_3CH(CH_2OH)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{20}O_2$	204.4	123—125/1	—	1.4432	0.9292	—	11
								68/0.4	—	1.4516	—	72.0	27
								81—83/2	—	1.4498	—	78.0	27
								70/0.5	—	1.4509	—	73.0	27
60	$CH_3CH(COOH)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{18}O_3$	218.4	—	142—143	—	—	83.0	26
								—	145	—	—	91.0	73
								—	143—144	—	—	80.0	25
								—	142—144	—	—	79.7	24
61	$CH_3CH(COOC_6H_5)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_{19}H_{26}O_2$	246.5	102/11	—	1.4392	0.9718	96.0	73
								75—77/0.5	—	1.4390	1.043	79.0	24, 27
62	$CH_3CH(CONH_2)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_6H_{16}N_2O_2$	217.4	—	137—140	—	—	90.0	26
63	$CH_3CH(CH_2NH_2)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_6H_{22}N_2O_1$	203.4	87—88/12	—	1.4518	—	75.0	26
								45/0.3	—	1.4521	—	70.0	27
64	$CH_3CH(COOK)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{17}K_1O_3$	256.5	—	—	—	—	~100	26
65	$CH_3C(CN)HCH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{17}N_1O_1$	199.4	105/12	55—56	—	—	71.0	26
								105—108/11	—	—	—	68.0	27
66	$CH_3C(CN)(COOH)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{17}N_1O_2$	243.4	—	131—131.5	—	—	72.0	26
								—	128.5—129.5	—	—	94.7	24, 25
67	$CH_3C(CN)(COOK)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{16}K_1N_1O_2$	281.5	—	—	—	—	98.0	26
								—	—	—	—	77.0	24
68	$CH_3C(CN)(CH_2OH)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{19}N_1O_2$	229.4	—	99—101	—	—	83.0	27
								—	100—101	—	—	89.0	27
69	$CH_3C(CN)(CONH_2)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{16}N_2O_2$	242.4	—	166—167.5	—	—	74.0	26
70	$CH_3C(CN)(CO_2CH_3)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_{10}H_{19}N_1O_2$	257.5	115—117/3	29—30	—	—	—	26
71	$CH_3C(CN)(CO_2C_6H_5)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_{15}H_{21}N_1O_2$	271.5	90/0.3	31—32	—	—	59.0	26
72	$CH_3C(CN)_2CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{16}N_2O_1$	224.4	—	138—138.5	—	—	27.0	27
73	$CH_3C(CN)(CH_3)CH_2$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{17}N_1O_1$	213.4	98—102/13	80—83	—	—	43.0	27
74	$CH_3C(CH_2OH)_2CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_8H_{22}O_2$	234.4	120/0.5	90—92	—	—	20.0	27
								—	93—94	—	—	75.0	27
75	$CH_3C(CH_2NH_2)(CH_2OH)CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_7H_{21}N_1O_2$	233.5	—	100—101	—	—	40.0	27
76	$CH_3C(CH_2NH_2)_2CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_7H_{20}N_2O_1$	232.5	112—114/2	—	1.4798	—	65.0	27
77	$CH_3C(COOC_2H_5)_2CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_2C_{13}H_{26}O_4$	318.5	134/6—7	—	1.4485	1.043	61.0	73
								95—97/1.5	—	1.4465	—	21.0	27
78	CH_3COCH_3	CH_3	CH_3	CH_3	CH_3	$Si_2C_7H_{16}O_2$	—	—	—	—	—	—	27
79	$CH_3Si(CH_3)_2CH_3$	CH_3	CH_3	CH_3	CH_3	$Si_3C_6H_{22}O_1$	218.4	90—93/45	—	1.4385	0.8844	25.9	72
								179—180	—13.5	1.4370	0.8760	67.8	50, 73
								179—180	—13.5	1.4370	0.8760	15.0	48, 50
								179—180	—13.5	1.4370	0.8760	87.3	50
								77/27	—	1.4371*	0.8720*	—	21

Table 1 (continued).

No.	X	R_1	R_2	R_3	R_4	Empirical formula	Mol. wt.	B.p., °C/mmHg	M.p., °C	n_D^{20}	d_4^{20}	Yield, %	References
80	$CH_2Si(C_2H_5)_2CH_2$	CH_3	CH_3	CH_3	CH_3	$Si_3C_{10}H_{24}O_1$	246.0	97—100/15	—	1.4524	0.8930	29.9	70
81	$CH_2Si(CH_3)(C_6H_5)CH_2$	CH_3	CH_3	CH_3	CH_3	$Si_3C_{13}H_{24}O_1$	280.6	134—138/8	—	1.5112	0.9607	10.5	70
82	$CH_2Si(CH_3)_2O$	CH_3	CH_3	CH_3	CH_3	$Si_3C_7H_{20}O_2$	220.4	156—157 156—157	—28.0	1.4113 1.4113	0.9040 0.9040	66.0 45.0	50, 71, 73 48, 50
83	$(CH_2)_4$	CH_3	CH_3	CH_3	CH_3	$Si_4C_8H_{20}O_1$	188.4	169/730	—	1.4340	0.8794	85.0	35
84	$(CH_2)_4$	CH_3	C_6H_5	CH_3	C_6H_5	$Si_3C_{13}H_{24}O_1$ *cis*	312.5	158—160/3	—	1.5473	—	—	90, 133
85	$(CH_2)_4$	CH_3	C_6H_5	CH_3	C_6H_5	$Si_3C_{16}H_{24}O_1$ *trans*	312.5	160—164/3	—	1.5479	—	—	90, 133
86	$(CH_2)_4$	CH_3	F	CH_3	F	$Si_3C_8H_{14}F_2O_1$ *cis*	196.2	55/15	—	1.4035	—	68.0	133
87	$(CH_2)_4$	CH_3	F	CH_3	F	$Si_3C_8H_{14}F_2O_1$ *trans*	196.2	—	—	1.4020	—	50.0	133
88	$CH_2Si(CH_3)_2OSi(CH_3)_2CH_2$	CH_3	CH_3	CH_3	CH_3	$Si_4C_{10}H_{28}O_2$	292.7	213—213.5 213—214/768 103—104/20 208—209 213—214 213—214	30.0 28.6—29.0 28—29 30.0 27.4 —	1.4341 1.4328* 1.4345 1.4345 1.4328*	0.9039 0.9035* 0.9048 0.9048 0.9042*	— 95.0 50.0 70.6 60.0 78.0	17, 36 45, 46 3, 44 41—43 48, 50, 71, 73 21
89	$CH_2Si(C_2H_5)_2OSi(C_2H_5)_2CH_2$	C_2H_5	C_2H_5	C_2H_5	C_2H_5	$Si_4C_{14}H_{36}O_2$	404.6	154—155/2 165/3	—84	1.4683 1.4662	0.9361 0.9330	74.3 —	40—43 40—43
90	$CH_2Si(C_4H_9)_2OSi(C_4H_9)_2CH_2$	C_4H_9	C_4H_9	C_4H_9	C_4H_9	$Si_4C_{34}H_{76}O_2$	629.2	214—216/1	—64	1.4649	0.8907	63.5	41—43
91	$OSi(CH_3)_2CH_2Si(CH_3)_2O$	CH_3	CH_3	CH_3	CH_3	$Si_4C_9H_{26}O_2$	294.7	192—193	—22.3	1.4182	0.9354	39.4	50, 71, 73
92	$CH_2Si(CH_3)_2CH_2Si(CH_3)_2CH_2$	CH_3	CH_3	CH_3	CH_3	$Si_4C_{11}H_{30}O_1$	290.7	235—236	37.0	1.4533**	0.8825**	38.8	50, 73
93	$[CH_3CH_2COCH_2CH_2Si(CH_3)_2]_2O$	CH_3	CH_3	CH_3	CH_3	$Si_4C_{16}H_{40}O_4$	432.9	—	129—130	—	—	23.0	86, 93
94	$[(CH_3)_2Si(CH_2)_2]_2O$	CH_3	CH_3	CH_3	CH_3	$Si_4C_{20}H_{44}O_2$	433.0	—	47.5—48.4	—	—	14.0	51
95	*o*-C_6H_4	CH_3	CH_3	CH_3	CH_3	$Si_2C_{10}H_{14}O_1$	208.4	91—94/20 117/53	33.0 38.5	1.4950 1.4892*	0.9727 0.960*	7.5	63 62
96	*o*-C_6F_4	CH_3	CH_3	CH_3	CH_3	$Si_2C_{10}H_{12}F_2O_1$	280.3	—	49—51			5.2	64
97	*m*-$C_6H_4(CF_2)_2$—*p*-C_6H_4	CH_3	CH_3	CH_3	CH_3	$Si_2C_{16}H_{20}F_6O_1$	434.5	—	80—81.5	—	—	12.0	67, 68
98		CH_3	CH_3	CH_3	CH_3	$Si_2C_{10}H_{16}O_1$	210.4	—	71—72	—	—	20.0	56
99		CH_3	CH_3	CH_3	CH_3	$Si_2C_6H_{22}B_{10}O_1$	274.5	—	—	—	—	75.0	66
100		CH_3	CH_3	CH_3	CH_3	$Si_3C_{10}H_{32}B_{20}O_1$	474.9	—	207—208	—	—	35.0	74
101	*m*-C_6F_4—$Si(CH_3)_2OSi(CH_3)_2$—*m*-C_6F_4	CH_3	CH_3	CH_3	CH_3	$Si_4C_{20}H_{24}F_8O_2$	560.6	— —	136—137 136.3—137	— —	— —	1.5 10.0	64 65
102	*p*-C_6H_4—$Si(CH_3)_2OSi(CH_3)_2$—*p*-C_6H_4	CH_3	CH_3	CH_3	CH_3	$Si_4C_{20}H_{32}O_2$	416.8	— —	207—208 208	— —	— —	10.0 4.0	60 61
103	*p*-C_6H_4—$Si(CH_3)_2OSi(CH_3)_2$—*p*-C_6H_4—$Si(CH_3)_2OSi(CH_3)_2$—*p*-C_6H_4	CH_3	CH_3	CH_3	CH_3	$Si_6C_{30}H_{46}O_3$	625.2	—	—	—	—	—	61
104	*p*-C_6H_4—$Si(CH_3)(OH)OSi(OH)(CH_3)$—*p*-$C_6H_4$	CH_3	OH	OH	CH_3	$Si_4C_{16}H_{34}O_6$	424.7	—	—	—	—	82.7	54
105	*p*-C_6H_4—$Si(C_6H_5)(OH)OSi(OH)(C_6H_5)$—*p*-$C_6H_4$	CH_3	OH	OH	CH_3	$Si_4C_{36}H_{34}O_6$	548.8	—	—	—	—	89.3	54
106	*p*-C_6H_4—$Si(C_6H_5)(OH)OSi(OH)(C_6H_5)$—*p*-$C_6H_4$	C_6H_5	OH	OH	C_6H_5	$Si_4C_{56}H_{50}O_6$	673	—	93—104	—	—	83.5	55
107	*p*-C_6H_4—$Si(CH_3)[OSi(CH_3)_2]_3OSi[OSi(CH_3)_3](CH_3)$—*p*-$C_6H_4$	CH_3	OH	OH	CH_3	$Si_8C_{22}H_{60}O_8$	569.1	—	—	—	—	83.5	70
108	*p*-C_6H_4—$Si(CH_3)[OSi(CH_3)_2]OSi[OSi(CH_3)](CH_3)$—*p*-$C_6H_4$	CH_3	$OSi(CH_3)_3$	$OSi(CH_3)_3$	CH_3	$Si_6C_{25}H_{66}O_6$	713.4	217—220/2	—	1.4610	0.9680	7.0	70
109		CH_3	CH_3	CH_3	CH_3	$Si_4C_{32}H_{46}O_2$	520	—	glass temp. 80—82°	—	—	19.7	57
110		CH_3	—	—	CH_3	$Si_4C_{26}H_{58}O_2$	420.2	—	subl. temp. 268	—	—	5.0	58, 132

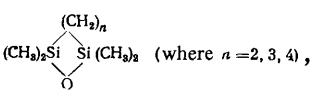
*At 25°C.
**At 40°C.

Table 2. Physical properties of polycyclic cyclocarbosiloxanes.

No.	Cyclocarbosiloxane	Empirical formula	Mol. wt.	B.p., °C/mmHg	M.p., °C	n_D^{20}	d_4^{20}	Yield, %	References
1		$Si_4C_{10}H_{24}O_4$	320.4	138—140/30	101—102	—	—	87.5	11, 31, 32
2	 R=CH_3	$Si_4C_{12}H_{36}O_3$	334.7	142/21	—	1.4429	0.9710	62.5	2, 11, 30, 31
3	R=C_6H_5	$Si_4C_{22}H_{34}O_3$	458.0	225—226/2	—	1.5222	1.070	—	11, 31, 32
4		$Si_4C_{15}H_{34}O_5$	418.8	160/0.8	—	1.4638	—	84.0	27
5	 R=CH_3	$Si_6C_9H_{24}O_6$	396.7	—	199—202	—	—	92.4	45, 46, 53, 69
6	R=C_6H_5	$Si_6C_{39}H_{36}O_6$	769.2	—	312—314	—	—	23.0	53, 69
7		$Si_6C_{16}H_{44}O_6$	557.2	125—126/2.5	—	1.4509	1.0350	20.0	45
8		$Si_6C_{13}H_{36}O_4$	425.0	120—121/8	54.2—54.8	—	—	31.0	45,46
9		$Si_6C_{24}H_{60}B_3N_3O_3$	639.8		122—124 124—125	— —	— —	98.0 69.0	26 27
10		$Si_6C_{27}H_{66}B_3N_3O_6$	723.7	230—240/1	157	—	—	70.0	27
11		$Si_8C_{30}H_{80}O_8$	763.5	—	—	—	—	88.6	70
12		$Si_{11}C_{72}H_{82}O_{11}$	1328.0	—	—	—	—		55
13	 (*cis*-)	$Si_2C_{10}H_{22}O_1$	210.0	—	—	—	—	~100	91

The thermal conductivities of the compounds in the gaseous state also decrease linearly with the number of methylene groups[50], except for cyclosiloxanes, the thermal conductivities of which are lower than those of the corresponding cyclocarbosiloxanes with a single methylene group.

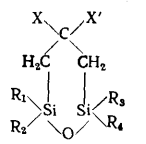
The infrared spectra have been widely employed by many investigators[9,11,18,24,35,48-58,60,62-69,71,79,87,92-99] to study the structures of various cyclocarbosiloxanes. In the spectra of compounds of this class the bands due to the stretching vibrations of the siloxane bonds are the most characteristic; in many cases useful information about the structure of cyclocarbosiloxanes may be obtained by analysing bands due to the carbon bridge. Comparison of the position of the band associated with the Si—O—Si bond in the compounds



showed that, with decrease of ring size, the band is displaced from 1018 cm^{-1} in the seven-membered ring[35] to 990 and 930 cm^{-1} in the six-membered[2,25-33] and five-membered[18,76-79,97,98] rings respectively. In the spectra of acyclic compounds the band due to the Si—O—Si group is observed in the region 1050—1100 cm^{-1}.[9,48,89,96,103-105] This shift is due to the fact that, with decrease of n, the Si—O—Si angle diminishes; it has been estimated[98,99] as 125° (for n = 4), 120° (n = 3), and 105° (n = 2). As a result, the strain in the above cyclocarbosiloxanes increases as n diminishes. For example the strain energy in five-membered cyclocarbosiloxanes is 8—12 kcal $mole^{-1}$.[18]

The Si—O—Si band in the spectrum of 1,1,3,3-tetramethyl-2-oxa-1,3-disilaindane has also been observed[63,97-99] in the region of 930 cm^{-1}.

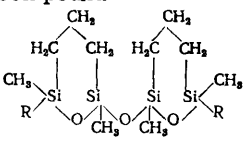
In six-membered cyclocarbosiloxanes of the type



X=H, CN;
X′=H, $COOCH_3$, $COOC_2H_5$, COOH, COOK,
$CONH_2$, CH_2NH_2
R_1, R_2, R_3, R_4 = alkyl, aryl, alkoxy-group.

the position of the maximum of the Si—O—Si band is almost independent of the nature of the substituents at the carbon or silicon atom[11,26-33,102] and is in the region 990 to 1000 cm^{-1}, which corresponds to an SiOSi angle of about 110—120°.[25,26,95] The 992 cm^{-1} absorption by the Si—O—Si group has also been observed in the infrared spectrum of the bicyclic compound *cis*-1,6-dimethyl-11-oxa-1,6-disilabicyclo[4,4,1]undecane[91].

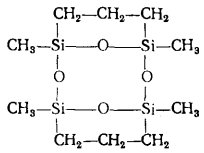
If the cyclocarbosiloxane molecule contains cyclic and acyclic siloxane bonds, the two corresponding bands are observed in the infrared spectrum as expected, the first being at a longer wavelength. Thus in the infrared spectrum of the compound



(R=CH_3, C_6H_5)

there are Si–O–Si absorption bands at 990 and 1080 cm^{-1} characterising the linear and cyclic structures respectively[2,11,30].

In the infrared spectrum of the compound



two Si–O–Si bands are also observed—at 1006 cm^{-1} (for the six-membered carbosiloxane ring) and at 1067 cm^{-1} (for the eight-membered siloxane ring).[11,32,97-99]

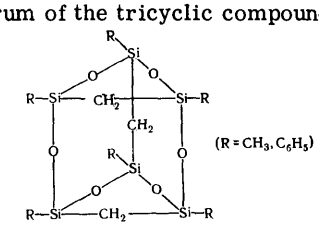
In the spectra of many six-membered compounds (I–IV) the band due to the asymmetric vibration of the Si–O bond[48-50,103-105] is in the region 1020–1030 cm^{-1}, while the CH_2 deformation vibration band is displaced from 980 to 1050 cm^{-1} [in the infrared spectra of compounds (II) to (IV)]. Thus the band due to the deformation vibrations of the ring CH_2 groups in the infrared spectra of compounds (II)–(IV) is more sensitive to changes in the skeleton of the cyclic structure than the siloxane band.

Calculation of the integral intensities of the bands associated with the asymmetric stretching vibrations of the Si–O bonds and the deformation vibrations of the endocyclic CH_2 groups in the infrared spectra of compounds (I), (II), and (IV) [for the spectrum of compound (III), such calculation is difficult owing to the impossibility of resolving the bands] shows that the integral intensity of the Si–O band remains constant, but the intensity of the CH_2 deformation vibration band is variable. The latter finding may be due to the effect of the conformational isomers on these vibrations.

Proton Magnetic Resonance Spectra

The ^1H NMR spectra of six- and eight-membered siloxanylmethylenecyclocarbosiloxanes (II), (III), and (VI)–(VIII) have two or more signals due to the non-equivalent methyl and methylene protons, the latter occurring in stronger fields[50,73]. With increase of ring size, the spin–spin coupling constant $J(^{13}CH_2)$ decreases, probably owing to an increase of the *p*-character of the carbon in the C–H bonds; there is a corresponding increase of $J(^{29}SiCH_2)$, which may be due to an increase of the *s*-character of the Si–C bond. On the basis of these results, it has been concluded that in the cyclocarbosiloxanes investigated the silicon atoms in the Si–C bonds in the ring have less *s*-character than in the Si–C bond directed to the methyl groups.

In the spectrum of the tricyclic compound

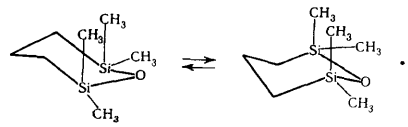


(R = CH_3, C_6H_5)

there are two signals of methylene protons, occurring at higher field (τ = 9.90 and 9.93 p.p.m.) than the signals of the methyl group protons (τ = 9.61 and 9.67 p.p.m.).[53,69]

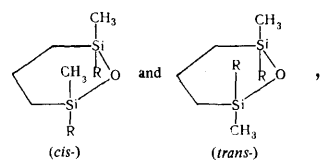
Analysis of the ^1H NMR spectra of a number of derivatives of oxadisilacyclohexane (see p. 121) led to the conclusion that such heterocycles have the "chair" conformation[26,106].

The ^1H NMR spectrum of 2,2,6,6-tetramethyl-1-oxa-2,6-disilacyclohexane[106] consists of a singlet due to methyl protons (δ = 0.07 p.p.m.), a multiplet due to α-methylene protons (δ = 0.45–0.72 p.p.m.), and a multiplet due to β-methylene protons (δ = 1.65–2.1 p.p.m.). Owing to the rapid "chair–chair" inversion, the axial and equitorial methyl groups are equivalent:



The activation energy for the conformational transitions of this compound has been estimated as about 3.5 kcal $mole^{-1}$, which is much lower than the corresponding value for 1,1,4,4-tetramethylcyclohexane (11 kcal $mole^{-1}$)[107,108] and approaches the activation energies for the "chair–chair" inversion in 1,1-dimethyl-1-silacyclohexane (5.5 kcal $mole^{-1}$)[109] and 1,1,4,4-tetramethyl-1,4-disilacyclohexane (6 kcal $mole^{-1}$).[110]

The *cis*- and *trans*-isomers of oxadisilacyclohexane,



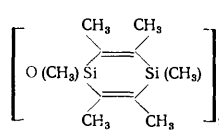
(*cis*-) (*trans*-)

where R = OAlk or C_6H_5, have characteristic ^1H NMR spectra[106]. The signal due to the protons of the methyl group located on the same side of the ring as the alkoxy-substituents is displaced towards lower field compared with the signal of a similar methyl group located in the *cis*-position with respect to a methyl or another alkyl group. In the spectra of methylphenyloxadisilacyclohexanes[106], the signal due to the methyl group in the *cis*-position is displaced towards higher field, while the signal of the *trans*-methyl group is displaced towards lower field.

The ^1H NMR method has also been used to analyse five-membered[9,18,78,79] and other cyclocarbosiloxanes[27,58,64,68,69].

Electron Spin Resonance

The application of the ESR method in studies of the radical-anions obtained from



by reduction with potassium in 1,2-dimethoxyethane solutions at –80°C, has been described[58]. The resulting radical-anion was stable for several hours at –80°C, disappearing rapidly on heating to room temperature. Analysis of the spectrum showed that the unpaired electron is fully delocalised owing to a transannular interaction, the delocalisation over the Si–O–Si bond being insignificant.

Mass Spectra

The application of mass spectroscopy to determine the molecular weight[11,58,97,111] and the mode of dissociation of

cyclocarbosiloxanes on electron impact[11,58,111] has been described. The latter is discussed in greater detail in Section IV.

IV. CHEMICAL PROPERTIES

The characteristic chemical properties of cyclocarbosiloxanes are determined primarily by the reactivity of the bonds forming the heterocycle. In the reactions investigated the Si–O bonds show the highest activity and the Si–C the lowest; the C–C bonds of the carbon bridge are as a rule stable in chemical reactions of cyclocarbosiloxanes. On the other hand, the reactions of cyclocarbosiloxanes can also involve functional groups linked to silicon and carbon atoms.

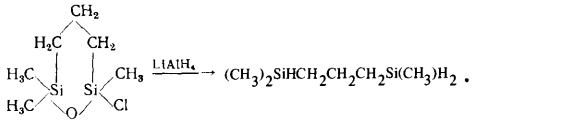
1. REACTIONS WITH CLEAVAGE OF THE HETEROCYCLE SKELETON

a. Heterolytic Cleavage of Si–C Bonds

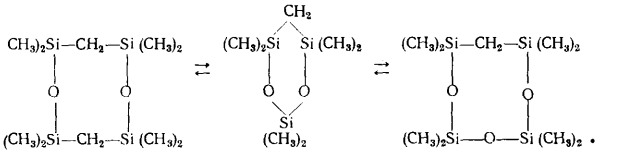
The opening of the carbosiloxane rings in the presence of electrophilic or nucleophilic agents takes place as a rule with cleavage of the siloxane bond. Like cyclosiloxanes, five-membered cyclocarbosiloxanes can be titrated with tetra-n-butylammonium hydroxide in pyridine[112]:

where R = CH_3 or C_6H_5.

When 6-chloro-2,2,6-trimethyl-1-oxa-2,6-disilacyclohexane is hydrogenated with lithium aluminium hydride in ether, not only the chlorine at the silicon atom is reduced but also the Si–O–Si bond, which results in the formation of a compound with a linear structure[11,33]:



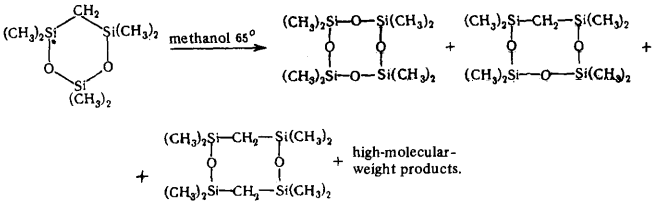
In pyridine solutions containing catalytic amounts of tetramethylammonium hydroxide, six- and eight-membered cyclocarbosiloxanes undergo a rearrangement with ring expansion or contraction even at 60°C:[50,113,114]



The rate of cleavage of heterocycles of the above type decreases with increase in the number of methylene groups in the molecule. Together with cyclic products, the rearrangement here gives rise also to high-boiling oligomers. It has been established that reactions of this kind are also accompanied by dissociation of the ring Si–C bond, as shown by the formation of six-membered heterocycles from eight-membered heterocycles (the cleavage of the Si–C bond of these cyclocarbosiloxanes by nucleophilic agents is described on p. 125).

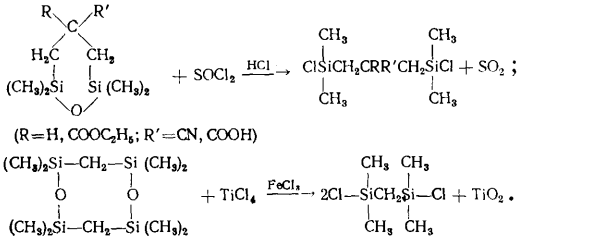
At the same time it is interesting to note that in the presence of an alcoholic solution of NaOH, KOH, and also H_2SO_4 (70%) and $H_2SO_4.SO_3$, 1,1,3,3,5,5,7,7-octamethyl-2,6-dioxa-1,3,5,7-tetrasilacyclo-octane is not cleaved[45,46,115].

In methanol solution, 1,1,3,3,5,5-hexamethyl-2,4-dioxa-1,3,5-trisilacyclohexane gives rise to rearrangement products[50,114]:



A compound having a similar structure and two methyl groups—1,1,3,3,5,5-hexamethyl-2-oxa-1,3,5-trisilacyclohexane—does not undergo any change under identical conditions. Probably the mechanism of this reaction is similar to that of the rearrangements of six-membered cyclosiloxanes in methanol[106,116-118].

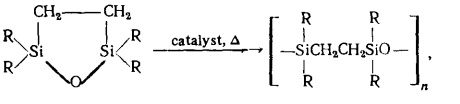
On treatment with chlorinating agents ($TiCl_4$, $SOCl_2$) in the presence of catalysts (HCl,[27] $FeCl_3$,[47] etc.) the siloxane bond of cyclocarbosiloxanes is cleaved and the corresponding linear dichlorides are formed in high yields (80–95%):



b. Polymerisation of Cyclocarbosiloxanes

This section deals with reactions involving the cleavage of the Si–O bond and leading to the formation of linear carbosiloxane polymers. Owing to the presence of the siloxane bond in the ring, cyclocarbosiloxanes can polymerise with ring opening in the presence of the usual catalysts for the polymerisation of cyclosiloxanes. Polymers whose main chain consists of alternating siloxane and carbosilane units have been obtained in this way. However, the polymerisation activity of cyclocarbosiloxane is as a rule lower than that of cyclosiloxanes with similar structures.

As already mentioned, five-membered cyclocarbosiloxanes are the most strained compounds of this class[18], as a result of which they readily polymerise in the presence of anionic [NaOH, KOH, LiOH, $(CH_3)_4NOH$, $(CH_3)_3SiONa$, $(CH_3)_3SiOK$] and cationic (H_2SO_4, CF_3COOH) catalysts[13,18]:



where R = CH_3 or C_6H_5.

The polymers obtained in the presence of anionic catalysts have a high molecular weight (up to about 10^6).

The ease of cleavage of the siloxane bond in these heterocycles depends on the nature of the substituents at the silicon and carbon atoms. Phenyl substituents at the silicon atoms increase the activity of five-membered

cyclocarbosiloxanes in anionic polymerisation[119]. Thus, 2,2,5,5-tetraphenyl-1-oxa-2,5-disilacyclopentane polymerises approximately 18 times faster than the corresponding tetramethyl-substituted cyclocarbosiloxane (Table 3).

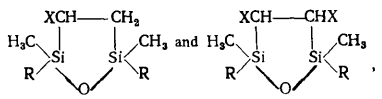
Table 3. Relative reactivities of five-membered cyclocarbosiloxanes and six-membered cyclocarbosiloxanes in base-catalysed polymerisation at 25°C.[119]

No. of cpd.	Monomer	Relative reactivity							
		I	II	III	IV	V	VI	VII	VIII
I	$^1/_3[(CH_3)_2SiO]_3$*	1.00	0.12	0.07	0.04	0.02	0.02	0.01	0.006
II	$(CH_3)_2SiCH_2CH_2(CH_3)_2SiO$	8.10	1.00	0.56	0.32	0.18	0.18	0.097	0.05
III	$(CH_3)_2SiCH_2CH_2(C_6H_5)(CH_3)SiO$	14.5	1.79	1.00	0.58	0.33	0.32	0.17	0.09
IV	$^1/_3[(C_6H_5)_2SiO]_3$	24.9	3.08	1.72	1.00	0.57	0.55	0.29	0.15
V	$(C_6H_5)(CH_3)SiCH_2CH_2(C_6H_5)(CH_3)SiO$	44.0	5.44	3.03	1.76	1.00	0.98	0.52	0.27
VI	$(CH_3)_2SiCH_2CH_2(C_6H_5)_2SiO$	45.0	5.56	3.11	1.82	1.02	1.00	0.53	0.28
VII	$(CH_3)(C_6H_5)SiCH_2CH_2(C_6H_5)_2SiO$	84.3	10.4	5.81	3.45	1.91	1.87	1.00	0.53
VIII	$(C_6H_5)_2SiCH_2CH_2(C_6H_5)_2SiO$	150.0	19.8	11.0	6.67	3.64	3.56	1.90	1.00

*Data obtained at 40°C in copolymerisation with compound (II).

On the other hand, the reactivity of five-membered cyclocarbosiloxanes under the conditions of cationic polymerisation increases when methyl substituents at the silicon atom are replaced by ethyl or phenyl groups.

In the series of C-substituted five-membered cyclocarbosiloxanes[9,76-79]

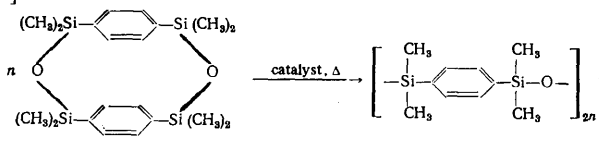


where R = CH_3, C_2H_5, C_6H_5, and X = C_4H_9, α-$C_{10}H_7$, or C_6H_5, the monosubstituted compounds show a greater tendency towards polymerisation. When they are polymerised in the presence of H_2SO_4, KOH, NaOH, and alkali metal silanolates, oily products with molecular weights in the range $(1.5-18)\times10^3$ are formed. Thermal polymerisation of the C-phenyl-substituted compound with R = CH_3 (molecular weight of the polymer up to 2×10^4) and its catalytic polymerisation in the presence of $AlCl_3$, BF_3, and $ZnCl_2$ + chloromethyl ether have been noted. In contrast to the monosubstituted derivatives, cyclocarbosiloxanes disubstituted at carbon atoms are not converted into polymers under the action of acids or bases.

In the copolymerisation of the cyclocarbosiloxanes $R_2SiCH_2CH_2SiR_2$ (R = CH_3 or C_6H_5) with six-membered cyclosiloxanes [hexamethyl(phenyl)cyclotrisiloxane] in the presence of basic catalysts, copolymers of different structures and molecular weights were obtained. The copolymerisation constants found were used to calculate the relative reactivities of the cyclocarbosiloxanes (Table 3).[119] Copolymers of the above type are suitable for conversion into rubbers and can also be used as moulding and casting resins, filling oils, and protective coatings[119,120].

Cyclocarbosiloxanes containing phenylene groups in the ring can also be polymerised in the presence of bases. Thus five-membered heterocycles with an *ortho*-phenylene bridge form at 100–140°C in the presence of 1% KOH low-molecular-weight polymers[11,62,63], while in the presence of H_2SO_4 the Si–C bonds in the ring are cleaved (see p. 125).

Cyclic carbosiloxane dimers and trimers with a *para*-phenylene bridge are converted in the presence of 0.01% potassium dimethylsilanolate at 180°C into high-molecular-weight soluble polymers [molecular weight $(0.7-4)\times10^5$]:[61]



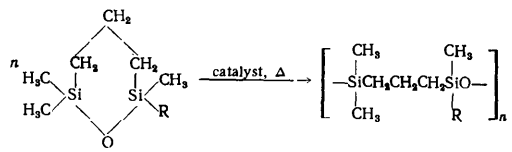
These polymers are thermally stable up to 350°C and are resistant to oxidation.

When 1,2-(1′,1′,3′,3′)-tetramethyldisiloxanyl-(1′,3′)-carborane is treated with bases, the Si–C bonds are dissociated and a siloxane polymer is formed[74] (see p. 125).

In the series of six-membered cyclocarbosiloxanes containing alternating siloxane and silmethylene groups, the polymerisation activity falls as oxygen atoms are replaced by methylene groups[50,113,114]. While the cyclocarbosiloxanes formed by replacing one oxygen atom in hexamethylcyclotrisiloxane by a methylene group polymerise more slowly in the presence of an anionic catalyst than their cyclosiloxane analogue and form a polymer with a molecular weight of 2×10^5, under analogous condition the corresponding compound in which two oxygen atoms have been replaced by methylene groups does not polymerise at all. It can be polymerised under more severe conditions (1.4% KOH, 120°C, 33 h) with formation of a low-molecular-weight oily product in a yield of 19%.[72] The formation of a condensation product of this compound has also been observed in the presence of 6 wt. % $AlCl_3$.

As in the case of five-membered cyclocarbosiloxanes[119], the replacement of a methyl group at a silicon atom by a phenyl group increases the reactivity of six-membered heterocycles in anionic polymerisation[72]. Six-membered heterocycles (oxadisilacyclohexanes) are also polymerised with greater difficulty[11,27,75,101] than hexamethylcyclotrisiloxane; they are less reactive than five-membered cyclocarbosiloxanes.

The anionic and cationic polymerisation of 2,2,6,6-tetramethyl-1-oxa-2,6-disilacyclohexane and certain other derivatives of this heterocycle has been investigated[11,102,109,121,122]:



where R = CH_3, C_2H_5, C_3H_7, C_4H_9, C_5H_{11}, C_6H_5, or C_6H_4Cl.

Under optimal polymerisation conditions (0.6% KOH, 110°C, 640 min), the yield of the polymer (with R = CH_3) was 93% and the molecular weight was 3×10^3. In the presence of sulphuric acid or polydimethylsiloxysulphonic acid, a polymer with a molecular weight of about 10^4 was formed.

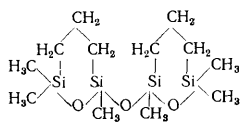
The rate of polymerisation of 2,2,6,6-tetramethyl-1-oxa-2,6-disilacyclohexane in the presence of KOH and H_2SO_4 is lower by two powers of 10 than the rate of polymerisation of hexamethylcyclotrisiloxane and the activation energies are respectively 21 kcal mole^{-1} for anionic

polymerisation and 7 kcal mole^{-1} for cationic polymerisation[11,101,121,122]. The intrinsic viscosity (molecular weight) of the polymers increases linearly with the degree of conversion. On this basis, the authors conclude that the polymerisation has a stepwise mechanism. In the initial stages the reaction is of first order with respect to the monomer; at higher conversions, the reaction order becomes fractional.

The effect of the substituent at the silicon atom on the rate of polymerisation of oxadisilacyclohexanes in the presence of cationic and anionic catalysts has been investigated[11,102]. Replacement of the methyl group by ethyl and higher alkyl groups lowers the rate of polymerisation in the presence of KOH approximately by a factor of 10. The introduction of electron-accepting substituents (phenyl, chlorophenyl) increases somewhat the rate of reaction. As was to be expected, in the case of cationic polymerisation aryl substituents lower the rate. It is interesting to note that electron-donating substituents also lower the rate of cationic polymerisation of oxadisilacyclohexanes, which has been explained by the swamping of the inductive effect by the steric effect.

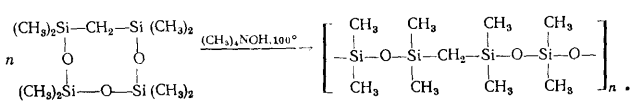
The linear relation between the logarithm of the relative rate of polymerisation of oxadisilacyclohexanes with phenyl substituents and the σ^* constant in the Hammett–Taft equation is evidence of a correlation between the rate of polymerisation and the inductive effect of substituents.

The polymerisation of the bicyclic compound



in the presence of KOH and polydimethylsiloxysulphonic acid takes place with formation of insoluble polymers[11,102].

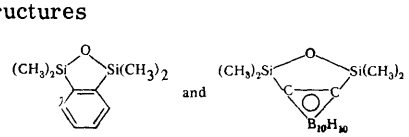
In the series of eight-membered methylenesiloxane heterocycles, only 1,1,3,3,5,5,7,7-octamethyl-2,4,6-trioxa-1,3,5,7-tetrasilacyclo-octane could be polymerised in the presence of anionic catalysts[50,113,114]:



A polymer with a molecular weight of 7.5×10^4 was obtained. The corresponding cyclocarbosiloxanes with two and three methylene groups are not polymerised under these conditions, i.e. in this case the polymerisation activity decreases with the number of methylene groups, probably owing to their positive inductive effect (relative to oxygen), which leads to an increase of electron density at the silicon atoms as a result, nucleophilic attack on the latter is hindered.

c. Heterocyclic Cleavage of Si–C Bonds

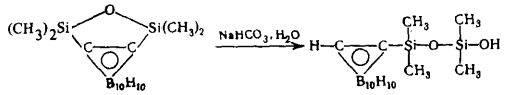
When cyclocarbosiloxanes with a carbon bridge having marked electron-accepting properties are treated with alkalis or acids, the ring Si–C bonds are cleaved. For example, in an attempt to polymerise compounds with the strained structures



(X) (XI)

in the presence of acids [compound (X)] or bases [compound (XI)], the formation of a polydimethylsiloxane and the removal of a phenyl or a carborane group respectively was observed[11,62,63,74].

At room temperature an aqueous solution of sodium bicarbonate also causes the dissociation of the Si–C bond[74]:

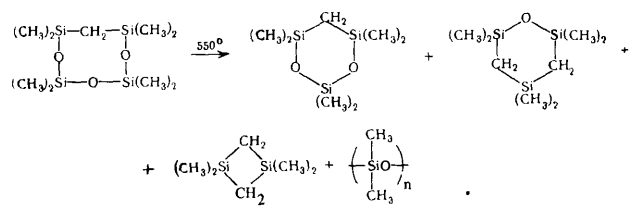


The cleavage of endocyclic Si–C bonds has likewise been observed when certain eight-membered cyclocarbosiloxanes were treated with nucleophilic agents[50,113,114]. In pyridine solutions containing catalytic amounts of $(CH_3)_4NOH$, 1,1,3,3,5,5,7,7-octamethyl-2,6-dioxa-1,3,5,7-tetrasilacyclo-octane gave rise to 1,1,3,3,5,5,7,7-octamethyl-2,4,6-trioxa-1,3,5,7-tetrasilacyclo-octane and 1,1,3,3,5,5,-hexamethyl-2,4-dioxa-1,3,5-trisilacyclohexane together with other products at a temperature as low as 60°C (see the scheme on p. 123). The formation of these heterocycles indicates the dissociation of Si–C bonds in the carbosiloxane ring. The weakening of endocyclic Si–C bonds in cyclocarbosiloxanes is probably due to the effect of the adjacent oxygen atom of the siloxane bond.

d. Thermal Reactions of Cyclocarbosiloxanes in the Gas Phase

At 500–600°C in the gas phase cyclocarbosiloxanes undergo rearrangements accompanied by the dissociation of endocyclic Si–O and Si–C bonds. In the first place this applies to cyclocarbosiloxanes consisting of alternating siloxane and silmethylene groups (p. 117).[48,50,88].

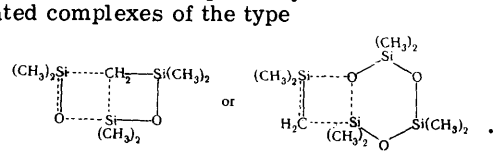
The principal effect of the rearrangements is ring contraction. Thus eight-membered cyclocarbosiloxanes form mainly six-membered compounds; in addition 1,3-disilacyclobutane and cyclosiloxanes are formed, for example:



$(n = 3,4)$

The characteristics of the thermal decomposition of cyclocarbosiloxanes are very similar to those of the thermal decomposition of cyclosiloxanes: the latter is a monomolecular process involving a four-centre mechanism[50,123,124].

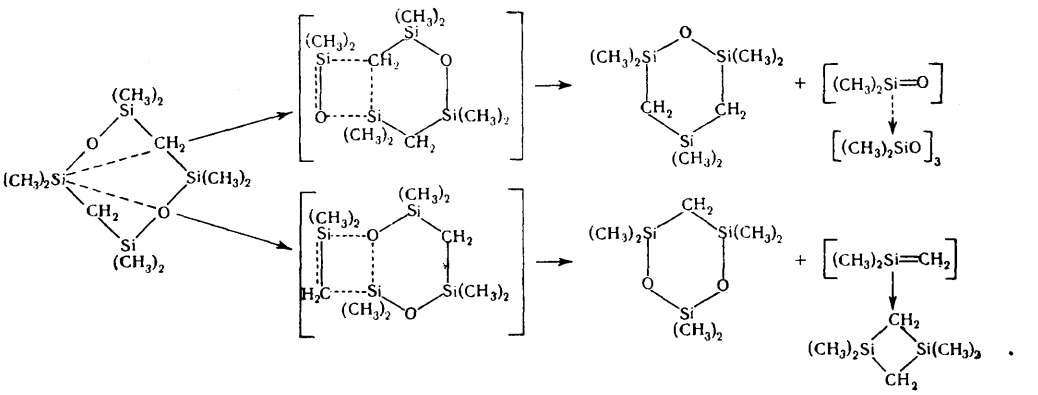
It has been suggested that the thermal rearrangement of cyclocarbosiloxanes has a similar molecular mechanism involving transannular interactions between the oxygen or carbon atoms on the one hand and silicon atoms on the other[50,88,124]. The latter probably lead to the formation of activated complexes of the type



A qualitative assessment of these activated complexes shows[125–127] that the activation energy for the dissociation

of the first is higher than for the second which is consistent with the higher thermal stability of six-membered cyclocarbosiloxanes noted in some investigations[50,88] compared with the eight-membered compounds. The proposed activation mechanism also accounts for the preferential dissociation of endocyclic bonds.

The structures of activated cyclocarbosiloxane complexes presented below show that their dissociation should lead to the formation of unstable intermediates: methylenedimethylsilane or dimethylsilanone, which are probably in fact responsible for the formation of 1,3-disilacyclobutane and cyclosiloxanes:



Oxadisilacyclohexanes behave differently in gas-phase thermolysis. Thus it has been noted[11,128] that the decomposition of 2,2,6,6-tetramethyl-1-oxa-2,6-disilacyclohexane begins with the removal of methylene groups, after which the siloxane bond is cleaved.

e. Dissociation of Cyclocarbosiloxanes on Electron Impact

The primary process occurring in the dissociative ionisation of cyclocarbosiloxanes (as for many other acyclic and heterocyclic organosilicon compounds) is the removal of a methyl group from the molecular ion (M^+):[11,58,67,111]

$$M^+ \xrightarrow{-CH_3} [M-15]^+.$$

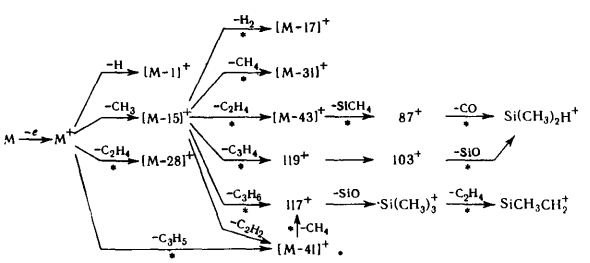
The resulting ion $[M-15]^+$ is more stable than the molecular ion; the formation of all other fragment ions can be as a rule explained by its decomposition and rearrangement. As in the case of cyclosiloxanes[129], the heaviest of the cyclocarbosiloxane fragment ions (II), (III), (VI)–(VIII) (see p. 117) are formed as a result of the loss of neutral fragments originating from the surrounding methyl group, but the cyclic skeleton of the molecule persists. With increase of the number of methylene groups in the ring, the intensity of the fragmentation of compounds (I)–(IV), due to the decomposition or rearrangement of the cyclic skeleton of the molecule, increases.

An interesting feature of the dissociative ionisation of these cyclocarbosiloxanes is the formation of metastable ions due to the loss of the neutral fragments $(CH_3)_2SiO$ and $(CH_3)_2SiCH_2$, which are structural elements of cyclocarbosiloxanes.

The mass spectra of the above six- and eight-membered cyclocarbosiloxanes contain a group of ions with the general formula $(CH_3)_3Si_2O_2{-}_n(CH_2)_n$ (n = 0, 1, or 2): the cyclosiloxane ion with m/e = 133, the cyclocarbosiloxane ion with m/e = 131, and the cyclocarbosilane ion with m/e = 129. The liberation of a considerable amount of kinetic energy on formation of the first ion[129] and the detection of an ion with a high intensity (m/e = 129) in the mass spectrum of 1,1,3,3-tetramethyl-1,3-disilacyclobutane[130] suggest that ions of this group have a cyclic structure.

Together with the above ions, doubly charged fragment ions formed by the successive removal of hydrocarbon groups from the $[M-2CH_3]^{2+}$ ions were observed in the mass spectrum. However, on passing from cyclosiloxanes to cyclocarbosilanes, the intensity of the doubly charged $[M-2CH_3]^{2+}$ ions falls. In addition, $[M-CH_3]^{2+}$ doubly charged ions were found in the mass spectra of six-membered cyclocarbosiloxanes [compounds (II) and (III)].[111] This is evidence of a particularly high resistance of the six-membered ring to dissociation on electron impact.

In the case of 2,2,6,6-tetramethyl-1-oxa-2,6-disilacyclohexane[11,128], the formation of the principal fragment ions is due to the decomposition of the $[M-15]^+$ ion and is associated with the removal from it of propene, ethylene, acetylene, and other fragments:

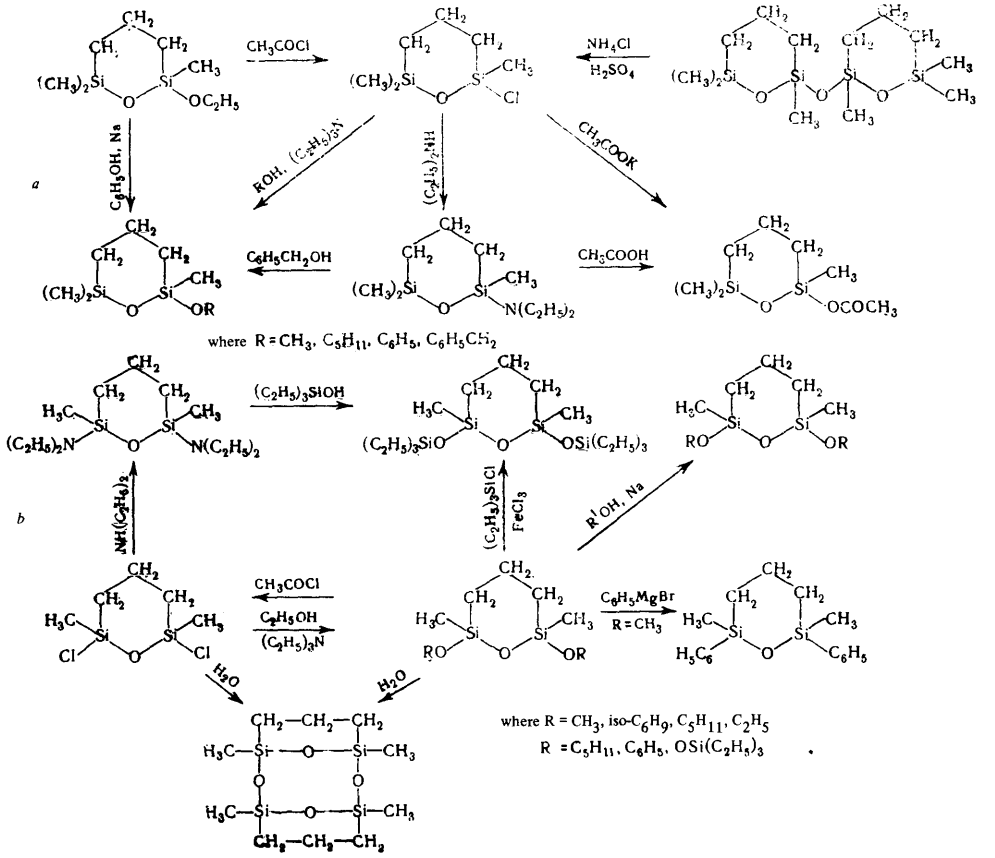


The stability of the siloxane skeleton in this compound has been noted. The number of ions containing the SiOSi group reached up to 85% of all the ions in the spectrum. An interesting feature of the mass spectrum of $[O(CH_3)Si\langle\equiv\rangle Si(CH_3)]_2$ is the presence of a fragment ion with m/e = 97 (an intensity of 14) to which the authors attributed the structure of silirene[58]:

2. REACTIONS INVOLVING THE RETENTION OF THE HETEROCYCLIC SKELETON

a. Reactions Involving Exocyclic Bonds at the Silicon Atom

As for acyclic compounds with functional groups at Si, a number of reactions of cyclocarbosiloxanes involving substitution at the silicon atom have been described; the majority of them can occur without the cleavage of the ring Si–O bonds. Thus reactions involving the substitution of halogen, alkoxy-, and amino-groups in six-membered oxadisilacyclohexanes have been described[11,31–33,54,55,70]: hydrolysis, alcoholysis, transesterification, amination, acetoxylation, alkylation with a Grignard reagent, heterofunctional condensation, and others, for example:

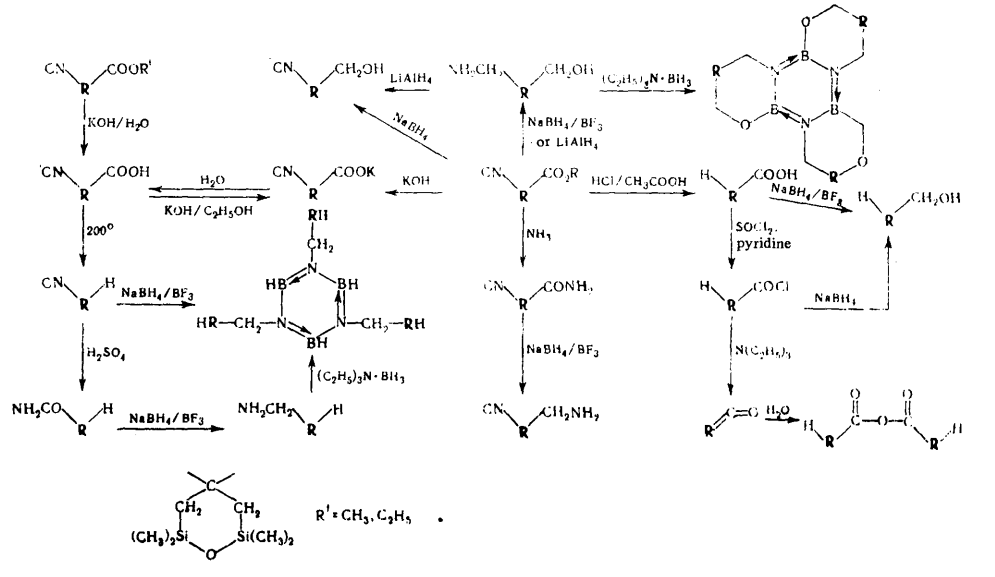


where R = CH_3, C_5H_{11}, C_6H_5, $C_6H_5CH_2$

where R = CH_3, iso-C_6H_9, C_5H_{11}, C_2H_5
R = C_5H_{11}, C_6H_5, $OSi(C_2H_5)_3$

b. Reactions of Groups and Atoms Linked to Carbon

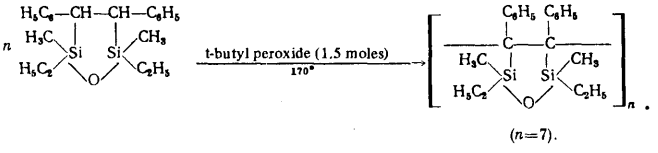
Numerous reactions of oxadisilacyclohexanes containing functional groups at the β-carbon atom of the ring have been investigated[24–27,75,131]:



$R' = CH_3, C_2H_5$

Despite the fact that many of these reactions take place under comparatively severe conditions, the carbosiloxane ring is not cleaved. In particular, it is interesting to note that, in contrast to cyclocarbosiloxanes with functional groups linked to silicon atoms[11,33], compounds with functional groups linked to carbon atoms can be reduced by $LiAlH_4$ without the cleavage of the ring siloxane bond.

When the hydrogen atoms of the methine groups of five-membered C-phenyl-substituted cyclocarbosiloxanes are attacked by free radicals, relatively unreactive cyclocarbosiloxane radicals of the benzyl type are formed and recombine, giving rise to condensation products[9,79]:



(n=7).

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During the preparation of the manuscript for the press, new studies on the synthesis and properties of cyclocarbosiloxanes were published[132-135].

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[Ref. 43 is missing from the original (Ed. of Translation).]

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N-Nitrenes

B.V.Ioffe and M.A.Kuznetsov

This review gives an exhaustive summary of data on unstable intermediate species RR'N-N:, containing a nitrogen atom with an incomplete electron shell, bonded to another nitrogen atom. These species are analogous to aminocarbenes, and play an important role in the chemistry of organic derivatives of hydrazine. Reactions in which the formation of N-nitrenes has been postulated have been systematised, and reactions involving their subsequent transformation with the separation of nitrogen, isomerisation, or addition to other reagents have been examined. The review covers papers dealing with the chemistry of N-nitrenes, published before mid-1971. The bibliography contains 145 references.

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I. INTRODUCTION

Progress in the chemistry of the carbenes in recent decades has led to an increase in interest in their analogues containing atoms with incomplete sextet electron shells, including the reactive intermediate compounds of formally univalent nitrogen R-N:, the so-called nitrenes (the subject of several reviews[1-5] and a recent monograph[6]).

Among the nitrenes, a unique position is occupied by the labile compounds in which the "sextet" nitrogen atom is bonded to another nitrogen atom:

(I)

Compounds of type (I) are called N-nitrenes or aminonitrenes, to distinguish them from C-nitrenes or O-nitrenes, containing C-N: and O-N: bonds respectively. The terms diazene, azene, azalene, and azamine have also been used in the literature for structures of type (I).[1] The term "diazene" is now applied to monosubstituted derivatives of di-imide R-N=NH, and this can lead to confusion. The other names have not been widely used.

We shall use the terms "N-nitrene" and "aminonitrene" as equivalent names, the nature of the radicals R and R' (I) being indicated in the name:

H_2N-N	aminonitrene
$(CH_3)_2N-N$	dimethylaminonitrene
C_6H_5NH-N	phenylaminonitrene etc.

In more complex compounds, in which the central nitrogen atom of the aminonitrene is present in a ring, it is convenient to use the names of the corresponding heterocyclic radicals, for example

N-pyrrylnitrene .

An increasing number of facts indicate that N-nitrenes play a prominent role in the chemistry of the organic derivatives of hydrazine. Although the existence of these very unstable intermediate compounds in many instances has been only tentatively assumed, the ideas regarding aminonitrenes make it possible to understand a large number of the reactions of hydrazines, used in the production of synthetic materials and medicinal products, and in agriculture. The assumption that N-nitrenes are formed as intermediate products reveals common features in apparently completely different reactions and provides possibilities for predictions, useful analogies, and generalisations. Without a systematisation of ideas regarding N-nitrenes, the study and further development of the organic chemistry of hydrazine would be impossible.

The brief data on N-nitrenes in reviews of nitrenes[1-5], and the sections devoted to these compounds in the monograph cited[7] are inadequate and incomplete. The detailed article by Lemal in Lwowsky's book[6], published before this review was complete, covers the literature only as far as early 1969.

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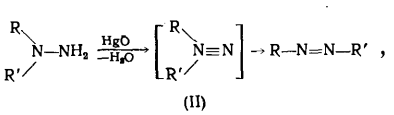
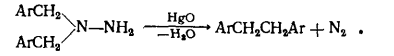
The first suggestion regarding the existence of unstable intermediate compounds with a nitrogen atom bound only to another nitrogen atom appeared as early as the end of the nineteenth century, with the need to explain the anomalous course of the oxidation of various hydrazines. In the oxidation of 1-allyl-1-phenylhydrazine and 1-allyl-1-*p*-tolylhydrazine with mercuric oxide, Michaelis and Luxemburg[8] obtained azo-compounds instead of the tetrazenes usually formed under these conditions, and they attributed this result to the rearrangement of a primary product with the unusual structure (II):



(II)

where $R = CH_2=CH-CH_2-$ and $R' = C_6H_5$ or p-$C_6H_4CH_3$. Formula (II) is not possible from the viewpoint of modern electronic theory, and it represents essentially the N-nitrene (I).

In the oxidation of dibenzylhydrazines with mercuric oxide, completely different anomalous products were obtained; nitrogen was liberated, and hydrocarbons were formed:

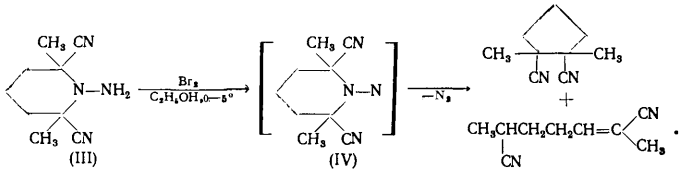


This reaction proceeds so smoothly that it was subsequently used for the preparation of derivatives of dibenzyl (the Busch-Weiss reaction)[10-12]. The replacement of one of the benzyl radicals by an aryl radical, however, leads

to the formation of arylhydrazones (or mixtures of arylhydrazones and tetrazenes)[13]:

$$\begin{matrix} Ar \\ Ar'CH_2 \end{matrix}\!\!>\!N\!-\!NH_2 \xrightarrow[0°,CHCl_3]{HgO} ArNHN{=}CHAr'\,.$$

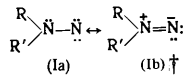
Later, it was established that the Busch–Weiss reaction is not restricted to benzylhydrazines; the oxidation of the cyclic hydrazine (III) with bromine leads to the liberation of nitrogen and the production of a mixture of dinitriles, which, in the opinion of the authors cited[14-17], are products of the decomposition of the N-nitrene (IV) formed as an intermediate product:



The hypothetical compound with a "sextet" nitrogen atom (V) was also regarded as an intermediate product in the thermal decomposition of a mixture of phenylhydrazine and its hydrochloride[18]:

$$[C_6H_5NH_2NH_2]^+ + C_6H_5NHNH_2 \rightarrow \underset{(V)}{[C_6H_5NH{-}N]} \rightarrow C_6H_5NH_2 + C_6H_6 + NH_3 + N_2 + H^+.$$

Since the nineteen-fifties, suggestions regarding the existence of intermediate species of this kind have begun to appear more frequently in papers on the chemistry of hydrazines. It has been considered that as a consequence of the presence of an unshared pair of electrons on the central nitrogen atom in these compounds, mesomerism is possible (Ia–Ib)



It has been suggested that mesomerism may lead to stabilisation and an increase in the lifetime of N-nitrenes compared with C-nitrenes or carbenes (see p. 106 of Ref. 7). Until recently, however, there was no information on the electronic structure of N-nitrenes or the relative roles of structures (Ia) and (Ib). In 1970, the structures of a number of the simplest N-nitrenes and their analogues were calculated[19] by the MO LCAO method with complete neglect of differential overlap and with allowance for all the valency electrons (the CNDO/2 method[20-22]). These calculations showed that aminonitrene itself $H_2N{-}N$ should have a planar configuration with N–N bond length 1.25 Å, which is smaller than the length of the N–N bond in hydrazine (1.46 Å) but longer than the length of the N=N bond in di-imide (1.2 Å)‡. The "sextet" nitrogen atom of the aminonitrene carries a fairly high negative charge (−0.217). For the nearest homologues of aminonitrene the negative charge on the terminal nitrogen atom is increased slightly as a consequence of the positive inductive effect of the alkyl substituents.

N-Nitrenes in which the unshared electron pair of the central nitrogen atom is involved in conjugation with substituents show the opposite effect—a definite, though small, decrease in the negative charge on the terminal nitrogen atom: −0.216 for N-pyrrylnitrene and −0.204 for phenylaminonitrene.

The populations of the π-AO of the terminal nitrogen atom in aminonitrene and its nearest homologues lie in the range 0.47–0.49, and the orders of the π-bonds between the nitrogen atoms in the range 0.81–0.84.

These results were obtained with the assumption that the ground state of the aminonitrenes is a singlet state. This assumption agrees with data on the stereochemistry of the addition reactions of various aminonitrenes at the double bond.

The comparatively large contributions of the polar structure (Ib), which reaches several percent, is an important characteristic feature of N-nitrenes, distinguishing them from C-nitrenes and from typical carbenes. The electrophilic properties characteristic of carbenes and associated with the presence of an incomplete electron shell can in the N-nitrenes be poorly defined and even masked by the distinct manifestation of the nucleophilic properties of the negatively charged terminal nitrogen atom with its high π-AO population. In this respect we must consider the nearest analogues of the N-nitrenes to be not the C-nitrenes but the so-called "nucleophilic carbenes", in particular the little-studied aminocarbenes.

Another characteristic structural feature of the N-nitrenes, which leaves a specific imprint on their reactions, is the presence of the nitrogen–nitrogen bond. As a consequence of the low energy of this bond, combined with the tendency, typical of many hydrazine derivatives, to decompose with the formation of the exceptionally stable nitrogen molecule, an extremely important role in the chemistry of the N-nitrenes is played by decomposition reactions, which are not characteristic of carbenes.

II. PREPARATION OF N-NITRENES

The fairly large number of reactions for which the formation of N-nitrenes in the intermediate stages has been postulated can be divided into two groups. One of these consists of reactions involving the formation and decomposition of unsymmetrically substituted hydrazine derivatives, including (formally at least) α-elimination according to the scheme

$$>\!N{-}N\!<^{X}_{Y} \rightarrow >\!N{-}N + XY\,.$$

These reactions invlude the oxidation of 1,1-disubstituted hydrazines by bromine in acid medium (XY = HBr), the alkaline cleavage of the hydrazides of sulphonic acids, the thermal decomposition of their N-sodium derivatives (XY = $NaSO_2P$), and also the incomplete reduction of N-nitrosamines in alkaline medium (X = OH, Y = H), the ozonolysis of hydrazones, and the reaction of secondary amines with difluoroamine HNF_2, in which the sources of the nitrenes—unstable hydrazine derivatives—are formed in the first stages of the processes.

† This mesomeric form can be regarded as a modern representation of the structure (II) proposed at an early date by Michaelis[8], whereas structure (Ia) is a more accurate general representation of structures of type (V).

‡ An interesting feature is that in an electron diffraction study of the compound N_2F_2, obtained by decomposing FN_3, it was found[23] that the intensity curves can correspond to a planar molecule of the form $\begin{matrix} F \\ F \end{matrix}\!\!>\!N{-}N$ with N–N bond length 1.16 Å.

Another less extensive group of methods for obtaining N-nitrenes consists of reactions involving the decomposition of various derivatives of hydrazine containing the fragment $\rangle N-N^{-}-Z^{+}$:

$$\rangle N-N^{-}-Z^{+}:$$

$$\rangle N-\bar{N}-\overset{+}{Z} \rightarrow \rangle N-N + Z \ .$$

The decomposition of N-azido-compounds (Z = N_2) and sulphoximines (Z = R_2SO) takes place according to this scheme.

1. Formation of N-Nitrenes in Oxidation Reactions

The first proof of the formation of N-nitrenes in oxidation reactions was obtained by McBride and Kruse[24]. In the oxidation of the simplest 1,1-dialkylhydrazines by halogens or alkali metal halates in strongly acidic medium (pH 0), the solutions showed characteristic absorption in the near ultraviolet, which could be interpreted as a consequence of the formation of the acid (VI) conjugate with (I):

$$\underset{R}{\overset{R}{\rangle}}N-NH_2 \xrightarrow[-2HBr]{H^+,Br_2} \underset{R}{\overset{R}{\rangle}}\overset{+}{N}=NH \rightleftarrows \left[\underset{R}{\overset{R}{\rangle}}N-\ddot{N} \leftrightarrow \underset{R}{\overset{R}{\rangle}}\overset{+}{N}=\bar{N}\right] + H^+ \ .$$

(VI) (I)

This acid, which was called the diazenium cation, is fairly stable in strongly acidic solutions. Neutralisation of the solutions gave the corresponding tetrazene $R_2N-N=N-NR_2$.

The existence of species of type (VI) was also proved as follows. Acid solutions of Me_2NNH_2 and Et_2NNH_2 were oxidised separately, then mixed and neutralised. The mixtures formed contained all three possible tetrazenes—the two symmetrical and the unsymmetrical.

Dimethyldiazenium perchlorate (VII) was isolated by the reaction of dimethylhydrazine with iodine and silver perchlorate:

$$Me_2NNH_2 + I_2 + 2AgClO_4 \rightarrow \underset{(VII)}{[Me_2\overset{+}{N}=NH]\,ClO_4^-} + 2AgI + HClO_4 \ .$$

Work on the electrochemical oxidation of 1,1-dimethylhydrazine[25] and 1,1-diphenylhydrazine[26,27] in acid solutions also established the formation of relatively stable products of the two-electron oxidation; the presence of these products was confirmed by coulometry and chronopotentiometry[25] and by ultraviolet spectroscopy. It was noted that these substances can be reduced to the original hydrazines in yields of up to 95%, but when the solutions are left to stand they slowly decompose.

Further proof of the formation of N-nitrenes in oxidation reactions is provided by the fact that they can be trapped in the form of stable products of addition to the multiple bonds[28-34] and the products of the cyclo-addition of diazenium salts at multiple bonds[27,35-39], and also by the reactions of N-nitrenes with dimethyl sulphoxide[28,31].

The oxidation of 1,1-disubstituted hydrazines by bromine in strongly acidic aqueous solutions has been dealt with in a number of papers[14,15,17,24,35,36,40-43]. Potassium iodate[44] and bromate[24,43,45] are sometimes used as oxidant, but yellow mercuric oxide is used most frequently[8-13,44,46-61]. The reaction with mercuric oxide is usually carried out in aqueous or absolute alcohol, and less frequently in CH_2Cl_2,[50,53,55,59] $CHCl_3$,[10,11] CCl_4,[12,56] ether[61], butanol, and dimethyl sulphoxide[57]. Activated manganese dioxide[32,53,56,59,60,62,63] and nickel dioxide[60,64] in CH_2Cl_2, potassium permanganate in acetone[16,55], N-bromosuccinimide[55,60], selenium dioxide and iodobenzene diacetate[60], *t*-butyl hypochlorite[17,65], chlorine[65], and per-acids[66] have also been used.

Lead tetra-acetate has recently been used for the oxidation of 1,1-disubstituted hydrazines[28-33,36,51,60,67-81]. The reaction is usually carried out in benzene or CH_2Cl_2.

1-Chlorobenzotriazole[82] and the diethyl ester and phenylimide of azodicarboxylic acid[83] have been used as oxidants.

In all instances it is assumed that intermediate formation of the N-nitrene takes place according to the general scheme

$$\underset{R'}{\overset{R}{\rangle}}N-NH_2 \xrightarrow[-2H]{-2e^-} \left[\underset{R'}{\overset{R}{\rangle}}N-\ddot{N} \leftrightarrow \underset{R'}{\overset{R}{\rangle}}\overset{+}{N}=\bar{N}\right] \ . \qquad (1)$$

The directions of the reactions of the N-nitrenes formed in the first stage of the reaction, and the structures of the final products, are determined by the conditions of the oxidation and also by the nature of the radicals R and R′ in the original hydrazine. If R and R′ are aliphatic or aromatic radicals, oxidation under mild conditions usually gives the tetrazenes, which are regarded as the "normal" products of the oxidation of unsymmetrical secondary hydrazines. N-Nitrenes with heterocyclic, benzyl, and certain other radicals, however, have a greater tendency to undergo other reactions, so that the oxidation of these hydrazines may take place "anomalously", with the formation of not tetrazenes but other nitrogen compounds or hydrocarbons.

The oxidation has been carried out with 1,1-dibenzylhydrazine and its derivatives[9-13,17,47-49,63,79], including optically active compounds[47,48], and also with heterocyclic compounds which can be regarded as analogues of 1,1-dibenzylhydrazine: 1-amino-2,6-diphenylpiperidine[44,46,54], 1-amino-2,5-diphenylpyrrolidine[58], and other compounds containing condensed aromatic rings[53,55,56,64,84]. The oxidation of 1-amino-2,5-diphenylpyrrole and 1-amino-2,3,4,5-tetraphenylpyrrole[56], 1-amino-1,3,4-triazole, and its 2,5-dimethyl- and 2,5-diphenyl-derivatives[78] has been studied. Studies have been reported of the oxidation of 1,1-dialkylhydrazine[24,25,34,35,40,41,45,61,83,85], 1-alkyl-1-benzylhydrazine[21,32], and also of 1,1-diarylhydrazine[26,27,63,86], and 1-aryl-1-benzylhydrazine[13]. The oxidation of 1,1-disbustituted hydrazines with allyl and aryl radicals was studied earlier[8,86].

Overberger and coworkers oxidised 1-amino-2,6-dicyano-2,6-dimethylpiperidine[14-17,42], 1-amino-2,6-dicyanopiperidine, and 1-amino-2,6-dicarbamidopiperidine[57]. The oxidation of N-aminopiperidine, N-aminomorpholine[63], and N-aminophthalimide[80] has been studied.

Considerable attention has been paid to the oxidation of compounds of the 1- and 2-aminobenzotriazole[60,68-72,77,82], 1-aminonaphtho[1,8,-*d*,*e*]triazine[73-75], and 1-amino-4,5-diphenyltriazole[82] series, in connection with the intermediate formation of dehydroaromatic systems—dehydrobenzene and 1,8-dehydronaphthalene.

1-Amino-oxindole and its derivatives[51,65] have been oxidised, and various 3-cinnolinols were obtained as final products.

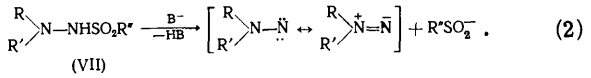
3-Aminobenzoxazoline-2-one[28,29,36], the N-aminoimides of various dibasic acids[29-32], and various other N-aminoheterocyclic compounds[29,32,33,67] were oxidised with the aim of carrying out addition reactions of the intermediate N-nitrene at the multiple bond.

3-Amino-benzo-1,2,3-triazine-4-one and its derivatives[76] were oxidised in an attempt to obtain benzocyclopropenone. The reaction of semicarbazide with per-acids has been carried out[66].

It should be emphasised that in early work on the oxidation of 1,1-disubstituted hydrazines the suggestion that N-nitrenes are formed in intermediate stages was used only to explain anomalous reactions, whereas it is now assumed that they are also formed in "normal" oxidation.

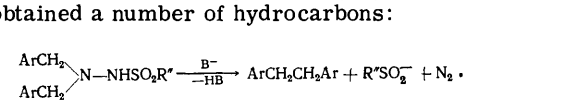
2. Decomposition of the Hydrazides of Sulphonic Acids and Their N-Sodium Derivatives

The action of alkalis on 1,1-disubstituted hydrazides of sulphonic acids (VII) leads not to their saponification but to their decomposition to the salts of the sulphinic acids and N-nitrenes, which undergo further reactions:

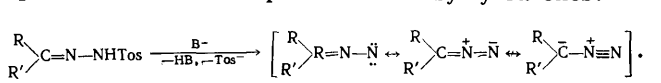


(VII) (2)

This reaction is named after its discoverer Carpino[87,88]. In the decomposition of dibenzylsulphonylhydrazines, Carpino obtained a number of hydrocarbons:



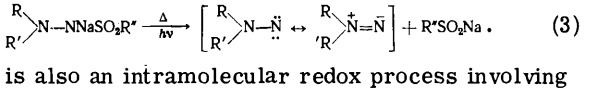
The formation of N-nitrenes from the hydrazides of sulphonic acids can be regarded as analogous to the preparation of diazo-compounds from tosylhydrazones:



In both instances an intramolecular redox process takes place, in which the hydrazine residue undergoes two-electron oxidation and the sulphonic acid residue is reduced to the sulphinate ion. In this sense the Carpino reaction is similar to the Busch–Weiss intermolecular oxidation of 1,1-disubstituted hydrazines; the final products of these reactions are also similar.

Lemal[89,90] observed a decrease in the rate of hydrolysis of 1,1-disubstituted hydrazides of sulphonic acids in strongly alkaline solutions. It was suggested that a condition for the reaction is the presence of alkali and free sulphonyl hydrazide.

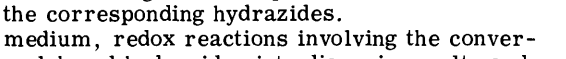
The alkaline decomposition of 1,1-disubstituted sulphonyl hydrazides is closely related to the thermal decomposition[75,90–93] or photolysis[75] of their N-sodium derivatives:



(3)

This is also an intramolecular redox process involving the oxidation of the hydrazine residue to the aminonitrene and the reduction of the sulphonic acid residue to the sodium salt of the sulphinic acid. The final products of this reaction are analogous to the products of the action of alkalis on the corresponding hydrazides.

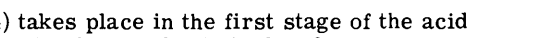
In acid medium, redox reactions involving the conversion of the sulphonyl hydrazides into diazenium salts and salts of sulphinic acids, which dissociate to give diazenium cations and sulphinate ions[94], also take place



(4)

Reaction (4) takes place in the first stage of the acid hydrolysis of 1-alkyl- and 1,1-dialkyl-2-tosylhydrazines, and the diazenium ion formed undergoes a number of further reactions.

Dissociation according to scheme (4) is also apparently the first stage of the ready exchange of sulphonic acid residues between sulphonyl hydrazides and salts of sulphinic acids[89,94]:



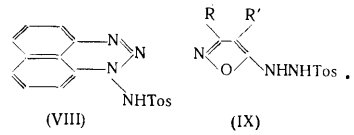
The exchange has been studied in alkaline and neutral media. The establishment of equilibrium in this exchange has been demonstrated by the NMR method, and the kinetics of exchange have been studied. It has been established that the reaction is of first order with respect to the original hydrazide and of zero order with respect to the salt (at a salt concentration greater than the equivalent concentration).

The action of alkali on 1,1-disubstituted sulphonyl hydrazides and the decomposition of their N-sodium derivatives have been most frequently studied with the readily available and easily purified tosyl hydrazides[55,56,59,62,75,87,88,91–93,95–101] and benzenesulphonyl hydrazides[87,88,91,96,101,102]. The hydrazides of alkylsulphonic acids have been less extensively studied[87,88,101].

The substituents on the tertiary nitrogen atom have been varied widely. Dibenzylhydrazides[87,88,95,96] and their derivatives[87,88] and analogues[55,62,92,97,98] have been studied. The alkaline cleavage of the 1-aryl-1-benzylhydrazides of sulphonic acids has been carried out[101,102]. The reactions of hydrazides with alkyl[90,91,96,102] and allyl[93] substituents have also been studied.

The Carpino reaction has been carried out with the tosylates of 1-aminopyrrole[91], 1-amino-2,5-diphenylpyrrole, and 1-amino-2,3,4,5-tetraphenylpyrrole[56], and also with 9-benzenesulphonimidocarbazole[91].

Hoffmann and coworkers[75] obtained 1,8-dehydronaphthalene by the alkaline hydrolysis of compound (VIII):



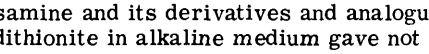
(VIII) (IX)

The alkaline cleavage of monosubstituted hydrazides was used in synthesis for the elimination of the hydrazine group in compound (IX)[99,100].

Most studies of the alkaline decomposotion of sulphonyl hydrazines have been carried out in aqueous or aqueous-alcoholic solutions of NaOH or KOH[55,56,59,62,87,88,91,92,97,98,101,102]. Other solvents used include ethylene glycol[56] and diethylene glycol[88], and, less frequently, aqueous K_2CO_3 solution[99,100], triethylamine in dimethylformamide[87], and pyridine[92].

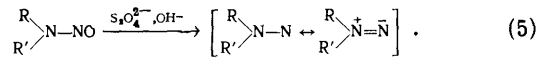
3. Formation of N-Nitrenes in the Reduction of N-Nitrosamines

In 1957 it was discovered[103] that the reduction of dibenzylnitrosamine and its derivatives and analogues with sodium dithionite in alkaline medium gave not the usual reduction products—unsymmetrical secondary hydrazines R_2NNH_2—but hydrocarbons of the dibenzyl series:



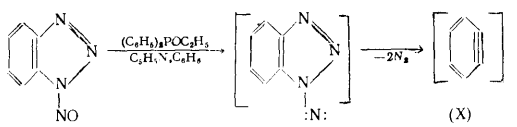
The anomalous reduction of nitrosamines to hydrocarbons has been called the Overberger–Lombardino reaction. Since the products were found to be the same as the products of the oxidation of the corresponding

hydrazines, it was suggested that the same intermediate compounds—N-nitrenes—are formed in the two instances:



(5)

Reactions involving the anomalous reduction of nitrosamines were observed with dithionite in alcoholic alkali[47,48,58,84,103,104], lithium in liquid ammonia[104], and a benzene solution of ethyl diphenylphosphinite $[(C_6H_5)_2POC_2H_5]$.[105] Anomalous reduction is undergone not only by dibenzylnitrosamine itself[103,104] but also by N-nitroso-derivatives of benzylphenylamine, diphenylamine, and 2,6-dimethylpiperidine[103], 2,6-diphenylpiperidine[103,104], 2,5-diphenylpyrrolidine[58], and the optically active α,α'-dimethyldibenzylamine[47,48]. The formation of dehydrobenzene (X) was observed in the reduction of 1-nitrosobenzotriazole[105]:

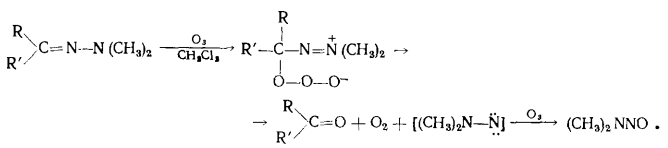


It is at present difficult to assess the possibility of formation of N-nitrenes in the reduction of N-nitrosamines taking place "normally", since the necessary experimental data are not available.

4. Ozonisation of Compounds Containing the $>C=N-N<$ Group

It has been known for a long time that in the ozonisation of compounds containing the $>C=N-N<$ group, aldehydes or ketones are formed[106,108]; the compositions of the other products of the reaction, and its mechanism, were not studied until recently. In 1961, papers were published on the ozonisation of the double bond in azines[109] and on the action of ozone on pyrazole and some of its homologues[110]; the authors of these papers assume that N-nitrenes are formed as intermediate products.

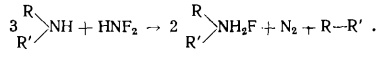
On the basis of kinetic data[111], the following mechanism for the ozonisation of the C=N bond in dimethylhydrazones was suggested:



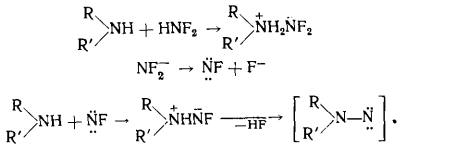
The N-nitrene formed may react with the solvent or be oxidised to the N-nitroso-compound[111].

5. Reaction of Difluoroamine with Amines and Phenylhydrazones

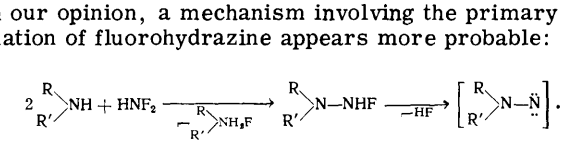
Bumgardner and coworkers[95] studied the reaction of primary and secondary amines with difluoroamine in an excess of the amine:



The deamination of dibenzylamine with difluoroamine, the reduction of N-nitrosodibenzylamine with sodium dithionite, and the alkaline cleavage of 1,1-dibenzylhydrazine tosylate give dibenzyl in similar yields. On this basis it was concluded that N-nitrenes are formed in an intermediate stage of the deamination. The authors cited[95,112] put forward the following mechanism:

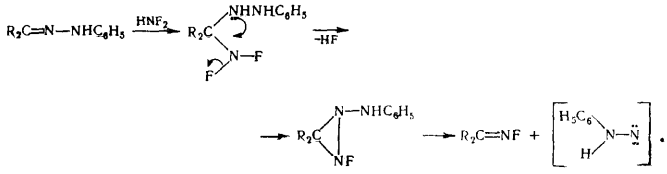


In our opinion, a mechanism involving the primary formation of fluorohydrazine appears more probable:



The reaction with difluoroamine has usually been carried out at room temperature. A variety of primary amines have been taken for the reaction—saturated[95] and unsaturated[37] amines, 3,5,5-trimethylpyrazoline[95], N-methylaniline[113], and the small-ring compounds azetidine[95] and aziridines[95,114].

It has also been assumed that N-nitrenes are formed in the reaction of difluoroamine with the phenylhydrazones of acetone and formaldehyde[113]:

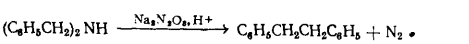


Stronger evidence in support of all the above reaction mechanisms is required.

6. Formation of N-Nitrenes in the Reaction of Angeli's Salt with Secondary Amines

Lemal[96,115] described the reactions of a number of secondary amines with Angeli's salt $Na_2N_2O_3$§. Dibenzylamine, pyrrolidine, piperidine, morpholine[96], pyrroline, and its *cis*- and *trans*-2,5-dimethyl-derivatives[115] were studied.

Dibenzyl was obtained from dibenzylamine:



Other amino-compounds also gave products identical to the products of the reactions of the corresponding N-nitrenes, so that Lemal, without putting forward a reaction mechanism, concluded that the formation of N-nitrenes as an intermediate stage of the reaction of amines with Angeli's salt is possible.

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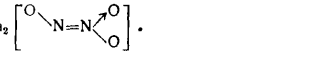
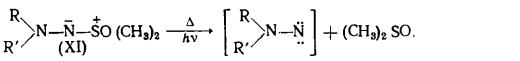
§ Angeli's salt has the sodium α-oxyhyponitrite structure[116]:

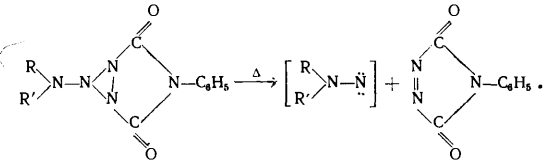


7. Formation of N-Nitrenes in the Decomposition of Their Adducts and N-Azides

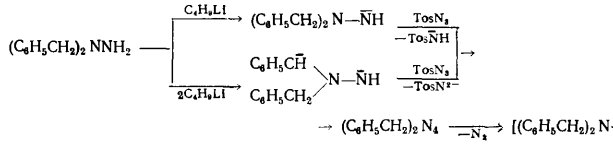
Sulphoximines (XI), obtained by the addition of N-nitrenes to dimethyl sulphoxide, give N-nitrenes again as a result of photolysis[29] or thermal decomposition[31,67]:



The formation of N-nitrenes in the decomposition of N-aminotriaziridines, obtained by the addition of N-nitrenes across an N=N bond, has been assumed[83]:



A recent paper[117] dealt with the decomposition of N-azides, giving N-nitrenes and their decomposition products. The N-azides were obtained by the exchange of hydrazide anions and $TosN_3$; the intermediate N-azide was not isolated. Dibenzylamino-N-azide and the corresponding N-nitrene were obtained in this way:



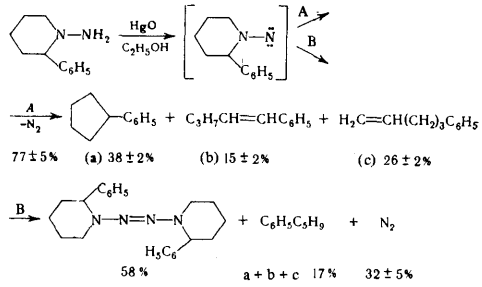
III. REACTIONS OF N-NITRENES

The previous section examined briefly reactions in which the intermediate formation of N-nitrenes has been assumed. The products of these reactions result from the subsequent transformation of the N-nitrenes. If we follow the traditional classification of chemical reactions according to the number of reactants and products, we can divide all known reactions of N-nitrenes into three types: 1) decomposition; 2) isomerisation; and 3) addition.

Examples of reactions of the first type are provided by the Busch–Weiss, Carpino, and Overberger–Lombardino reactions, in which the N-nitrenes decompose to hydrocarbons and nitrogen. The rearrangement of N-nitrenes to the isomeric hydrazones belongs to the second of the reaction types listed above, and examples of the third type are fairly widely encountered: they include the formation of tetrazenes, characteristic of N-nitrenes, and also the addition of various aminonitrenes across double bonds.

The direction of the reaction depends on many factors, which can be classified as internal factors, determined by the nature of the N-nitrene (its structure), and external factors determined by the conditions under which the reaction is carried out. The role of the medium has been little studied and is difficult to take into account. The same N-nitrenes react in different ways under different conditions, and even such an unstable species as dibenzylaminonitrene can be reduced to 1,1-dibenzylhydrazine without decomposition, whereas the comparatively stable aromatic imidonitrenes, under the conditions of the thermal decomposition of sulphoximines at 400–450°,[118] decompose with the liberation of nitrogen.

The lifetime of a given N-nitrene, and hence the reactions which it can undergo, can vary over a wide range, particularly under the conditions of heterogeneous reactions. If the probability that the N-nitrene meets and reacts with another molecule is appreciable, intermolecular reactions are observed, whereas if this probability is low, the N-nitrene decomposes before it is able to react with another molecule. This obvious situation is effectively illustrated by data on the oxidation of 1-amino-2-phenylpiperidine (XII) by yellow mercuric oxide[52].



When compound (XII) is added rapidly to a suspension of mercuric oxide in alcohol, the N-nitrene formed is able, before decomposition, to meet a molecule of the original hydrazine and react with it, giving chiefly the product of the bimolecular reaction—the tetrazene—and the decomposition products (hydrocarbons) are obtained in only 17% yield (path B). When the reagent is added slowly, the probability of the above encounter is low, and the decomposition of the N-nitrene is almost complete (path A).

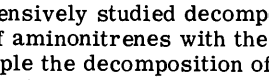
Thus in order to predict the direction of a reaction it is necessary to take into account many factors; these often have opposite effects which cannot yet be estimated quantitatively. Moreover, the picture is usually complicated by various secondary processes.

With all this in mind, we shall consider below the chief reactions of N-nitrenes and the small amount of information which has accumulated on the reaction mechanisms.

1. Decomposition of N-Nitrenes

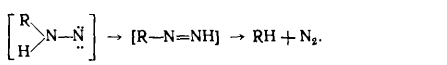
One of the most interesting and general features of N-nitrenes is their ability to decompose with the liberation of nitrogen and the formation of hydrocarbons. This reaction has been observed for N-nitrenes obtained in the most varied ways. In summarising the available data, it may be noted that the mechanism of the decomposition of N-nitrenes depends on the nature of the substituents and may vary from a completely concerted mechanism to a biradical mechanism.

The most extensively studied decomposition is the decomposition of aminonitrenes with the rupture of two bonds, for example the decomposition of dibenzylaminonitrene and its derivatives into dibenzyl and nitrogen:



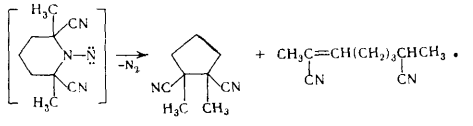
This reaction, discovered by Busch and Weiss in 1900, has attracted the attention of many research workers in subsequent decades. Dibenzyls have been obtained in the oxidation of 1,1-disubstituted hydrazines[9–12,47–49,88,104], in the anomalous reduction of nitrosamines[47,48,84,104], in the Carpino reaction[55,62,87,88,97,101], in the deamination of dibenzylamine by difluoroamine[95] or $Na_2N_2O_3$,[96] and in the decomposition of dibenzylamino-N-azide[117].

Decomposition to the corresponding hydrocarbons is also undergone by monosubstituted N-nitrenes, possibly after their rearrangement into the azo-compound[18,37,95,99,100,113,114]:



Problems related to the existence and stability of compounds of the type R–N=NH have been examined[119].

In the decomposition of N-nitrenes, in addition to combination of the residues R and R′, disproportionation with the formation of unsaturated compounds may also take place. Reactions of this kind were first observed in the oxidation of 1-amino-2,6-dicyano-2,6-dimethylpiperidine by bromine[14–17], when 2,6-dicyanoheptene-2 was obtained in addition to *cis*- and *trans*-1,2-dicyano-1,2-dimethylcyclopentanes:

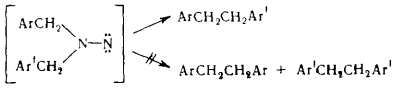


A large number of examples of reactions of this kind were subsequently studied[42,44,46–48,52,54,57,58].

The question of the mechanism of the decomposition of N-nitrenes was first raised in 1955, when a radical mechanism was proposed for the decomposition of 2,6-dicyano-2,6-dimethylpiperidyl-N-nitrene[17]. Later[44], however, it was suggested that the decomposition of aminonitrenes of this kind, and also of aminonitrenes with substituents of the benzyl type is a three-centre concerted decomposition. The data at this stage of the studies were summarised by Overberger[120]. Later, an E_2-mechanism was proposed[42], but this was later rejected when it could not explain new experimental facts[52,54,57].

A criterion for the correctness of a mechanism for the decomposition of aminonitrenes with radicals of the benzyl type must be consistent with the following experimental facts.

1. In the decomposition of aminonitrenes with different radicals, it has not been possible to isolate mixed cross-products of the combination[49,84,93,104]:

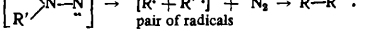


2. Decomposition with combination of the radicals takes place only if both[49,50,52,93] or at least one[52] of the substituents in the N-nitrene is capable of stabilising the intermediate state. These substituents are the benzyl, allyl, and nitrile radicals, and the carbamide and furfuryl groups. It is also known that in order to obtain a high yield of the products of the combination, the substituents should have a small volume, otherwise alkenes are formed preferentially[57].

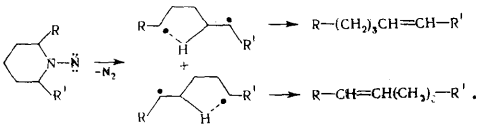
3. For N-nitrenes with R and R′ radicals of the benzyl type, no definite conclusion can be reached regarding the influence of the inductive or mesomeric effect of a substituent in the ring on the rate of decomposition or the yield of hydrocarbons[87,88,101]. The absence of a relationship of this type is characteristic of radical reactions.

4. The stereospecificity of the decomposition of aminonitrenes in which the substituents form a cyclic system is extremely high[44,46,57,58,103,104]. For the optically active α,α'-dimethyldibenzylaminonitrene, the stereospecificity of the decomposition decreases sharply[47,48,84].

Almost all these results are consistent with the radical mechanism of decomposition, proposed by Overberger, with a strong cage effect, which prevents the formation of cross-products and increases the stereospecificity of the reaction[58]:

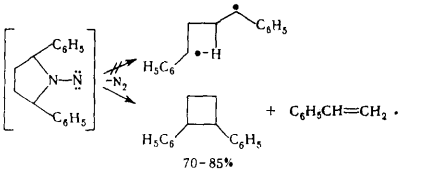


The formation of alkenes in the decomposition of six-membered rings, in Overberger's opinion, involves a five-membered intermediate state:



The relative amounts of combination products and alkenes will in this instance depend on steric factors.

In the decomposition of N-(2,5-diphenylpyrrolidino)nitrene, 1,4-diphenylbutenes are not formed[58], apparently due to the highly strained nature of the corresponding intermediate state (which must be four-membered):

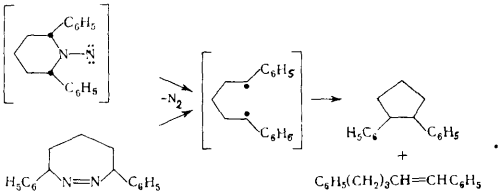


The process proceeds further with the partial formation of styrene.

The decomposition of N-nitrenes can be compared with the decomposition of the corresponding azo-compounds, the radical mechanism of which was established by the EPR method[121].

At first, the non-stereospecific nature of the thermal decomposition of the azo-compounds was noted[122,123]. Later, however, a number of authors[121,124–129] showed that under conditions favouring a marked cage effect, the decomposition of azo-compounds is extremely stereospecific. The model compounds in this work were *cis*- and *trans*-2,5-disubstituted Δ^1-pyrazolines[121,124–128] and 3,6-dicyano-3,6-dimethyl-3,4,5,6-tetrahydropyridazine[129].

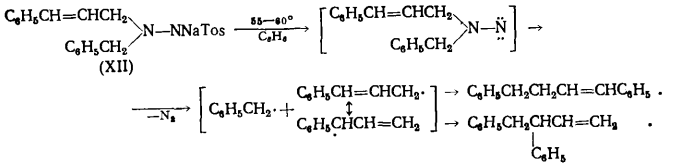
Evidence that the mechanisms of these reactions are the same is provided by the similarity in the isomeric composition of the products obtained in the decomposition of N-(*cis*-2,6-diphenylpiperidyl)nitrene[44,46,103,104] and in the decomposition of *cis*-3,7-diphenyl-1,2-diazacyclohept-1-ene[124]:



The products of the decomposition of N-(*cis*-2,5-diphenylpyrrolidino)nitrene[58] and the thermal decomposition of *cis*-3,6-diphenyl-3,4,5,6-tetrahydropyridazine[130] are also similar.

The proposed radical mechanism is effectively confirmed by the results of the decomposition of the sodium derivatives of tosylhydrazines with different allyl and benzyl radicals[93]. Thus the decomposition of compound

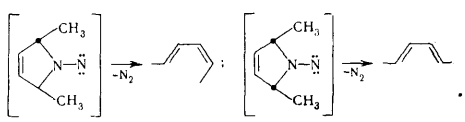
(XII) gave not only 1,4-diphenylbut-1-ene but also 3,4-diphenylbut-1-ene, in the ratio 3 : 1, with a total yield of ~ 100%:



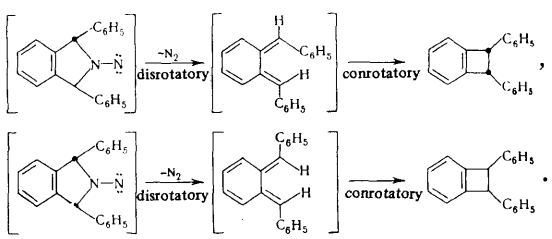
This result indicates the intermediate formation of free allyl and benzyl radicals. The absence of the cross-products—dibenzyl and diphenylhexadienes—indicates a strong cage effect.

The biradical decomposition of the aminonitrenes should however be regarded only as one possible extreme. The other extreme possibility is the concerted mechanism of decomposition.

The decomposition of a number of aminonitrenes obeys the Woodward–Hoffmann rules for concerted processes. These rules define the stereochemistry of the decomposition and are observed in those instances where these processes for the aminonitrene are allowed and are energetically more favourable than the radical processes. A common feature of the concerted processes of the decomposition of aminonitrenes is the formation of a system with a greater unsaturation than the original system. The polyene obtained may react further, and its subsequent reactions are also determined by the Woodward–Hoffmann rules. Examples of such processes are the decomposition of various N-(3-pyrrolino)nitrenes[115,132] and N-(1,3-dihydroisoindolino)nitrenes[53,55,59,64,92,98]. Lemal[115] established by means of correlation diagrams that the decomposition of N-(3-pyrrolino)nitrene should be disrotatory, and he confirmed this experimentally. The model compounds were N-(*cis*- and *trans*-2,5-dimethylpyrrolino)nitrenes:

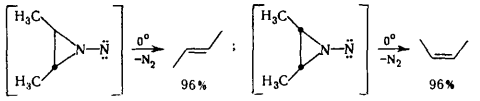


The decomposition of N-(1,3-dihydroisoindolino)nitrenes has attracted considerable attention, since it was expected to give various benzocyclobutenes. This process takes place in two stages, and for the example of N-(*cis*- and *trans*-1,3-dihydro-1,3-diphenylindolino)nitrenes it was shown[53,59,92,98] that the stereochemistry of both stages obeys the Woodward–Hoffmann rules. The yields and compositions of the products depend markedly on the conditions of the reaction[59]:

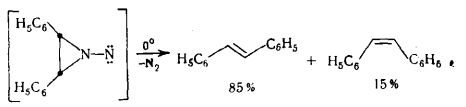


The decomposition of unsubstituted N-(1,3-dihydroisoindolino)nitrene[53,55,92,98] and the tri- and tetraphenyl-derivatives with substituents in the 1,3-positions[64] has also been studied. The intermediate products showed a tendency to undergo other concerted reactions, also possible in these systems, with the formation of various polycyclic compounds.

The decomposition of N-aziridinonitrenes gives alkenes. Data on the stereochemistry of the decomposition of three-membered rings with the formation of alkenes are contradictory, and there is still lack of agreement regarding its mechanism. Until recently it was considered that the decomposition of N-aziridinonitrenes was completely stereospecific, and this was demonstrated by the deamination of *cis*- and *trans*-2,3-dimethylaziridines by difluoroamine[114] (see also Ref. 133):

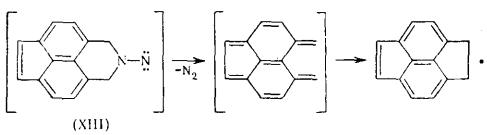


The decomposition of N-(*cis*-2,3-diphenylaziridino)nitrene is non-stereospecific, however[32]:



It was shown that under the conditions of the reaction, the isomerisation of *cis*-stilbene into the *trans*-isomer does not take place. Here, it is true, it may be assumed that the mechanism of the decomposition is intermediate between the biradical and the purely concerted mechanisms, but even this does not explain all the results obtained.

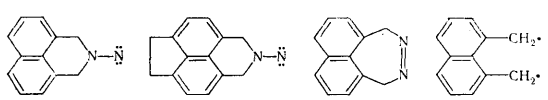
The decomposition of aminonitrenes with large rings has been little studied up to the present and has not been examined from the viewpoint of the preservation of orbital symmetry. The only example as yet is the decomposition of the aminonitrene (XIII), which gives dihydropyracylene in 8–15% yield[62]:



(XIII)

It may be assumed that this reaction takes place in two stages: linear cheletropic[131] decomposition of the aminonitrene takes place first, followed by electrocyclic closure of the ring with 12 π-electrons.

It should be noted that the aminonitrenes (XIV) and (XV) with similar structures do not decompose to nitrogen and hydrocarbons[55,62,97].

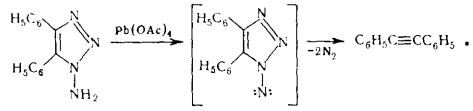


(XIV) (XV) (XVI) (XVII)

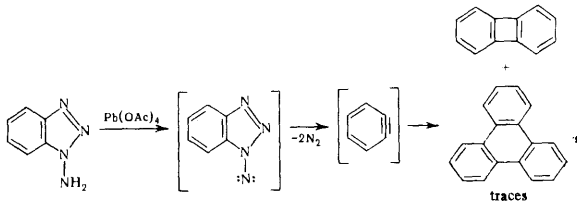
Concerted decomposition in these systems is impossible, but it is not clear why biradical decomposition does not take place. The decomposition of the aminonitrene (XIV) and the corresponding azo-compound (XVI) should take place by the same mechanism with the formation, in the first stage, of the biradical (XVII) and a molecule of nitrogen. The thermal decomposition of compound (XVI), however, as expected, gives the acenaphthene in 59% yield[55], and the aminonitrene (XIV) does not decompose to give nitrogen and hydrocarbons. No explanation for this has yet been put forward.

Let us now consider processes, involving the decomposition of aminonitrenes, in which more than two bonds in the original molecule are broken. This group includes the cleavage of 1- and 2-(1,2,3-triazolyl)nitrenes, and various other reactions.

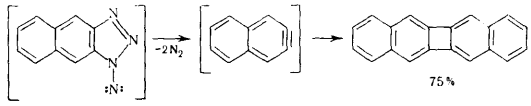
1-(1,2,3-Triazolyl)nitrene decomposes with the liberation of two molecules of nitrogen and the formation of hydrocarbons. In this way, 1-amino-4,5-diphenyl-(1H)-triazole gave tolane[82]:



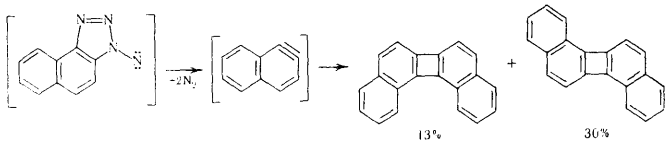
Hydrocarbons were obtained by the following reactions: from 1-aminobenzotriazole[60,69-71,82,105]:



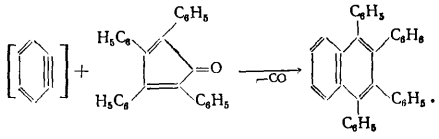
from 1-amino-[1H]-naphtho[2,3-*d*]triazole[72]:



from 1-amino[1H]-naphtho[1,2-*d*]triazole[72]:

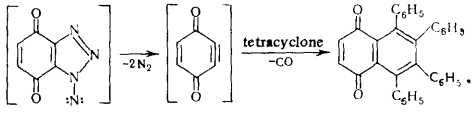


All these products are dimers of the corresponding dehydro-derivatives. The "arenes" obtained can also be trapped by "tetracyclone" (2,3,4,5-tetraphenylcyclopentadienone)[69,82,105]:

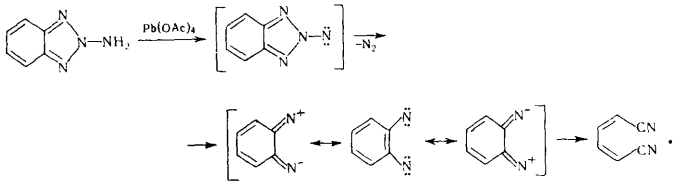


The yield of tetraphenylnaphthalene is almost quantitative, indicating the quantitative formation of dehydrobenzene in this reaction.

1-Aminobenzotriazoles with different substituents in the benzene ring also undergo splitting[69,71,77]. A similar method gave "benzynequinone" (dehydroquinone)[68,77], which with tetracyclone gave tetraphenylnaphthaquinone in 40–60% yield:

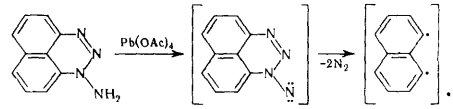


The oxidation of 2-aminobenzotriazole gives the dinitrile of *cis-cis*-mucic acid[70,71,82]:



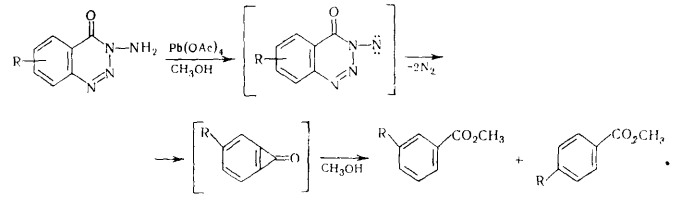
Oxidation by lead tetra-acetate leads to the partial formation of the *cis-trans*-dinitrile, apparently as a consequence of isomerisation under the conditions of the reaction. The milder conditions of oxidation by iodobenzene diacetate give only the *cis-cis*-isomer[71]. The formation of the dinitrene in an intermediate stage of the reaction is confirmed by the fact that the dinitrile of mucic acid was also obtained by the oxidation of *o*-phenylenediamine[71] by lead tetra-acetate and by the thermal decomposition of *o*-phenylenediazide[134]. Both of these reactions involve the intermediate formation of the dinitrene. *cis-cis*-2,5-Dimethoxymuconitrile was obtained by oxidising 1,4-dimethoxy-2,3-phenylenediamine[77].

The oxidation of 1-aminonaphtho[1,8-*d*,*e*]triazine gives 1,8-dehydronaphthalene[73-75]:

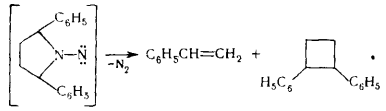


1,8-Dehydronaphthalene could not be obtained either by the thermal decomposition or by the photolysis of the sodium derivative of the tosylate of this compound. 1,8-Dehydronaphthalene is an exceptionally reactive compound. It reacts with solvents[73,74] and also adds on to C=C[73-75] and N=N[74] bonds.

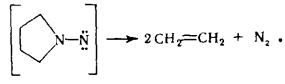
In 1969, an attempt was made to prepare benzocyclopropenone by the oxidation of 5- or 6-substituted 1-aminobenzotriazolin-8-ones, but the reaction in methanol gave only the methyl esters of the corresponding benzoic acids[76]:



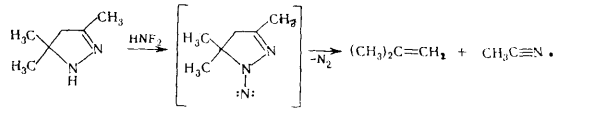
The decomposition of aminonitrenes containing a five-membered ring with different degrees of unsaturation is of considerable interest. This is important for the study of systems in which concerted decomposition is impossible. It was noted above that one of the products of the decomposition of N-(2,5-diphenylpyrrolidino)nitrene is styrene[58]:



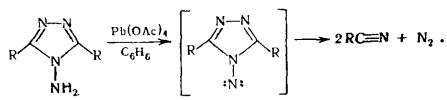
With unsubstituted N-(pyrrolidino)nitrene, dissociation into three components is the only route taken in the splitting:



This splitting with rupture of the 1–2, 1–5, and 3–4 bonds is fairly typical of nitrenes with a five-membered ring. It has been established[95] that when 3,5,5-trimethyl-Δ^2-pyrazoline is treated with difluoroamine, the N-nitrene formed decomposes to nitrogen, acetonitrile, and isobutene:



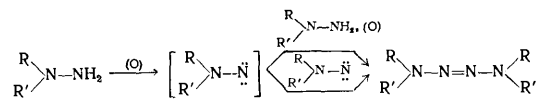
In the oxidation of 1-amino-1,3,4-triazoles with different substituents in positions 2 and 5, the liberation of 55–90% of the nitrogen and the formation of the corresponding nitriles was observed[78]:



1-Aminopyrrole derivatives, however, do not decompose in this way, but form tetrazenes and subsequently pyrrole derivatives[56,78,91]. It was therefore suggested that, other conditions being equal, the direction of the reaction is determined by the ease of rupture of the bond 3–4.[78] The explanation for the decomposition of the triazole derivatives is that the energy of the N–N bond here is smaller by 40 kcal mole^{-1} than the energy of the C–C bond 3–4 in pyrrole. This hypothesis, however, cannot explain the decomposition of aminonitrenes in the two previous instances, where the energy of the bond 3–4 is fairly high.

2. Formation of Tetrazenes

Since the time of Fischer[135] it has been known that Δ^2-tetrazenes are the chief products of the oxidation of 1,1-disubstituted hydrazines by a wide variety of oxidising agents. This "normal" oxidation is now also regarded as involving the interaction of the initially formed N-nitrenes with the original hydrazine or (which is less likely) their dimerisation[7,52]:

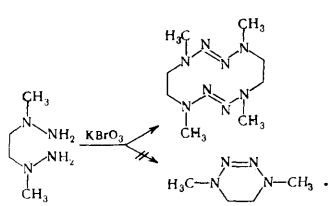


Tetrazenes are also formed in other instances on dimerisation of intermediate N-nitrenes, if the latter are sufficiently stable under the conditions of the reaction[24,55,56,66,91].

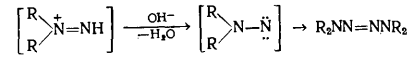
Fairly frequently, the tetrazenes formed are unstable under the conditions of the reaction and decompose with the separation of a molecule of nitrogen and the formation of secondary amines[56,78,90,91].

The possible stereoisomerism of Δ^2-tetrazenes has not been studied until recently, but recent papers deal with the isolation of *cis*- and *trans*-3,3-azobis-(2-oxazolidinone)[136] and the *cis*- and *trans*-isomers of the tetrazene obtained by oxidising N-aminophthalimide[80]. The oxidation usually gives the thermodynamically more stable *trans*-structure, but the *cis*-form can also be obtained on heterogeneous oxidation[80,136].

An attempt to prepare the *cis*-tetrazene by the oxidation of 2,5-diamino-2,5-diazahexane (this would be 1,4-dimethyl-1,4,5,6-tetrahydro-1,2,3,4-tetrazine) gave the twelve-membered cyclic bis-tetrazene[45]:

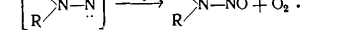


McBride developed a method for preparing tetra-alkyltetrazenes by oxidising 1,1-dialkylhydrazines with bromine in acidic aqueous solution followed by neutralisation[24,34,40,44]. The diazenium ion formed in the first stage, on neutralisation, gives the N-nitrene, which then dimerises to give the tetrazene:



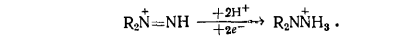
3. Oxidation and Reduction of N-Nitrenes

These reactions have been insufficiently studied. The oxidation of N-nitrenes to the corresponding nitrosamines was observed under ozonisation conditions[110,111]:



It was suggested that in the electrochemical oxidation of 1,1-dimethylhydrazine in acid medium, one possible reaction of the diazenium ion is its oxidation to the nitrosamine[25].

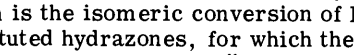
Reduction of N-nitrenes apparently takes place in the reduction of N-nitrosamines to hydrazines. It is known that diazenium ions in acid medium can be reduced by chemical (by $SnCl_2$ or Zn in H_2SO_4) or electrochemical methods[25,26]. The corresponding 1,1-disubstituted hydrazines are obtained in yields close to 100%:



4. Rearrangements of N-Nitrenes

The rearrangements of N-nitrenes have been studied in considerable detail, but a satisfactory mechanism has not yet been proposed for any of these reactions.

The most widely encountered and relatively fully studied reaction is the isomeric conversion of N-nitrenes into monosubstituted hydrazones, for which the name "diazene–hydrazone rearrangement" has been proposed[90]:

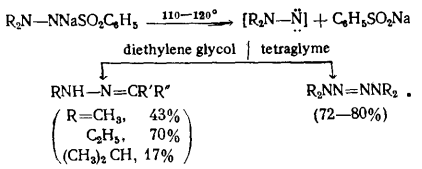


The formation of hydrazones in the oxidation of 1-aryl-1-benzylhydrazines by mercuric oxide was detected at an early date[13]. Later, examples of this rearrangement were studied for arylbenzylaminonitrenes[101,102], arylalkylaminonitrenes[101,113], and dialkylaminonitrenes[25,85,89,90,102]. The rearrangement has usually been carried out in alkaline medium, and only one example in acid medium is known[25].

That the rearrangement is intramolecular is indicated by the absence of the products of the cross-reaction in the alkaline cleavage of a mixture of the tosylates of 1-benzyl-1-*p*-chlorophenylhydrazine and 1-*p*-chlorobenzyl-1-phenylhydrazine (only benzaldehyde *p*-chlorophenylhydrazone and *p*-chlorobenzaldehyde phenylhydrazone were isolated)[101]. The reaction is of first order with respect to the hydrazide anion, and the rate-determining step is the separation of the sulphinate ion.

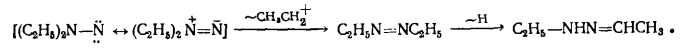
The mechanism of the diazene–hydrazone rearrangement was the subject of a special study[90] in which the N-sodium derivatives of the 1,1-dialkylhydrazides of benzenesulphonic acids were heated to 110–120° in the organic solvents tetraglyme and diethylene glycol. It was found that the composition of the decomposition products depends markedly on the nature of the solvent: in the aprotic tetraglyme, tetrazenes were obtained in good

yields, whereas in diethylene glycol, only the hydrazones or a mixture of the hydrazone and the tetrazene were obtained:

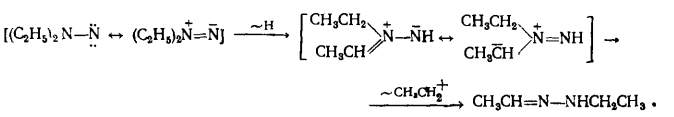


Three possible mechanisms for the rearrangement of the aminonitrenes to hydrazones were examined[90].

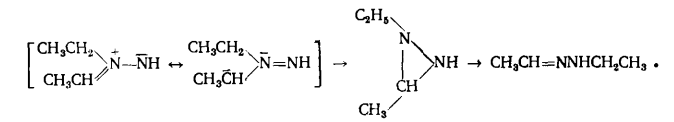
1. Migration of one of the substituents on the central nitrogen atom to a neighbouring atom carrying a negative charge, in the form of the carbo-cation; the azo-compound formed then undergoes isomerisation to the hydrazone:



2. A mechanism which differs from the preceding mechanism in the order of migration of the proton and the carbo-cation and which assumes the intermediate formation of not the azo-compound but an unstable ylide:

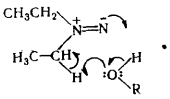


3. A mechanism involving a valency rearrangement of the initially formed ylide into the diaziridine, which then undergoes isomerisation to the hydrazone:



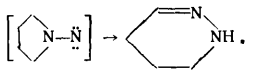
Neither azo-compounds nor diaziridines were detected among the products of the rearrangement. Since special experiments showed that under the conditions of the rearrangement[90] azoethane undergoes only partial isomerisation, and the corresponding diaziridine does not undergo isomerisation at all, mechanisms 1 and 3 were rejected.

The role of the hydroxyl-containing solvent is regarded as being to facilitate the migration of the proton by the formation of a six-membered cyclic intermediate complex with the participation of the aminonitrene:



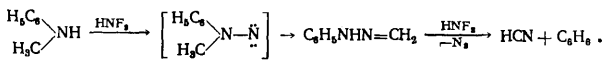
Experiments with compounds labelled with ^{15}N,[102] however, did not confirm the second proposed mechanism either. From the mechanism with the primary formation of an ylide, it follows that for a nitrene with a labelled terminal nitrogen atom the hydrazone formed should contain the tracer atom in the amino-group RCH=N–N*HCH$_2$R, but the labelled atom was found to be the imide nitrogen atom of the hydrazone RCH=N*–NHCH$_2$R, that is the rearrangement as it were involved not the carbo-cation RCH_2^+ but the alkylidene residue RCH$\langle$. Further study of the mechanism of the rearrangement of aminonitrenes to hydrazones is thus required.

Some heterocyclic aminonitrenes can undergo diazene–hydrazone rearrangement with expansion of the ring as a result of the inclusion of a second nitrogen atom in it. Thus Δ^2-tetrahydropyridazine was obtained from derivatives of N-aminopyrrolidine[96]:



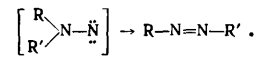
The yield was 55–70%, depending on the method used to generate the nitrene. This reaction indicates new methods for the preparation of heterocyclic nitrogen compounds which are difficult to obtain.

The diazene–hydrazone rearrangement has been postulated in the reaction of difluoroamine with N-methylaniline[113]:

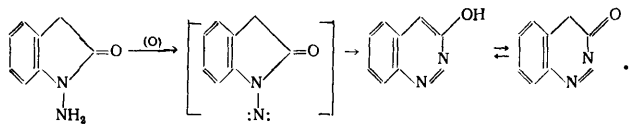


It should however be noted that formaldehyde phenylhydrazone was not obtained in the alkaline cleavage of 1-phenyl-1-methylhydrazine tosylate[101].

Another form of rearrangement of N-nitrenes involves their conversion into azo-compounds:

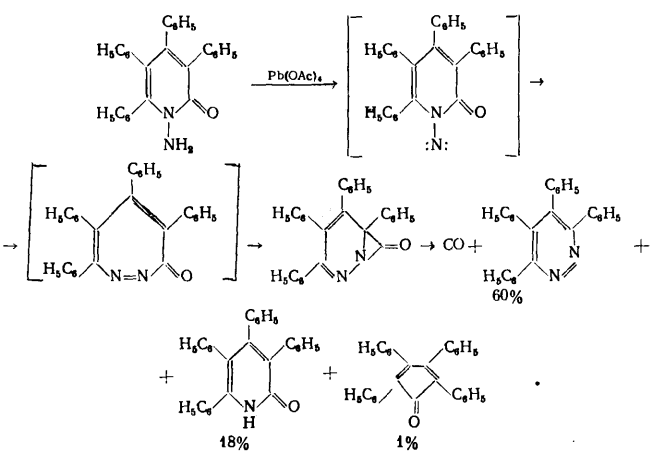


Historically, the first example of this reaction can be taken to be the formation of azo-compounds from 1-allyl-1-arylhydrazines on oxidation with mercuric oxide[8,86]. After this, no new example of the preparation of azo-compounds from 1,1-disubstituted hydrazines was described, although the analogous reactions of heterocyclic compounds were discovered by Baumgarten[51,65] and Rees[67]. In the oxidation of 1-amino-oxindole and its derivatives by lead tetra-acetate[51], *t*-butyl hypochlorite, and chlorine[65], Baumgarten observed rearrangement to 3-cinnolinol:



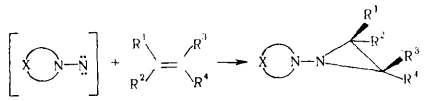
An interesting feature is that oxidation by chlorine gave the highest yield (up to 93%).

Rees and Yelland[67] discovered a similar rearrangement in the oxidation of N-amino-2,3,4,5-tetraphenylpyridone:



5. Addition of N-Nitrenes Across Multiple Bonds

The first report of the addition of N-nitrenes across the C=C bond of alkenes and conjugated dienes appeared only in 1967[28], but a fairly large amount of data has now accumulated[28,29,31-34,137], indicating the important synthetic and theoretical aspects of these reactions.



Preliminary reports of the addition of aminonitrenes to N=N[83] and C≡C[30] bonds have also appeared. All these reactions are (1+2)-cyclo-addition reactions.

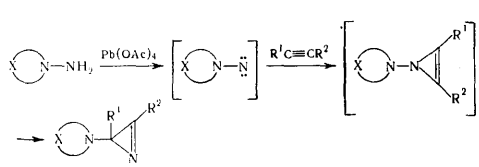
The specific features of the addition of N-nitrenes to multiple bonds are determined to a considerable extent by the negative charge on the sextet nitrogen atom and the high population of its π-orbital[19], as a consequence of which the simplest aminonitrenes exhibit nucleophilic, and not electrophilic properties, like the carbenes. In addition reactions, aminonitrenes with electron-accepting substituents which increase the electrophilic nature are used—most frequently N-amido- and N-imidonitrenes and similar compounds[28-34,137]. The addition of other types of aminonitrene to multiple bonds has not yet been observed. Aminonitrenes with very similar structures often show quite different behaviour, however, and it is difficult to predict the direction of a reaction.

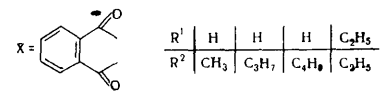
Both nucleophilic[28,29,32-34,97] and electrophilic[23,31,33,34,137] alkenes and dienes[28,29,34] have been taken for the addition reactions. Recently, to increase the yield of products, attempts have been made to use alkenes with electron-accepting substituents, but an unambiguous relationship between the yield of products and the electrophilic nature of the alkene has not yet been established[34]. An interesting feature is that *trans*-1,2-dichloroethylene and trichloroethylene give aziridines in 60–90% yield, whereas 1,1-dichloroethylene and *cis*-1,2-dichloroethylene do not form adducts at all[34]. It must be assumed that the yield of aziridines apparently characterises not so much their formation directly in the addition reaction as the stability of the resulting extremely unstable[33,34,137] aziridines under the conditions of the reaction, on isolation and purification.

The reaction of aminonitrenes and dienes gave the corresponding vinylaziridines in 35–71% yields. Adducts across both double bonds, or products of 1,4-addition, are not formed[28,29,34].

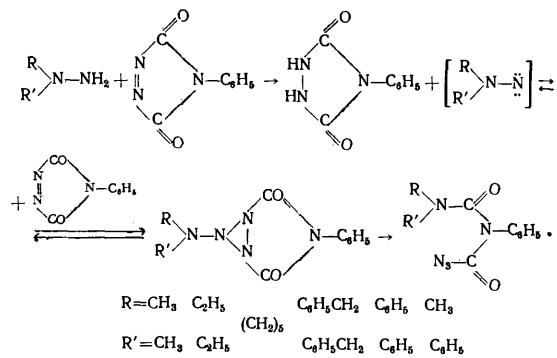
A remarkable feature is the complete stereospecificity of the addition of aminonitrenes to the C=C bond[28,29,31-34,137]. If Skell's postulates[138,139] regarding the stereochemistry of the addition of carbenes across multiple bonds are extended to aminonitrenes, it may be assumed that aminonitrenes react with a double bond exclusively in the singlet state[29,34].

In the addition of aminonitrenes across the C≡C bond, 2H-azirines are obtained in relatively low yields (5–15%)[30]. These reactions are of interest in that the 1H-azirine formed in the first stage is antiaromatic, so that it immediately undergoes rearrangement into the 2H-azirine, which is the final reaction product:



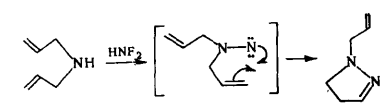


It is stated[83] that the products of the addition of aminonitrenes to the N=N bond are triaziridines. The diethyl ester and phenylimide of azodicarboxylic acid have been used as aminonitrene acceptors. In the last instance the reaction is represented:



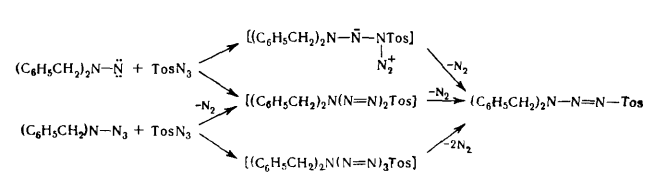
The triaziridines were isolated and characterised by their ultraviolet spectra and melting points.

With dialkylaminonitrenes, intramolecular reaction of the N-nitrene with the multiple bond was observed; the reaction mechanism was not discussed[37]:

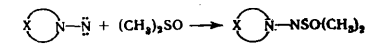


6. Reactions of N-Nitrenes with Tosyl Azide and Dimethyl Sulphoxide

In the reaction of dibenzylaminonitrene, formed from dibenzylamino-N-azide, or possibly, of the azide itself with tosyl azide at 0°, one of the products is 3,3-dibenzyl-1-tosyltriazene (yield 13–28%)[117]:

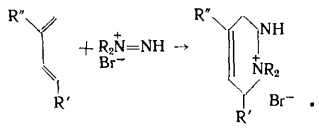


The aminonitrenes which can add to double bonds were taken for the reaction with dimethyl sulphoxide[29,31,67]. The products obtained were called sulphoximines[29,67] or iminoxysulphuranes[31]:

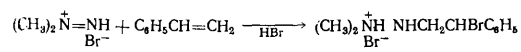


7. Reactions of Diazenium Salts

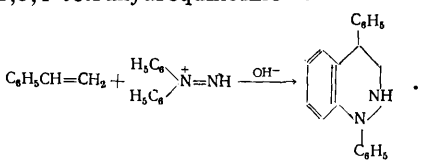
The diazenium cations formed on protonation of N-nitrenes have proved to be very active dienophiles, and this has been used for the preparation of quaternary Δ^4-tetrahydropyridazinium salts [35,36,38,39]:



The ability of 1,1-dimethyldiazenium bromide to undergo the Diels–Alder reaction with isoprene or divinyl under mild conditions was discovered by McBride and Urry [35] and later studied in detail by Zelenin and Bezhan [38,39,140] with many 1,1-dialkyldiazenium bromides, isoprene, chloroprene, and piperylene. Even cyclohexa-1,3-diene, which reacts only with very active azo-compounds, gives an adduct with 1,1-dimethyldiazenium bromide in 80% yield. The structural direction of these reactions is the usual direction for diene synthesis: 1-substituted dienes (piperylene) give the ortho-isomers, and 2-substituted dienes (isoprene and chloroprene) the para-isomers. The product of the oxidation of 1,1-di-isopropylhydrazine in acid medium, however, did not undergo the diene synthesis. The branched structure of the framework of the diazenium cations is apparently of considerable importance [39,140]. In the reaction of dimethyldiazenium bromide with isoprene, the formation of small quantities (12%) of tiglic aldehyde dimethylhydrazone was observed [35]. The reaction of the 1,1-dimethyldiazenium cation with styrene and indene leads to the formation of hydrazinium salts [36]:



When the solution is neutralised, these salts may be converted into diazetidinium salts, and also undergo more extensive decomposition. The reaction of styrene with 1,1-diphenyldiazenium perchlorate in acetonitrile, however, leads after neutralisation to the formation of 1,4-diphenyl-1,2,3,4-tetrahydroquinoline [27]:



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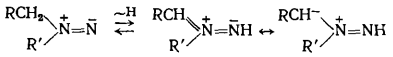
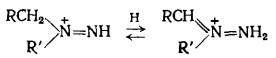
A number of papers published in 1971 supplement and extend our knowledge of aminonitrenes.

New data on the conversion of dialkylaminonitrenes into dialkylhydrazones [141] indicate that this reaction is a general reaction for aminonitrenes generated under different conditions, and can be regarded as indicating the important role of tautomeric equilibria



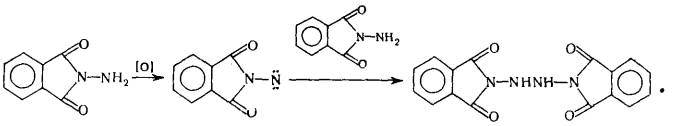
in the subsequent reactions of the aminonitrenes.

The analogous tautomerism of the protonated forms of aminonitrenes—the diazenium cations:



is apparently the first stage of the splitting of diazenium cations at the C=N$^+$ bond with the formation of carbonyl compounds when solutions of diazenium salts and the corresponding 2,4-dinitrophenylhydrazones are boiled—in the reaction with 2,4-dinitrophenylhydrazine [142].

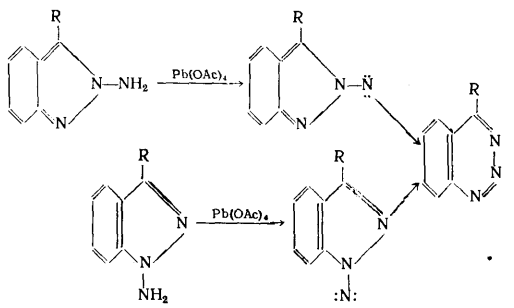
In the oxidation of various N-aminolactams with lead tetra-acetate and iodobenzene diacetate, the corresponding tetrazanes were isolated [143]:



These are capable of undergoing further oxidation to Δ^2-tetrazenes, providing evidence in support of the previously proposed mechanism of oxidation of 1,1-disubstituted hydrazines to Δ^2-tetrazenes via the tetrazanes, obtained in the reaction of intermediate N-nitrenes with the original hydrazines [7,52] (see also section III, 2 of this review).

The formation of esters of benzoic acid in the oxidation of 5- and 6-substituted 1-aminobenzotriazolin-8-ones with lead tetra-acetate in CH_2Cl_2 [144] may take place not only via the decomposition of intermediate aminonitrenes to cyclopropenones and two molecules of nitrogen [76] but also via the formation of indazolones, which have been isolated as the adducts with tetracyclone.

In the oxidation of 3-substituted 1- and 2-aminoindazoles, instead of the liberation of nitrogen, expected by analogy with the behaviour of the corresponding aminobenzotriazoles [69–72], the reaction gave 1,2,3-benzotriazines [145] in almost quantitative yields



This rearrangement of the intermediate aminonitrenes is extremely similar to other examples of ring expansion in aminonitrenes [51,65,67].

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Mass-spectrometric Determination of the Configuration of Steroid Alcohols

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A large number of epimeric secondary alcohols of the 3-, 11-, 12-, 14-, 15-, 16-, 17-, 20-, and 24-hydroxy-steroid series, derivatives of androstane, pregnane, or cholestane, and also tertiary alcohols of the oestrane series which are epimeric at $C_{(17)}$ show that, in all cases in which the hydroxyl is situated in a conformationally sufficiently rigid part of the steroid skeleton, mass spectrometry can be used to establish the configuration of the steroid alcohols. The main conclusions can be drawn on the basis that, in most cases of electron impact an axial hydroxyl is split off more readily than is an equatorial hydroxyl, as a consequence of the possibility of a mechanism of 1,3- or 1,4-*cis*-diaxial elimination of the elements of water. A list of 31 references is included.

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1. INTRODUCTION

Mass spectrometry, which is widely employed in solving structural problems of organic chemistry and especially the chemistry of naturally occurring compounds, has hitherto found only limited application to the solution of stereochemical problems. The primary reason is that aliphatic stereoisomers differ little if at all in internal energy. As a consequence the mass spectra of optical enantiomers are usually identical not only to each other, but also to the spectrum of their racemic mixture[1]. The presence of two or more asymmetric carbon atoms is sometimes sufficient to produce differences, though slight, in the mass spectra of the diastereomers. Thus Ryhage and Stenhagen[2] observed slight differences in the mass spectra of dimethyl *meso*- and (−)-3,4-dimethyladipates (I) and methyl 2L, 9L- and 2L, 9D-dimethyltetracosates (Ia)

$$MeOCOCH_2CHMeCHMeCH_2COOMe \quad (I);$$

$$Me[CH_2]_{14}CHMe[CH_2]_6CHMeCOOMe \quad (Ia).$$

As could be expected, alicyclic compounds exhibit sharper differences in the mass spectra of stereoisomers, which are larger the greater the conformational stability of the cyclic system. The difference in internal energy between epimeric molecules may depend significantly on the nature of the substituent, its spatial arrangement, and the character of non-bonded interactions, and this in turn leads to variation in the intensities of the characteristic peaks in the mass spectrum.

Differences in the mass spectra of cyclic epimers are due primarily to variation in the ease of elimination of substituents at the asymmetric atom, a process often accompanied by ejection of a hydrogen atom (detachment of water, hydrogen sulphide, and acetic acid from alcohols, thiols, and acetates respectively). Therefore, although all modes of fragmentation of one epimer on electron impact are usually characteristic also of the other epimer, the intensities of the corresponding peaks ($M - CH_3$, $M - H_2O$, $M - H_2S$, $M - CH_3COOH$, etc.) are different. The extent to which the migrating hydrogen atom or group of atoms is involved in specific rearrangement of the given compound may be as important as the purely energetic factor. In this case the peak intensity of the corresponding rearranged ion usually depends on the distance between the hydrogen-donating and the hydrogen-accepting atoms.

The above discussion can be summarised in the conclusion that the differences in the way in which molecular ions of epimers break down on electron impact are governed ultimately by two factors—an energy factor and a so called "distance factor"[3,4].

In one of the earliest mass-spectrometric investigations of epimeric cyclic alcohols Biemann and Seibl[5] showed, with epimeric secondary alcohols of bicyclo[3,3,0]octan-2-ol, bicyclic terpenes, and steroids as examples, that the peak due to the molecular ion is less intense in the mass spectrum of the epimer having the more "compact" configuration than in the spectrum of the less "compact" epimer.

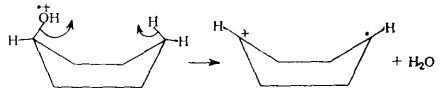
Before passing to a detailed examination of work on the mass spectrometry of steroid alcohols, we must first consider the mechanism of the dehydration of alcohols under conditions of mass spectrometry.

2. MECHANISM OF THE DEHYDRATION OF ALCOHOLS ON ELECTRON IMPACT

Momigny[6], McFadden et al.[7,8], Meyerson and Leitch[9], and also Benz and Biemann[10] showed, by means of deuterated analogues of straight-chain aliphatic alcohols, that in dehydration under the influence of electron impact ~ 90% of hydrogen atoms are lost from position 4: i.e. a mechanism of dehydration involving a six-membered transition state is preferred.

Natalis[11,12] was early able to show that all the deuterium atoms are retained when 2,2,5,5-tetradeuterocyclopentanol undergoes dehydration. It was suggested that 1,3-*cis*-diaxial elimination of water is the most probable process in the case of cycloalkanols. This question has been studied in greater detail by Shannon et al.[13] and by Djerassi et al.[14].

Investigation of 2,2,6,6-tetra- and 1,4,4-tri-deuterocyclohexanols showed[13] that the dehydration of the molecular ion of cyclohexanol (under conditions excluding random migration of hydrogen atoms) is effected by 1,3- and 1,4-elimination in the proportions 0.7 : 1. If the latter process does not involve preliminary opening of the ring, it must be assumed that the molecular ion of cyclohexanol has the boat conformation (we are concerned, of course, with the reactive conformation):

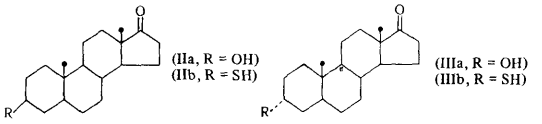


In this case *trans*-cyclohexane-1,4-diol should be more easily dehydrated than its *cis*-isomer on electron impact. In fact, the peak due to the $[M - DOH]^{+}$ ion in the spectrum of *trans*-1,4-dideuterocyclohexane-1,4-diol exceeds the corresponding peak in the spectrum of the *cis*-diol by a factor of 8.

By means of the mass spectra of deuterated cyclohexanols containing deuterium in various positions Djerassi[14] confirmed the suggested 1,3- and 1,4-mechanism for the elimination of water. However, his results indicated that the relative probabilities of the ejection of a hydrogen atom from positions 3 and 4 were 0.5 : 1.

3. 3-HYDROXY-STEROIDS

As remarked above, Biemann and Seibl[5] observed significant differences in the mass spectra of epimeric steroid alcohols. Thus the intensity ratio of the peaks $I_{M-H_2O}/I_{M^+} = 0.11$ for epiandrosterone (IIa) with an equatorial 3β-hydroxy-group, but the ratio is 0.19 for androsterone (IIIa) with a 3α-hydroxyl.

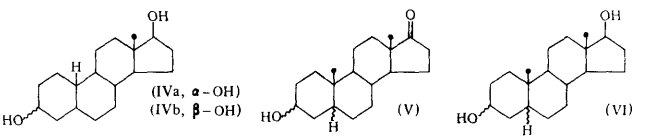


These workers found a similar but still more clearly defined difference in the mass spectra of the acetates of (IIa) and (IIIa), where elimination of a molecule of acetic acid occurs far more readily from the epimer having an axial acetoxy-group.

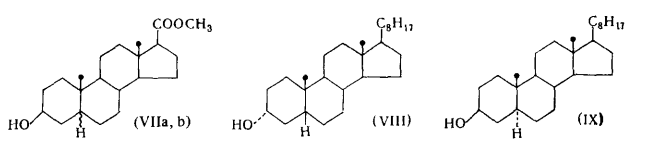
However, the work of Egger and Spiteller[15] casts about on the reliability of Biemann and Seibl's results. The mass spectra of epiandrosterone (IIa) and androsterone (IIIa), obtained by the later workers by direct introduction of the specimen into the ion source at 70°C, were completely identical, showing no difference in the intensity ratio of the peaks due to M^+ and $[M - H_2O]^{+}$ ions. Thermal effects obviously played a quite important part in Biemann and Seibl's experiment, since they used an instrument with a heated metallic admission system. Therefore their mass spectra represented a difference in thermal dehydration rather than in the degree of dehydration on electron impact.

An independent study of the mass spectra of the epimeric androsterones (IIa) and (IIIa) was made by Zaretskii and Zaikin[16]. They also detected no difference between the mass spectra of the epimers while using a system of direct introduction of the test material into the ion source† (at a temperature 20–30 deg below the melting point). Nor were differences evident in the mass spectra of their thio-analogues (IIb) and (IIIb). Thus the mechanism of the elimination of hydrogen sulphide from thiols on electron impact is evidently similar to the mechanism of the elimination of water.

In view of the results obtained by Shannon[13] and by Djerassi[14] we may suppose that the dehydration of androsterone (IIIa)[15,16], containing an axial hydroxyl, takes place mainly by the 1,3-type of elimination. On the other hand, the dehydration of epiandrosterone (IIa) may be accompanied by transition of ring A into the boat form, which evidently increases the probability of elimination of the 3β-hydroxyl, since hydrogen atoms from other rings, situated closest to the hydroxyl-group, may also be involved in the dehydration. The ultimate result is that the ratio I_{M-H_2O}/I_{M^+} is almost the same in the spectra of the 3α- and 3β-epimers. The spectra of 19-norandrostane-3α,17β- and -3β,17β-diols (IVa) and (IVb) provide some support for this view.



The peak due to the $[M - H_2O]^{+}$ ion is considerably larger in the spectrum of the 3α-hydroxy-epimer (IVa) than in that of the 3β-hydroxy-epimer (IVb)[15]. If it is assumed that on electron impact the ring A is in the boat form, conditions are favourable in the β-epimer for 1,4-elimination of water involving the 10β-hydrogen atom (which, incidentally, is absent from androstanes containing a 19-methyl group). In steroids having *cis*-fusion of rings A and B a hydrogen atom may be removed from $C_{(9)}$ (if ring A is also in the boat form). Such a possibility is not available to alcohols having *trans*-fusion of these rings, so that the 5β-alcohols undergo dehydration more easily than do their 5α-epimers. Nor are differences observed in the spectra of 3-hydroxyandrostan-17-ones (V) and of androstane-3,17β-diols (VI), whether of the 5β- or of the 5α-series, these compounds being epimeric at $C_{(3)}$.



However, compounds having the same configuration of the 3-hydroxyl but isomeric with respect to the fusion of rings A and B have significantly different spectra: dehydration under the influence of electron impact takes place more readily in the 5β-series. A more intense $M - H_2O$

† In all the work discussed below the mass spectra were obtained with direct entry of the specimen into the ion source.

peak and a less intense M^+ peak are observed also in the mass spectra of methyl 3β-hydroxy-5β-etianate (VIIa) and coprostan-3α-ol (VIII) in comparison with those of the stereoisomeric methyl 3β-hydroxy-5α-etianate (VIIb) and cholestan-3β-ol (IX) respectively[15].

The problem of elucidating the mechanism of the elimination of water on electron impact with epimeric cholestan-3-ols have been examined by Djerassi et al.[17] In order to exclude the effect of thermal dehydration preceding electron impact, these workers consider the dehydration of the $[M - CH_3]^+$ ion, not that of the molecular ion as is usually done. The mass spectra of the deutero-derivatives of cholestan-3α-ol showed (Table 1) that 73% of hydrogen atoms involved in formation of the ion $[M - CH_3 - H_2O]^+$ came from the 5α-position (ion a) and 7% from $C_{(1)}$ (ion a'). In the case of cholestan-3β-ol formation of the $[M - CH_3 - H_2O]^+$ ion involves the loss of 28% of hydrogen atoms from position 1 and 11% of 5α-hydrogen atoms (Table 2). The remaining hydrogen atoms involved in dehydration of the ion $[M - CH_3]^+$ are eliminated from other rings. If ring A is in the chair form, 1,3-diaxial detachment of hydrogen involving the 5α-hydrogen atom is possible with cholestan-3α-ol. This possibility is clearly absent from the cholestan-3β-ol molecule, where the opening of ring A and random ejection of hydrogen atoms from the other rings constitute the more probable mechanism[17].

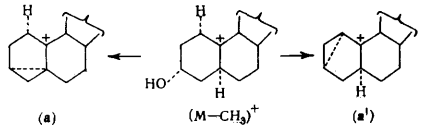
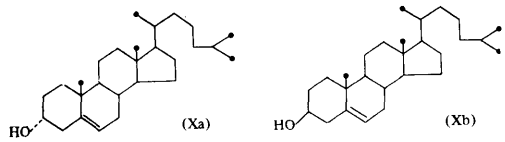


Table 1. Intensity of $[M - CH_3 - HDO]^+$ peak as percentage of $[M - CH_3 - H_2O]^+$ peak in the spectra of labelled cholestan-3β-ols.

2,2,4,4-Tetradeuterated	0
1,1,3β-Trideuterated	7 ± 2
1α-Monodeuterated	4.5 ± 2
5α-Monodeuterated	73 ± 2

It follows from the above discussion that the configuration at $C_{(3)}$ has little effect on the ease of elimination of water on electron impact with epimeric saturated 3-hydroxy-steroids.



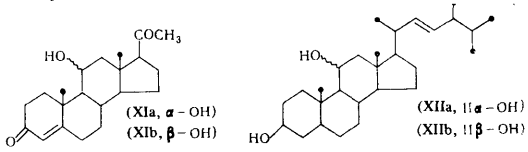
The introduction of a double bond at the 5–6 position of a steroid molecule fixes the conformation of ring A, which changes the situation significantly. In fact the mass spectra of epicholesterol (Xa) and cholesterol (Xb)[16] differ in the relative intensities of the peaks due to $[M - H_2O]^{+\cdot}$ and $M^{+\cdot}$ ions. In the case of (Xa) (axial hydroxyl) the intensity of the peak due to the former ion is 90% of that due to M^+, whereas in the spectrum of (Xb) (equatorial hydroxyl) the corresponding ratio is 50%. Thus, on the assumption that water is removed in this case by a process of 1,3-elimination (involving hydrogen from $C_{(1)}$), the axial 3α-hydroxy-group is more easily removed, owing to the 1,3-*cis*-diaxial arrangement of the groups undergoing elimination.

Table 2. Intensity of $[M - CH_3 - HDO]^+$ peak as percentage of $[M - CH_3 - H_2O]^+$ peak in the spectra of labelled cholestan-3β-ols.

2,2,4,4-Tetradeuterated	0
3α-Monodeuterated	0
5α-Monodeuterated	11
1,1-Dideuterated	28

4. 11-HYDROXY-STEROIDS

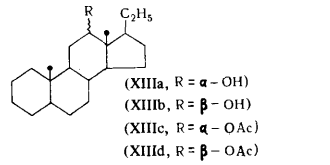
The mass spectra of steroid alcohols containing the hydroxyl in conformationally fixed rings, unlike those of 3-hydroxy-steroids, differ markedly among themselves, primarily in the peak intensity ratio $I_{M - H_2O}/I_{M^+}$. Comparison of the mass spectra of 11α- and 11β-hydroxy-progesterone (XIa) and (XIb) shows[18-20] that the alcohol (XIb), whose molecule contains an axial hydroxyl, readily eliminates a molecule of water on electron impact, whereas the molecular ion of its epimer (XIa), containing an equatorial hydroxyl, is more stable, and is dehydrated to a less extent (the intensity ratios for (XIa) and (XIb) are respectively 0.7 and 5.7).

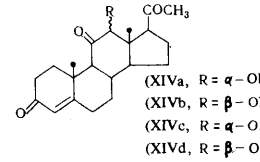


The mass spectra of ergost-22-ene-3β,11α-diol (XIIa) and of the corresponding 3β,11β-diol (XIIb), which were studied by Fitches[21], also differ in the ratio of the $M - H_2O$ and M^+ peaks: the intensity ratio is considerably smaller in the spectrum of the 11α-epimer (XIIa) (equatorial hydroxy-group) than in that of the 11β-epimer (XIIb) (axial hydroxyl).

5. 12-HYDROXY-STEROIDS

Studies have been made of the mass spectra of pregnan-12α- and 12β-ols (XIIIa and XIIIb), their acetates (XIIIc and XIIId), 12α- and 12β-hydroxypregn-4-ene-3,11,20-triones (XIVa and XIVb), and also the acetates of the latter compounds (XIVc and XIVd)[16]. The pregnan-12-ols (XIIIa) and (XIIIb) are easily dehydrated on electron impact (in both cases the peak due to the $[M - H_2O]^{+\cdot}$ ion considerably exceeds the M^+ peak). However, the $I_{M - H_2O}/I_{M^+}$ ratios in the spectra of the epimers differ markedly. As has been noted with 11-hydroxyprogesterones, an axial hydroxy-group is also eliminated more easily in the series of pregnan-12-ols.





A curious feature of the mass spectra of (XIIIa) and (XIIIb) is the difference in intensity of the peak having $m/e = 257$, corresponding to ejection of an ethyl radical from the $[M - H_2O]^{\cdot+}$ ion: this peak is considerably more intense in the spectrum of (XIIIa). It may be expected that, as a consequence of the *cis*-arrangement of the 12β-hydroxyl and the 17β-ethyl group, the elimination of water from the molecular ion of pregnan-12β-ol will be accompanied, at least partly, by loss of a hydrogen atom from the side-chain; whereas the 17β-ethyl group located *trans* to a 12α-hydroxyl is not involved in dehydration of the molecular ion of pregnan-12α-ol. This situation is probably responsible also for the diminution in the intensity of the elimination of the ethyl group from the $[M - H_2O]^{\cdot+}$ ion in the case of (XIIIb).

The mass spectra of the acetates (XIIIc) and (XIIId) differ little between themselves. Both epimers eliminate a molecule of acetic acid so easily on electron impact that the peak of the molecular ion cannot be recorded. However, breakdown of the $[M - CH_3COOH]^{\cdot+}$ ion, accompanied by ejection of an ethyl radical, occurs rather more readily with the 12α-hydroxy-epimer, as for the free alcohols.

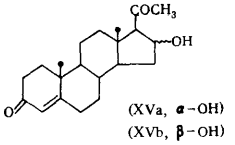
Table 3. Intensity ratios $I_{M - H_2O(CH_3COOH)}/I_{M^+}$ in the mass spectra of (XIIIa)–(XIVd).

Compound	$I_{M - H_2O(AcOH)}/I_{M^+}$	Compound	$I_{M - H_2O(AcOH)}/I_{M^+}$
(XIIIa)	57	(XIVb)	0.6
(XIIIb)	14	(XIVc)	7.3
(XIVa)	0.3	(XIVd)	4.3

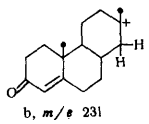
The dependence on configuration of the ease of dehydration on electron impact, which has been reported for pregnan-12-ols, is not maintained in the 12-hydroxypregn-4-ene-3,11,20-triones (XIVa and XIVb)[16]. In this case the mass spectrum of (XIVb) (equatorial hydroxyl) exhibits double the $I_{M - H_2O}/I_{M^+}$ ratio shown by (XIVa) (Table 3). This phenomenon is obviously explained by the ease of tautomerisation of α-hydroxy-ketones, on electron impact, to the corresponding 11-hydroxy-12-keto-isomers. This hypothesis is supported indirectly by the mass spectra of the acetates (XIVc) and (XIVd) of (XIVa) and (XIVb), in which high intensity of the peak due to the $[M - CH_3COOH]^{\cdot+}$ ion is characteristic of the 12α-acetoxy-epimer (XIVc) (axial acetoxy-group) (Table 3).

6. 16-HYDROXY-STEROIDS

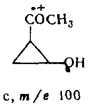
The mass spectra of 16α- and 16β-hydroxyprogesterones (XVa) and (XVb)[18,19], while indicating that both epimers are easily dehydrated on electron impact, exhibit significant differences. Firstly, the ease of dehydration of the molecular ion of (XVa) (16α-hydroxyl) exceeds that of its β-epimer (XVb) by a factor of 3 (Table 4). This indicates that an α-bond at $C_{(16)}$ is almost axial in character, and a β-bond almost equatorial.



(XVa, α-OH)
(XVb, β-OH)



b, *m/e* 231



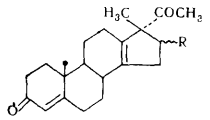
c, *m/e* 100

Secondly, the mass spectrum of (XVa) contains an intense peak due to the ion (b) having $m/e = 231$, which is almost completely absent from the spectrum of (XVb). The fragment (b) contains the rings A–C and is formed by rupture of the 13–17 and 14–15 bonds with migration of a hydrogen atom from position 16 to the charged fragment. However, rupture of the same bonds but with the charge localised on the fragment containing the atoms $C_{(15)}$–$C_{(17)}$, $C_{(20)}$, and $C_{(21)}$ yields the ion (c) having $m/e = 100$, whose peak is quite intense in the spectrum of 16α-hydroxyprogesterone (XVa) and is almost completely absent from the spectrum of its 16β-epimer (XVb).

Table 4. Intensity ratio $I_{M - H_2O}/I_{M^+}$ and intensities of peaks due to characteristic ions (% of Σ) in mass spectra of (XVa) and (XVb).

Cpd	I_{M-H_2O}/I_{M^+}	Ion (b) (*m/e* 231)	Ion (c) (*m/e* 100)
XVa	13	4.6	3.2
XVb	4.3	0.65	0.6

The above results were used to determine the configuration at position 16 in the pregnen-16-ol derivatives (XVIa) and (XVIb)[16]. In the mass spectrum of (XVIa) the ratio $I_{M - H_2O}/I_{M^+} = 20$, whereas in the spectrum of (XVIb) this ratio is only 8.7. By analogy with the 16-hydroxyprogesterones (XVa and XVb), therefore, the alcohol (XVIa) should have the α-configuration of the hydroxy-group, and the alcohol (XVIb) the β-configuration.



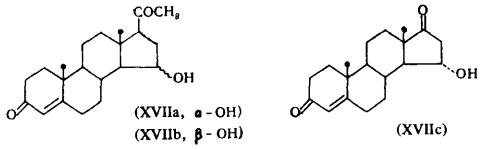
(XVIa, R = α-OH)
(XVIb, R = β-OH)
(XVIc, R = α-OAc)
(XVId, R = β-OAc)

Further confirmation of the configuration at position 16 was obtained by comparing the mass spectra of the corresponding acetates (XVIc) and (XVId). Primarily, the ratio of the peaks due to the ions $[M - CH_3COOH]^{\cdot+}$ and M^+ is different in the spectra of the epimers (120 and 36 respectively). Therefore the acetate (XVIc) must be assigned to the 16α-series, and its epimer (XVId) to the 16β-series. Another striking feature of the spectra of the four compounds (XVI) is the difference in intensity of the peak due to the ion $[M - COCH_3]^+$. The great intensity of this peak in the spectra of the 16α-OR′ epimers (XVIa and XVIc) is evidently due to the *cis*-arrangement of the 17α-acetyl and the 16α-OR′ groups, which facilitates elimination of the 17-acetyl group.

7. 15-HYDROXY-STEROIDS

Studies have been made of the mass spectra of 15α- and 15β-hydroxyprogesterones (XVIIa) and (XVIIb), and also of 15α-hydroxyandrost-4-ene-3,17-dione (XVIIc)[18,19]. The 15β-hydroxy-epimer (XVIIb) had a high $I_{M - H_2O}/I_{M^+}$ ratio (Table 5). The explanation is that the hydroxy-group

is equatorial in character in the (XVIIa) molecule, but axial in (XVIIb).



(XVIIa, α-OH)
(XVIIb, β-OH)

(XVIIc)

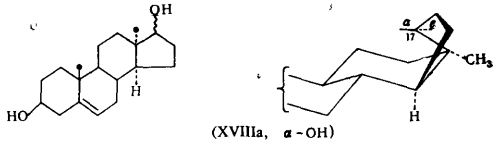
Table 5. Intensity ratio I_{M-H_2O}/I_{M^+} and intensities of peaks due to characteristic ions (% of Σ) in mass spectra of (XVIIa–(XVIIc).

Cpd.	I_{M-H_2O}/I_{M^+}	Ion (b) (*m/e* 231)	Ion (c) (*m/e* 100)
XVIIa	0.21	0.7	0.3
XVIIb	4.9	3.0	1.3
XVIIc	0.07	0.2	—

A similar situation is found in the mass spectrum of (XVIIc), in which the intensity of the peak due to the $[M - H_2O]^{+\cdot}$ ion is only 7% of the intensity of the M^+ peak, which dominates the spectrum. The characteristic difference in the mass spectrum of (XVIIb), as in the case of its 16α-hydroxyl analogue (XVa), is the considerable intensity of the peaks due to the ions (b) and (c), the mechanism of whose formation is similar to that described for (XVa) and (XVb) (Table 5).

8. 17-HYDROXY-STEROIDS

The behaviour of epimeric 17-hydroxy-steroids of the normal series on electron impact has not been studied. However, it is noteworthy that steroids of the 17β-hydroxy-series (oestradiol, 19-nortestosterone)[22], in which the hydroxyl is equatorial in character, eliminate water with difficulty under these conditions.



(XVIIIa, α-OH)
(XVIIIb, β-OH)

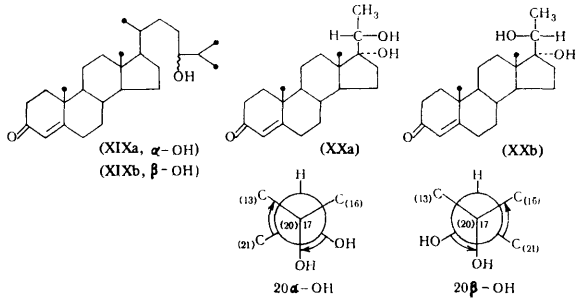
Comparison of the mass spectra of epimeric alcohols of the 13-iso-series—13-isoandrost-5-ene-3β,17α- and -3β,17β-diols (XVIIIa and XVIIIb)[16]—shows that electron impact has different dehydrating effects: the M^+ peak is more intense than the peak due to the $[M - H_2O]^{+\cdot}$ ion in the mass spectrum of (XVIIIa), but the opposite situation is observed in the spectrum of (XVIIIb). This observation is fully consistent with the equatorial character of an α-bond at $C_{(17)}$ in steroids of the 13-iso-series, and the axial character of a β-bond (in relation to ring C—see above scheme). Thus in this case also an axial hydroxyl is more easily eliminated as water than is an equatorial hydroxyl. A similar relation is found in several other fragments formed when molecular ions of compounds (XVIIIa) and (XVIIIb) break down. Thus the ratios

$$I_{M-2H_2O}/I_{M-H_2O} \text{ and } I_{M-H_2O-CH_2-H_2O}/I_{M-H_2O-CH_3}$$
$$I_{m/e\,197}/I_{m/e\,205} \text{ and } I_{m/e\,161}/I_{m/e\,179},$$

change similarly to I_{M-H_2O}/I_{M^+} on passing from (XVIIIa) to (XVIIIb). In these two cases ions having m/e = 205 and 179 are characteristic of steroids having a 5–6 double bond and contain the ring C together with parts of rings A and B[23–25].

9. 20- AND 24-HYDROXY-STEROIDS

Epimeric aliphatic alcohols containing a single asymmetric centre usually have completely identical mass spectra. This held for 24α- and 24β-hydroxycholest-4-en-3-one (XIXa and XIXb), which contain a hydroxy-group in the aliphatic side-chain. Nevertheless, 17α,20α-dihydroxypregn-4-en-3-ones show significantly higher I_{M-H_2O}/I_{M^+}, I_{M-2H_2O}/I_{M-H_2O}, and also I_{M-CH_3CHOH}/I_{M^+} ratios in the mass spectrum of the 20α-hydroxy-epimer (XXa) than in that of the 20β-epimer (XXb).



(XIXa, α-OH)
(XIXb, β-OH)

(XXa)

(XXb)

20α-OH

20β-OH

Inspection of Dreiding models shows that an intramolecular hydrogen bond is possible between the 20β- and 17α-hydroxyls in (XXb), whereas this possibility is difficult to realise in the case of the 20α-epimer (XXa), owing to steric hindrance caused by the close mutual approach of the 20-methyl and angular 13-methyl groups (see above scheme). Formation of a hydrogen bond is probably the reason why a water molecule and a CH_3CHOH radical are not ejected from the molecular ion of the 20β-hydroxy-epimer (XXb).

10. TERTIARY ALCOHOLS OF THE D-HOMO-SERIES

Study of epimeric tertiary alcohols derived from (±)-17a-alkyl-3-methoxy-D-homo-oestra-1,3,5(10),8-tetraen-17a-ols—(XXIa), (XXIb), (XXIIa), and (XXIIb)—revealed exceptionally large differences between the mass spectra of epimers[26–28]. First of all, the intensity of the peak due to the $[M - H_2O]^+$ ion in the spectra of alcohols having an axial hydroxyl (XXIa and XXIb) far exceeds that of the M^+ peak, whereas the opposite situation is found with

epimers having an equatorial hydroxyl (XXIIa and XXIIb) (Table 6).

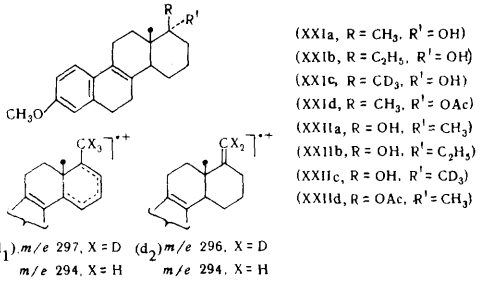


Table 6. Intensity ratios I_{M-H_2O}/I_{M^+} and $I_{M-H_2O-(17a\text{-Alk})}/I_{M-H_2O}$ in mass spectra of (XXIa)–(XXIIb).

Cpd	I_{M-H_2O}/I_{M^+}	$I_{M-H_2O-(17a\text{-Alk})}/I_{M-H_2O}$
(XXIa)	3.2	2.3
(XXIIa)	0.4	0.6
(XXIb)	2.3	3.5
(XXIIb)	0.2	0.6

The mass spectra of the 17a-trideuteromethyl analogues (XXIc and XXIIc) of (XXIa) and (XXIIa) were studied in order to elucidate the mechanism of dehydration on electron impact. Comparison of the mass spectra of (XXIc) and (XXIIc) (Figs. 1 and 2) shows that the readily dehydrated epimer (XXIIc)—and hence also (XXIa) and (XXIb)—form almost exclusively the $[M-H_2O]^{\cdot+}$ ion having m/e = 297 (ion d_1) on dehydration of the molecular ion.

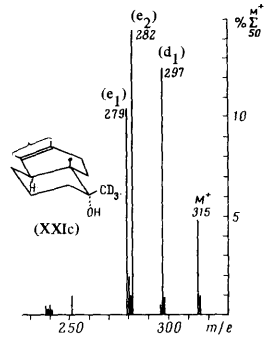


Figure 1.

Since dehydration takes place mainly by a mechanism of 1,3-elimination, the loss of hydrogen in this case takes place most probably from the atom $C_{(16)}$ or $C_{(14)}$. The epimer (XXIIc)—and hence also (XXIIa) and (XXIIb)—which eliminates water with far greater difficulty on electron impact, forms not only the ion d_1 but also the $[M-DOH]^{\cdot+}$ ion having m/e = 296 (ion D_2) with an exocyclic double bond. The formation of the fragment d_1 (not d_2) from the molecular ion of (XXIc) suggests an axial arrangement of the 17a-hydroxyl (since only then can one of the axial hydrogen atoms of the D ring be removed together with the hydroxy-group), and thus provides fresh evidence of the configuration at position 17a in the molecule of this compound. The appearance of twin $M-H_2O$ and $M-DOH$ peaks in the mass spectrum of (XXIIc) indicates an *ax*-alkyl-*eq*-hydroxyl configuration at position 17a.

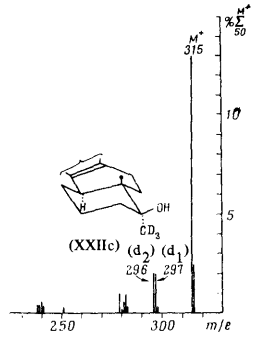
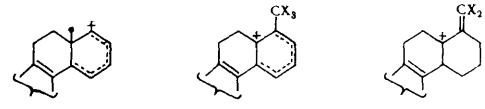
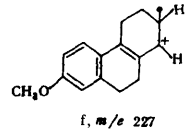


Figure 2.

The mass spectra of these compounds differ also in the relative intensities of the ions $[M-H_2O-17a\text{-Alk}]^+$ (e) and $[M-H_2O]^{\cdot+}$. In the case of epimers having an axial hydroxyl (XXIa and XXIb) the intensity of the former peak far exceeds that of the latter, but the opposite relation is found in epimers having an equatorial hydroxyl (XXIIa and XXIb) (Table 6). Comparison of the mass spectra of the deuterated analogues (XXIc and XXIIc) with those of the unlabelled compounds (XXIa and XXIIa) shows that the peak due to the ion (e) is composite, representing the formation of ions of the types (e_1), (e_2), and (e_3). In the spectra of epimers having an axial hydroxyl this peak represents the ions (e_1) and (e_2). In alcohols having an equatorial hydroxyl, however, removal only of the angular methyl group (ion e_3) is possible after the elimination of water, since the presence of an exocyclic double bond in the ion (d_2) makes loss of the 17a-alkyl group impossible.



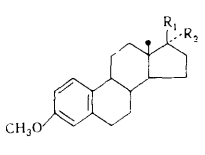
Another characteristic peak in the mass spectra of (XXIa), (XXIb), (XXIIa), and (XXIIb), whose intensity depends on the configuration of the epimer, is that due to the ion (f) having m/e = 227. Its intensity in the spectrum of the epimer with an equatorial hydroxyl is 16% (of $\Sigma_{50}^{M^+}$), whereas in the spectrum of the epimer having an axial hydroxyl it is only 1.2%. The ion (f) is formed directly from the molecular ion by detachment of ring D and migration of the hydrogen atom from the 17a-hydroxyl.



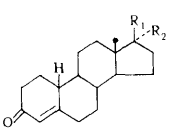
Comparison of the mass spectra of the acetates (XXId) and (XXIId)[30] reveals easier elimination of an axial than of an equatorial acetoxy-group as acetic acid on electron impact, similarly to the behaviour of the free alcohols. The mass spectra of (XXId) and (XXIId) differ also in the intensity of peaks due to ions of type (e), formed by ejection of a methyl group from ions of type (c) $[M - CH_3COOH]^{\cdot+}$. As with the free tertiary alcohols, the peak (e) is composite, the difference in its intensity being due to a difference in the mechanism of the elimination of acetic acid from the molecular ions of the epimers.

11. TERTIARY ALCOHOLS OF THE NORMAL SERIES

In contrast to alcohols of the D-homo-series, tertiary alcohols which are epimeric at $C_{(17)}$—(±)-17-alkyl-3-methoxyoestra-1,3,5(10)-trien-17-ol (XXIIIa,b–XXXVa,b) and (±)-17-alkyl-19-nortestosterone (XXXVIa,b–XXVIIa,b)[29] derivatives—have essentially similar mass spectra[29], differing only in the intensity ratio of the peaks due to $[M - H_2O]^{\cdot+}$ and M^+ ions. The ratio is higher in alcohols having an α-hydroxyl (XXIIIa–XXVa) than in their β-hydroxy-epimers (XXIIIb–XXVb) (Table 7). This result is consistent with general views on the conformation of bonds at the $C_{(17)}$ atom (an α-bond is axial in character, and a β-bond equatorial).



(XXIIIa, $R_1 = CH_3$, $R_2 = OH$)
(XXIIIb, $R_1 = OH$, $R_2 = CH_3$)
(XXIVa, $R_1 = C_2H_5$, $R_2 = OH$)
(XXIVb, $R_1 = OH$, $R_2 = C_2H_5$)
(XXVa, $R_1 = CH_2C(=CH_2)CH_3$, $R_2 = OH$)
(XXVb, $R_1 = OH$, $R_2 = CH_2(=CH_2)CH_3$)



(XXVIa, $R_1 = CH_3$, $R_2 = OH$)
(XXVIb, $R_1 = OH$, $R_2 = CH_3$)
(XXVIIa, $R_1 = C_2H_5$, $R_2 = OH$)
(XXVIIb, $R_1 = OH$, $R_2 = C_2H_5$)

Table 7. Intensity ratio I_{M-H_2O}/I_{M^+} in mass spectra of (XXIIIa)–(XXVb).

Compound	I_{M-H_2O}/I_{M^+}	Compound	I_{M-H_2O}/I_{M^+}
(XXIIIa)	45	(XXIVb)	21
(XXIIIb)	14	(XXVa)	62
(XXIVa)	41	(XXVb)	21

In the 19-nortestosterones (XXVIa,b–XXVIIa,b) the I_{M-H_2O}/I_{M^+} ratios show smaller differences in the spectra of epimers. In this case, however, the 17α-hydroxy-epimer undergoes dehydration more readily on electron impact.

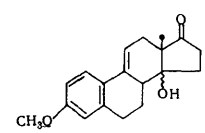
The spectra of epimers of this group differ more markedly in the ratio of the peaks due to the ions $[M - H_2O - 17\text{-Alk}]^+$ ($m/e = 255$) and $[M - H_2O]^{\cdot+}$ (Table 8). The considerable decrease in this ratio in the spectra of the 17β-hydroxy-epimers (XXVIb and XXVIIb) in comparison with the 17α-epimers (XXVIa and XXVIIa) is obviously due to a difference in the mechanism of the dehydration of their molecular ions. The process probably resembles that described for the D-homo-alcohols: removal of an α-hydroxyl from a molecular ion is accompanied by that of a hydrogen atom from the ring D, with formation of an ion of type (d_1); whereas in the case of the β-hydroxy-epimers an ion of type (d_2) having an exocyclic double bond is also formed. Ejection of the 17-alkyl is impossible in the latter case, and therefore the peak at $m/e = 255$ becomes less intense.

Table 8. Intensity ratios I_{M-H_2O}/I_{M^+} and $I_{M-H_2O-17\text{-Alk}}/I_{M-H_2O}$ in mass spectra of (XXVIa)–(XXVIIb).

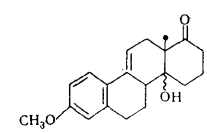
Compound	$\frac{I_{M-H_2O}}{I_{M^+}}$	$\frac{I_{M-H_2O-17\text{-Alk}}}{I_{M-H_2O}}$
(XXVIa)	36	1.8
(XXVIb)	17.4	0.3
(XXVIIa)	21	1.8
(XXVIIb)	15	0.9

12. 14-HYDROXY-STEROIDS

Mass spectrometry has been used also to determine the configuration at positions 8 and 14 in 14-hydroxy-derivatives of 3-methoxyoestra-1,3,5(10),9(11)-tetraen-17-one (XXVIII) and 3-methoxy-D-homo-oestra-1,3,5(10),9-(11)-tetraen-17-one (XXIXa and XXIXb)[31].

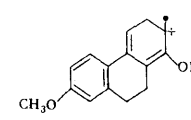


(XXVIII)



(XXIX, a α-OH; b β-OH)

The mass spectra of the hydroxy-ketones (XXIXa) and (XXIXb) differ substantially in the intensity of the peak due to the ion (g) having $m/e = 241$

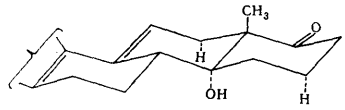


g, m/e 241

formed by cleavage of the bonds 13–17a and 14–15 in the molecular ion. The fivefold increase in this ion on passing from (XXIXa) to (XXIXb) enables us to assign the former to the *trans*-C–D series (14α-hydroxyl), and the latter to the *cis*-C–D series (14β-hydroxyl), by analogy with *cis*- and *trans*-α-decalins, 14α- and 14β-equilenins, 8α- and 8β-oestrones, etc.

Furthermore, the spectra of (XXIXa) and (XXIXb) differ in the intensity ratio of the $[M - H_2O]^+$ and M^+ peaks (1.2 and 0.3 respectively). The 8-deuterated analogues have been used to establish that the 8-hydrogen atom is not involved in dehydration. The other possible 1,2-elimination, involving the 15-hydrogen atom, is obviously also improbable. Ejection of DOH is not observed from the 17,17-dideutero-analogues, which refutes the possibility of 1,4-elimination. The most probable process is therefore the 1,3-elimination of water involving a 12- or 16-hydrogen

atom. This supports the conclusion that the ease of dehydration of the hydroxy-ketone (XXIXa) is associated with the α-configuration of the 14-hydroxyl (*trans*-C–D fusion), when the hydroxyl is located axially with respect to both rings C and D, with the preferred 1,3-*cis*-diaxial orientation of the groups undergoing elimination.



The insignificant dehydration of the molecular ion of the hydroxy-ketone (XXIXb) is evidently due to the equatorial orientation of the 14-hydroxy-group with respect to the ring which donates the hydrogen atom in the elimination of water on electron impact. This condition is feasible only with *cis*-C–D ring fusion (14β-hydroxy-configuration), since in any of the theoretically possible conformations of (XXIXb) the 14-hydroxyl is located equatorially with respect to one of the rings (C or D).

The mass spectrum of the hydroxy-ketone (XXVIII) is very similar to that of (XXIXb), so that *cis*-C–D fusion of the rings and equatorial orientation of the hydroxy-group can be attributed to the former.

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Although sufficient experimental results are not yet available, it can be concluded from the above survey that mass spectrometry can be used to establish configuration in all cases in which the steroid alcohol molecule contains a sufficiently rigid cyclic system, since in most cases electron impact eliminates an axial more readily than an equatorial hydroxyl.

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Electron Spin Resonance of the Excited Triplet State of Biologically Important Molecules

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The excited triplet states of molecules play an important role in the mechanisms of any photochemical reaction. These states are responsible for the occurrence of two-quantum photsensitisation, photoionisation, and photoreduction reactions. The present review compiles and gives a systematic account of the principal results obtained in the application of ESR to the study of the excited triplet state of biologically important molecules.
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I. INTRODUCTION

The application of the method of electron spin resonance (ESR) in the study of the excited triplet state of molecules began with the pioneer work of Hutchison and Mangum[1,2] more than ten years ago and has yielded much information about its properties and role in the photochemistry of organic molecules. The ESR method revealed the splitting of the lowest triplet level in the absence of an external magnetic field and the effect of the size of the conjugated system, the substituents in the molecule, and the properties of the solvents on the zero-field splitting energy. Data were obtained on the direction of the transition moment, molecular symmetry, and the distribution of spin density in the lowest excited triplet state. The ESR method provided valuable information about the lifetimes, probabilities of transition to the triplet state, and quenching and energy transfer processes.

The successful application of the ESR method in the study of the mechanism of the photochemical reactions in solid solutions several years later led to the discovery of two-quantum photosensitisation, photoionisation, and photoreduction reactions[2-8] proceeding via the triplet state of aromatic compounds, including biologically important substances, such as porphyrins, chlorophyll[8-11], aromatic aminoacids[9,11-14], nucleic acid bases[15], phenoxazine, phenothiazine, and flavins[16]. The phenomenon of triplet–triplet annihilation, leading to the formation of one molecule in a highly excited singlet, triplet, or quintet state from two molecules in a phosphorescent triplet state was first observed at approximately the same time. It attracted the attention of investigators as a possible method of using low-energy quanta to achieve reactions requiring a considerable energy expenditure[17]. It was suggested that this phenomenon may play a role in photobiological reactions.

There are many biological processes where the first stage involves the transition of specific molecules to an excited electronic state. This is the photodynamic effect—inactivation of proteins by radiation, photodimerisation of nucleic acid bases, vision, and bioluminescence. Photosynthesis, which provides energy to virtually all living things on earth, takes place owing to the absorption, transfer, and storage of the energy of sunlight by the photosynthetic apparatus of plant and bacterial cells. At the molecular level this involves tetrapyrrole pigments—chlorophyll and bacteriochlorophyll in an excited state.

All these findings—the vast scope of the new research technique, the discovery reactions proceeding via the triplet state, and finally the suggested role of the triplet state in biological processes—stimulated in recent years a profound interest by photobiologists in the study of biologically important substances in an excited triplet state. Owing to the extreme complexity involved in the observation of the phenomenon at an electronic level in real biological structures, it still remains unknown whether primary photochemical reactions *in vivo* take place at a singlet or triplet electronic level. However, such information is undoubtedly important for the understanding of the mechanism of the phenomena.

To date, more than 100 publications have appeared on ESR studies of molecules in an excited triplet state, both experimental and theoretical. A systematic and critical review of these investigations is necessary for future work. This review cannot give a complete analysis of all the studies and therefore we shall consider only briefly the advances in this field of research and shall deal in greater detail with data concerning biologically important substances.

The properties of molecules in singlet and triplet excited states are significantly different. These differences concern primarily their electronic structure: the charge distribution, spin density, and the symmetry of the π-electron cloud, and hence the donor–acceptor properties of the molecules, their reactivity, lifetime, and other characteristics determining the rate of the photochemical process. The great importance of the excited triplet state in the initial stage of the photochemical process is due to the fact that it is long-lived compared with the excited singlet state.

Fig. 1*A* presents a typical scheme of the molecular energy levels originally proposed in a simplified form by Jablonski[18] to explain the prolonged afterglow of organic molecules in rigid matrices. The radiative $T_1 \rightarrow S_0$ transition is of an intercombination type and is forbidden by the spin selection rules. The lifetime of the molecule in the lowest triplet state is therefore longer than that of the excited singlet state (about 10^{-9} s), increasing to between 10^{-4} s and several seconds, particularly at low temperatures where the probability of the non-radiative $T_1 \rightarrow S_0$ transition, the $T_1 \rightarrow S_1$ thermal transition, and quenching processes of different kinds diminishes. Since the transition to the T_1 triplet state involves the inversion

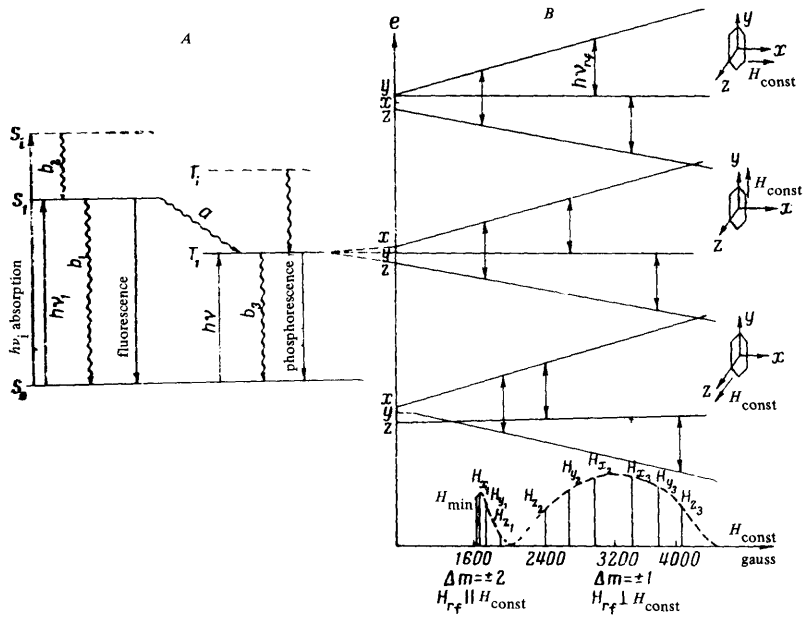

Figure 1. Schematic representation of the energy levels and transitions in an aromatic molecule. *A*—optical transitions; *B*—radio frequency ($h\nu_{rf}$) transitions in the presence of a constant magnetic field (H_{const}) and a radio frequency field (H_{rf}); S_0, S_1, S_i—the singlet energy levels; T_1, T_i—the triplet levels; *a*—intercombination non-radiative transition to a triplet state; b_1, b_2, b_3—non-radiative transitions to the corresponding lower state.

of the spin of the excited electron the overall spin of the system is unity and the multiplicity of the level is 3. Hence the term triplet is applied to this system of energy levels.

The mechanism of the transition to the phosphorescent state has been considered [19-21]. Terenin suggested that the metastable T_1 level be identified as a triplet level and put forward the hypothesis that the triplet state, characterised by unpaired spins, should play a significant role in photochemical reactions [22,23]. Lewis et al. [24] demonstrated for the first time by a static magnetic method the occurrence of light-induced paramagnetism.

We may note here also other characteristics of the excited triplet state. Firstly, as a result of the Coulombic repulsion of the unpaired electrons occupying the same orbital level, the T_1 level always has a lower energy than the first excited singlet level and therefore requires a lower activation energy. Secondly, since the lifetime in the triplet state is longer by a factor of 10^6–10^9 than the lifetime in the singlet state, favourable conditions are created for the involvement of the molecule in photochemical reactions, the rates of which are limited by diffusion processes at a low concentration of the reactants. Moreover, the energy of the triplet excitation may be readily transferred to another, unexcited molecule. Although the cross-section of the triplet–triplet transfer is lower than that of the singlet–singlet transfer, there is sufficient time for the energy of the long-lived triplet state to migrate over a long distance and therefore there is a high probability of its reaching the reaction centre.

We have already noted that the overall spin of the molecule in the triplet state S is unity and in a constant magnetic field the levels are split into three sublevels with $\Delta m = \pm 1.0$ projections of the spin on to the direction of the constant magnetic field. For molecules with a symmetry lower than spherical, the degeneracy is removed even in the absence of an external field. The zero-field splitting is due to dipole spin–spin interaction between the electrons in the triplet state, which is fairly well described by the two-electron spin Hamiltonian [1,2]

$$\hat{\mathcal{H}} = g\beta \mathbf{H}\hat{S} + DS_z^2 + E(S_x^2 - S_y^2). \qquad (1)$$

The first term defines the Zeeman energy of the interaction of the total spin S with the constant magnetic field **H** and the second, the dipole spin–spin interaction. S_X, S_Y, and S_Z are components of the overall spin S in the molecular system of coordinates, g is the spectroscopic splitting factor, and β the Bohr magneton. The zero-field splitting constant D defines the average dipole interaction between the spins along the molecular axis z and E takes into account the deviation of the spin–spin interaction tensor from axial symmetry [25,26]. The constants D and E can be readily determined from ESR spectra (the relevant equations are quoted below).

The Hamiltonian (1) transformed relative to the principal molecular axes is [26]

$$\hat{\mathcal{H}} = \mathbf{g}\beta \mathbf{HS} - (XS_x^2 + YS_y^2 + ZS_z^2), \qquad (2)$$

where X, Y, and Z are the principal values of the spin–spin interaction tensor diagonalised in the molecular

system of coordinates. They are related to the constants D and E in the following way:

$$X = {}^1/_3D + E,\ Y = {}^1/_3D - E,\ Z = -{}^2/_3D\ . \qquad (3)$$

If the constant magnetic field is directed along one of the molecular axes, for example x, eigenvalues for the triplet levels become [28]

$$e_1 = X,\ e_2 = e_3 = \frac{Y+Z}{2} \pm \sqrt{\frac{(Y-Z)^2}{4} - (g\beta H)^2}\ . \qquad (4)$$

Similar expressions can be found for the case where the field is directed along the y and z axes. Magnetic dipole transitions are allowed between two adjacent sublevels of the triplet level and involve a change in the magnetic quantum number: $\Delta m = \pm 1$. The transition moment, for example $x \rightarrow y$, is perpendicular to the xy plane (see Fig. 1*B*). When a variable magnetic field at a frequency ν such that

$$h\nu = g\beta H\,\Delta m \qquad (5)$$

is applied at right angles to the constant magnetic field, resonance absorption of electromagnetic energy takes place and is recorded by the ESR method. As a result of the occurrence of the zero-field splitting, the resonance absorption for different orientations of the constant magnetic field H_{const} relative to the three molecular axes will be observed for different values of H_{const} (Fig. 1*B*). If a single crystal is placed in the cavity and excited, being successively oriented so that the x, y, and z axes are parallel to H_{const}, three pairs of lines may be observed in the ESR spectrum—H_{x_2}, $H_{x_3}(H_{\text{const}} \parallel x)$, H_{y_2}, $H_{y_3}(H_{\text{const}} \parallel y)$, H_{z_2}, $H_{z_3}(H_{\text{const}} \parallel z)$ respectively (Fig. 1*B* below). However, the $\Delta m = \pm 1$ selection rules hold rigorously when the interaction between the spins and the external magnetic field is much greater than the intrinsic interaction between the spins, and the component of the spin angular momentum of the electrons $m(h/2\pi)$ in the direction of the field remains constant. Such transitions in a single crystal of a dilute solid solution of naphthalene in durene were observed by Hutchinson and Mangum [1,2]. However, the possibilities of growing diluted single crystals are limited. Van der Waals and de Groot [27,28] deduced theoretically and observed experimentally for the first time the forbidden transitions between the lowest and highest sublevels of the triplet level corresponding to a change in the magnetic quantum number $\Delta m = \pm 2$. The transition is observed at much weaker fields when the intrinsic interaction of the electrons is comparable to their interaction with the external magnetic field. The component of the spin angular momentum $m(h/2\pi)$ is not a constant of motion and the selection rules break down. The $\Delta m = \pm 2$ transitions are polarised parallel to the constant magnetic field and are observed in parallel fields (Fig. 1*B*). In particular, it follows from Eqn. (4) that the transitions between the sublevels take place for values of H_{const} defined by the equation

$$(e_2 - e_3)^2 = (h\nu)^2 = \frac{1}{4}(Y-Z)^2 + (g\beta H)^2\ . \qquad (6)$$

We shall employ as an example the data of Hutchison and Mangum [2] for naphthalene:

$$\frac{X-Z}{hc} = 0.0863\ см^{-1},\ \frac{Y-Z}{hc} = 0.1143\ см^{-1},\ \frac{h\nu}{hc} = 0.3221\ см^{-1} = 2.0033.$$

On substituting the numerical values in Eqn. (6), we find that the resonance absorption for naphthalene with $\Delta m = \pm 2$ will be observed for $H_{x_1} = 1602$ G, $H_{y_1} = 1650$ G, and $H_{z_1} = 1707$ G. Thus, whereas the $\Delta m = \pm 1$ transitions are recorded in the range of H_{const} from 2354 to 4490 G and the overall line width is 2196 G, for $\Delta m = \pm 2$ transitions the latter value is 105 G, i.e. the anisotropy of the transitions is smaller by a factor of 20. [27,28] Therefore,

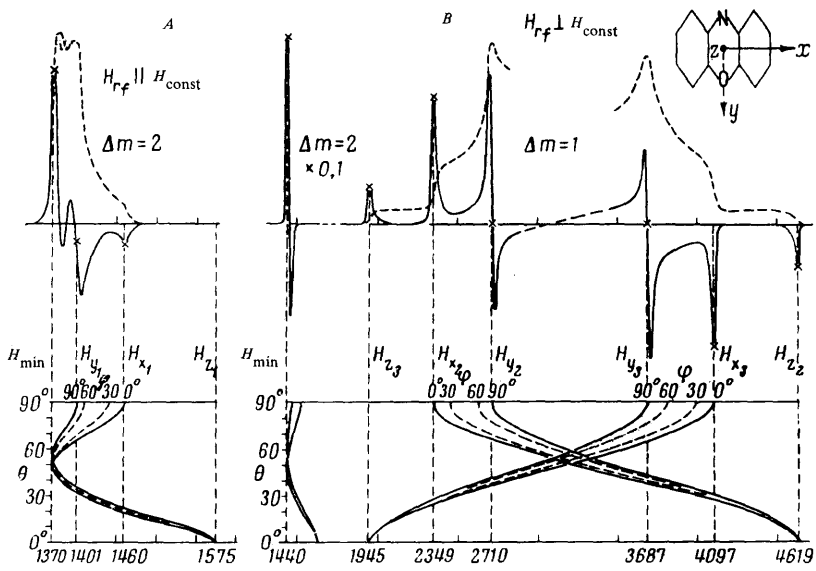

Figure 2. ESR spectrum of phenoxazine in the triplet state (molecular symmetry less than that for three axes: $x \neq y \neq z$). Below: distribution of resonance fields $F(\delta, H)$ as a function of $f(\theta, \varphi)$ for the specified ν = const.

despite the fact that the intensity of these transitions is lower by two powers of ten than that of the $\Delta m = \pm 1$ transitions, the ESR signal may be observed in specimens with a random orientation—solid solutions[28].

For an arbitrary orientation of H_{const} relative to the molecular axes, Kottis and Lefevre[29,30] used the operator (2) to find the distribution function of the resonance fields in terms of the spatial orientation of the x, y, and z axes relative to the constant magnetic field (the angles φ and θ, Fig. 2*B*). For a fixed value of the microwave quantum ($h\nu$), such a function makes it possible to determine the resonance fields for specified X, Y, and Z parameters. Figs. 1 and 2B show that, for $h\nu > D$, three resonance values of the field correspond to each molecular orientation. Two of these correspond to the $\Delta m = \pm 1$ transitions ($H_{const} \perp H_{rf}$) and the third to $\Delta m = \pm 2$ ($H_{const} \parallel H_{rf}$). Finally, there is resonance absorption for a minimal value of H_{const} (H_{min}) at the specified frequency (Fig. 2*B*). In this case the intensity of ESR absorption is independent of the relative orientations of H_{const} and H_{rf}:

$$H_{min} = (2g\beta)^{-1}[(h\nu)^2 + 4(XY + XZ + YZ)]^{1/2} = (2g\beta)^{-1}\left\{(h\nu)^2 - 4\left[\frac{D^2}{3} + E^2\right]\right\}^{1/2}. \quad (7)$$

Expressions for the calculation of the resonance fields or, if their values are known from ESR spectra, of the zero field splitting constants and energies are:

$$H_{x_1} = (2g\beta)^{-1}[(h\nu)^2 - (D-E)^2] = (2g\beta)^{-1}[(h\nu)^2 - (Y-Z)^2]^{1/2},$$
$$H_{x_2} = (2g\beta)^{-1}[(2h\nu - D - 3E)^2 - (D-E)]^{1/2} = (2g\beta)^{-1}[(2h\nu - 3|X|)^2 - (Y-Z)^2]^{1/2},$$
$$H_{x_3} = (2g\beta)^{-1}[(2h\nu + D + 3E)^2 - (D-E)^2]^{1/2} = (2g\beta)^{-1}[(2h\nu + 3|X|)^2 - (Y-Z)^2]^{1/2}. \quad (8)$$

H_{X_1} corresponds to the $\Delta m = \pm 2$ transition and H_{X_2} and H_{X_3} to the $\Delta m = \pm 1$ transition. The expressions for the H_{Y_1}, H_{Y_2}, H_{Y_3}, H_{Z_1}, H_{Z_2}, and H_{Z_3} resonance fields are similar to Eqn. (8) and can be obtained by a cyclic interchange of X, Y, and Z.

Subsequently it was found that the $\Delta m = \pm 1$ transitions can be observed not only for single crystals but also specimens with a random orientation. In a solid solution the molecules are fixed relative to one another and magneto-selection takes place. Molecules whose corresponding axes lie within 5° of the constant magnetic field contribute to the intensity of the canonical peak[27]. This was observed experimentally for the first time by Yager et al.[31] for naphthalene, coronene, and triphenylene. Similar spectra were recorded for biologically important compounds: magnesium-aetioporphyrin[32] and later for other porphyrins[33,34], chlorophyll[34], orotic and polyadenylic acids, adenosine and guanosine monophosphates[35-37], aromatic aminoacids, and certain proteins[38].

ESR absorption in a field corresponding to a g-factor of 2.0023 has been observed for certain aromatic substances[33,34,39]. This is the so called two-quantum transition ($H_{t.q.}$) caused by the simultaneous absorption of two radiofrequency quanta. The following relation must hold for a two-quantum transition to be observed:

$$(g\beta H_{t.q.})^2 = (h\nu)^2 - \frac{1}{3}D^{*2} \quad (D^* = \sqrt{D^2 + 3E^2}). \quad (9)$$

The molecular orientations for which the energy differences between two pairs of adjacent sublevels are similar or identical make a dominant contribution to the $H_{t.q.}$ absorption line.

Thus for molecules with a lower than third-order symmetry, the ESR spectrum in perpendicular fields consists of eight peaks. Such line shape corresponds to the static case where during the radiofrequency transition the nuclei of the atoms in the molecule do not undergo significant conformational, rotational, or other displacements. However, de Groot and van der Waals[40] showed that the line shape of the ESR spectra of the triplet state of certain aromatic compounds, for example benzene, triptycene, and aromatic ions, can vary significantly with temperature owing to different dynamic effects. The line shape of the ESR spectra of substances whose triplet state is orbitally degenerate varies in the same way[40]. In this case the Jahn–Teller effect leads to the instability of the fully symmetrical non-linear molecule and to the removal of the orbital degeneracy due to nuclear displacements. The high molecular symmetry breaks down, which leads to a change in the line shape of the ESR spectrum and in the zero-field splitting constants. The dynamic effect has been treated theoretically by Kottis and Lefevre[30].

Having examined the principal characteristics of the line shape of the ESR spectra common to all aromatic substances, we shall proceed to consider the characteristics of the ESR and the properties of the excited triplet state of biologically important compounds.

II. ELECTRON SPIN RESONANCE OF THE TRIPLET STATE OF BIOLOGICALLY IMPORTANT MOLECULES

1. Porphyrins

The first data on the excited triplet state of porphyrins observed by the ESR method were published in 1963.[32] Evacuated solutions of aetioporphyrin, mesoporphyrin, and protoporphyrin and their magnesium complexes, zinc-aetioporphyrin, haematoporphyrin and its mercury complex, and tetraphenylporphyrin(TPP) and its zinc complex, frozen at 77°K, were investigated[42-46]. In fields of about 1600 G (klystron frequency ν = 9260 MHz), ESR absorption corresponding to the $\Delta m = \pm 2$ transition was observed. The ESR signal consisted of a single slightly asymmetric line with a half-width ΔH = 10–12 G between the points of maximum slope. The intensity of the ESR signal did not vary with time on illumination with visible light ($\lambda \geq 400$ nm).

Among the porphyrins investigated Mg-aetioporphyrin proved to have the highest concentration of paramagnetic centres (about 10^{16} spins in a 0.03 cm^3 specimen at a porphyrin concentration of 2×10^{-3} M). For other porphyrins, the number of paramagnetic centres in the specimen at a concentration of 10^{-3} M was 5×10^{14}–7×10^{15} spins, in agreement with the shorter lifetime $\tau_{phosph} = 5 \times 10^{-2}$–$10^{-2}$ s compared with τ_{phosph} of Mg-aetioporphyrin (2×10^{-1} s).[41] The ESR absorption of the triplet states of the copper complexes of aetioporphyrin and haematoporphyrin could not be observed although it is known that the intensity of the phosphorescence of such copper complexes greatly exceeds that of the magnesium complexes and the bases. Since τ_{phosph} for the copper complexes is 10^{-4}–5×10^{-5} s, the steady-state concentration of the excited triplet molecules is lower by 2–3 powers of ten than that of the bases and magnesium complexes. Within the limits of the concentration range investigated (5×10^{-5}–10^{-3} M), the amplitude of the ESR signal is directly proportional to the concentration of the pigment[42]. The concentration-induced quenching for various porphyrins begins when a concentration of 10^{-3} M is reached. The ESR signal amplitude then falls[42,46].

For reactions proceeding via an excited triplet state, it is important to know the characteristics of molecules in the triplet state such as τ and the steady-state concentration n_{st}. Indeed, in the porphyrin series magnesium complexes are the most active, compared with the bases and zinc complexes, while the copper complexes are the least active[32,42]. This applies in particular to two-quantum reactions, since in the case of high values of τ there is a considerable population of the triplet level and hence a high probability that a second energy quantum will be absorbed.

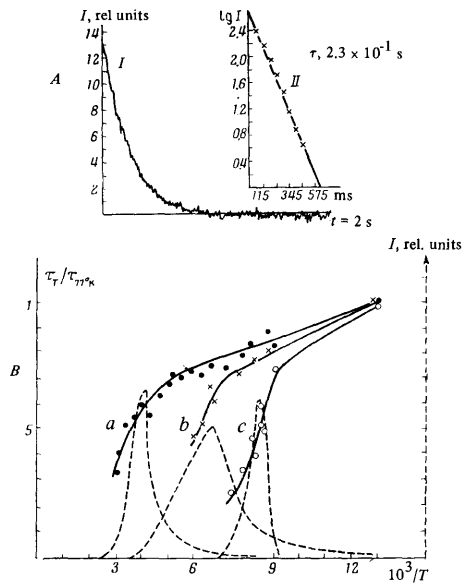

Figure 3. *A*) Kinetics of the decay of the ESR signal of the triplet state ($\Delta m = \pm 2$) of Mg-aetioporphyrin in ethanol at 77°K (I) and the same plot on a logarithmic scale (II); *B*) variation of $\tau_T/\tau_{77°K}$ with $1/T$ for Mg-aetioporphyrin in poly(methyl methacrylate) (a), in highly viscous methyl methacrylate (the initial stage of polymerisation) (*b*), and in ethanol (*c*). Lower curves —variation of the yield of radicals with temperature.

The authors of the review developed a method for the measurement of τ by ESR using a spectrum accumulator and a mechanical shutter[47]. The variation of τ and n_{st} with the concentration of the pigment and oxygen, the properties of the matrix, and temperature was investigated[47-49]. τ was determined from the time required for the amplitude of the $\Delta m = \pm 2$ ESR signal to diminish by a factor e after switching off the illumination. Fig. 3*A* presents a typical decay curve for the ESR signal of Mg-aetioporphyrin at 77°K. For all the porphyrins investigated, the decay curves are exponential. The values for τ for the triplet state are listed in Table 1. We may note that the variation of the pigment concentration in the range 5×10^{-5}–10^{-3} M, the nature of the solvent [ethanol, cyclohexanol, and poly(methyl methacrylate) (PMT)], and the presence of oxygen in the specimen at 77°K do not affect the value of τ for the triplet state.

With increase of temperature the lifetime diminishes. Table 2 presents the values of τ for Mg-aetioporphyrin dissolved in ethanol and PMT at different temperatures.

Table 1. Zero-field splitting constants and the values of τ for the triplet state of porphyrins at 77°K and 320°K.

Compounds	D/hc, cm^{-1} $\Delta m=\pm1$ 77° K	D^*/hc, cm^{-1} $\Delta m=\pm2$ 77° K	D^*/hc, cm^{-1} $\Delta m=\pm2$ 320° K	$10^{-2}\tau$, s 77° K	Solvent
Metal complexes					
Mg-aetioporphyrin	0.036	0.036	0.033	23.5	Ethanol, PMT
Zn-aetioporphyrin	0.036	0.038	—	—	Ethanol, ethanol + pyridine
Mg-protoporphyrin	—	0.036	—	—	Isobutyl alcohol
Zn-protoporphyrin	—	0.036	—	—	Ethanol + isobutyl alcohol
	—	0.038	—	—	Ethanol + pyridine
Mg-mesoporphyrin	0.036	—	—	—	Ethanol
Zn-tetraphenylporphin	—	0.031	0.025	6.2	Ethanol, PMT
Mg-phthalocyanine		0.027	—	—	Ethanol + pyridine
Dications					
$2H^+$-aetioporphyrin	0.033*	0.036	—	—	Ethanol + HCl
$2H^+$-mesoporphyrin	0.033	0.036	—	3.0	Ethanol + HCl
$2H^+$-haematoporphyrin	0.033	0.033	—	—	Ethanol + HCl
Bases					
Aetioporphyrin	0.048	0.047	0.042	3.2	Ethanol + pyridine, PMT
Mesoporphyrin	0.048	0.047	0.041	2.5	Ethanol + pyridine, PMT
Protoporphyrin	—	0.046	—	—	Ethanol + pyridine
Haematoporphyrin	—	0.047	—	—	Ethanol

*For freshly prepared specimens, $D^*/hc = 0.033$ cm^{-1}; for specimens stored for a long time in solutions with HCl, $D/hc = 0.036$ cm^{-1}.

Table 2. Variation of τ for Mg-aetioporphyrin in the temperature range 77–335°K.

Ethanol						
Temperature, °K	77	108	120	127	131	135
10τ, s	3.35 ±0.03	1.75 ±0.06	0.95 ±0.1	0.8 ±0.1	0.6 ±0.1	0.55 ±0.1
Poly(methyl methacrylate)						
Temperature, °K	77	120	180	250	320	333
10τ, s	2.35 ±0.03	1.85 ±0.06	1.55 ±0.06	1.4 ±0.06	1.0 ±0.1	0.75 ±0.1

The steady-state concentration of the triplet molecules varies with τ. The parallel variation of these quantities with temperature is evidence that the factors responsible for the temperature-induced quenching are the same. A deviation from the parallel variation is observed in ethanol solutions. In all cases the $\tau_T°K/\tau_{77°K} = f(1/T)$ curves are complex and have two sections. The variation along the slow section is close to exponential[47,48], which corresponds to purely temperature-induced quenching[51] (Fig. 3B). In addition, the effectiveness of the quenching depends on the viscosity of the medium and proves to be highest in ethanol and lowest in PMT. The presence of oxygen also sharply increases the effectiveness of the quenching in ethanol and cyclohexanol, but does not affect the quenching in a polymeric matrix when there is no diffusion of oxygen. The sharp inflection in curves describing the variation of τ (and also n_{st}) (Fig. 3B) is noteworthy. The temperature at which the inflection occurs is associated with the onset of formation of free porphyrin radicals. It has been

shown[48-50] that the formation of free radicals has a two-quantum mechanism. Together with pigment radicals, the polymeric matrix stabilises the radicals of methyl methacrylate. It is noteworthy that temperature-induced quenching of the triplet molecules of the photochemically less active Zn-tetraphenylphorphin is less effective, owing to the formation of free radicals, than for Mg-aetioporphyrin. Thus the temperature-induced quenching of τ and n_{st} is analogous to the temperature-induced quenching of the phosphorescence of aromatic compounds[51] and is determined, apart from the effect purely due to temperature and associated with the redistribution of the vibrational energy of the molecule, by the structural properties of the medium, the oxygen effect, and quenching due to photochemical reactions.

The ESR spectra of $\Delta m = \pm 1$ transitions. The ESR spectra in high magnetic fields (2900–3800 G) due to $\Delta m = \pm 1$ transitions were first observed for Mg-aetioporphyrin[8,43] (as already mentioned, this substance gives rise to the highest ESR signal in low fields). Later the same investigators[33] and also Lhoste et al.[52] (for haematoporphyrin) recorded $\Delta m = \pm 1$ transitions for bases, dications, and other metal complexes of porphyrins dissolved in ethanol, pyridine, cyclohexanol, and their mixtures and also in PMT. The ESR spectra at room temperature have been recorded exclusively in PMT. The cationic forms of porphyrins have been investigated in acid ethanol solutions. The method of signal accumulation has been used to record the spectra of molecules with low values of n_{st}, particularly at room temperature[47,48].

Fig. 4 presents high-field ESR spectra of porphyrins in an excited triplet state. For the metal complexes of porphyrins with D_{4h} symmetry (Mg-aetioporphyrin, Zn-aetioporphyrin, and Zn-tetraphenylporphin), the ESR spectrum has the expected line form, i.e. four canonical peaks: H_{X, y_2} and H_{X, y_3} for the x and y molecular axes directed along the constant magnetic field and H_{Z_2} and H_{Z_3} for $z \parallel H_{const}$. The intensity ratio corresponds to the expected inequality $I_{H_{X,y}} > I_{H_Z}$. Indeed, in the absence of an external magnetic field the triplet level splits into two sublevels separated by a distance D. Since the molecular symmetry is D_{4h}, one of the sublevels remains doubly degenerate (the molecular x and y axes in the plane of the molecule are physically equivalent. We may note that, at room temperature in PMT, the $H_{X, y}$ lines are considerably narrowed (Fig. 4*b*, curve *2*). Two tetrapyrrole pigments—Zn-aetioporphyrin and chlorophyll (discussed in greater detail below)—exhibit two-quantum transitions in the region of $\Delta m = \pm 1$ (Fig. 4*c*).

For porphyrin bases with D_{2h} symmetry (according to spectroscopic data[53]), one should expect the appearance of a six-line spectrum with H_X, H_Y, and H_Z canonical peaks. However, the experimental ESR spectrum consists of four lines, which corresponds to cylindrical symmetry of the molecule in the triplet state. In the light of the latest theoretical concepts and X-ray diffraction data[54], the porphyrin bases may be represented by a superposition of structures *A*, *B*, and *C* (Fig. 4*f*) with statistical weights of 19, 32, and 49% respectively. Structures *B* and *C* with D_{4h} symmetry then represent the porphyrin bases to the extent of 80%. This finding is satisfactorily consistent with ESR data.

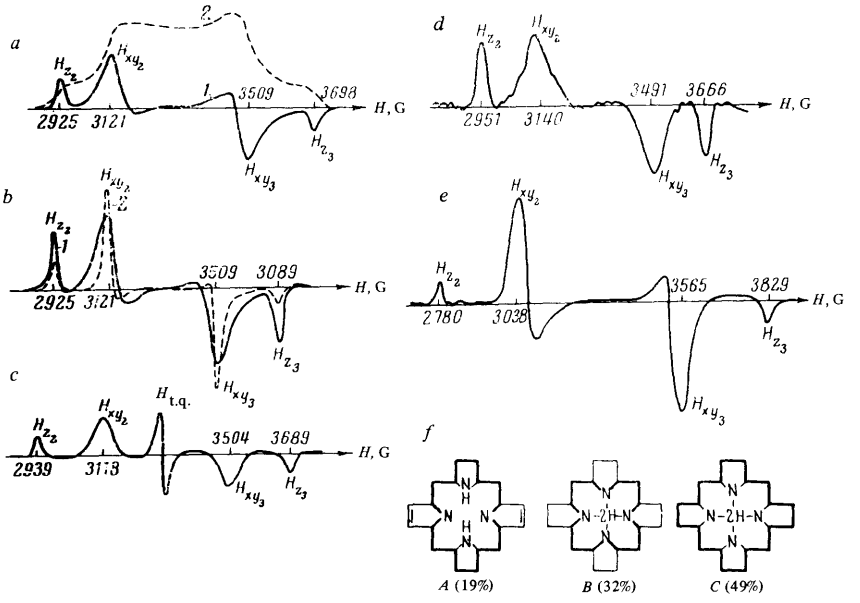

Figure 4. ESR spectra ($\Delta m = \pm 1$) of aetioporphyrins in an excited triplet state: *a*) Mg-aetioporphyrin in ethanol at 77°K [1) first derivative of the ESR spectrum; 2) the spectrum in the integral form]; *b*) Mg-aetioporphyrin in poly(methyl methacrylate) [1) at 77°K; 2) at 330°K]; *c*) Zn-aetioporphyrin in ethanol at 77°K; *d*) $2H^+$-aetioporphyrin in ethanol solution of hydrochloric acid at 77°K; *e*) aetioporphyrin in a pyridine—ethanol mixture at 77°K; *f*) π-electron structure of porphyrins.

The ESR spectra of the $\Delta m = \pm 1$ and $\Delta m = \pm 2$ transitions were also recorded at higher temperatures (up to 350°K)[33, 45, 55]. It must be emphasised that, with increase of temperature, the spectrum as a whole is displaced towards higher fields (the constant D^*/hc diminishes), the number of peaks does not change, but the lines themselves become markedly narrower and their intensity ratios change (Fig. 4*b*, curve *2*).

The zero-field splitting constants calculated from the ESR spectra are summarised in Table 1. The average values of D^*/hc calculated from the $\Delta m = \pm 1$ spectrum agree satisfactorily with the D^*/hc values calculated from the $\Delta m = \pm 2$ spectra. Analysis of the data in Table 1 leads to the following findings: (1) lateral substituents of the porphyrin ring such as CH_3, CHO, C_2H_5, and CH_2COOH do not affect the constant within the limits of experimental error, i.e. they do not affect significantly the dimensions and symmetry of the π-electron cloud of the molecule; (2) all metal complexes with aliphatic substituents also have the same zero-field splitting constants. On the other hand, phenyl substituents in Zn-tetraphenylporphin and Mg-phthalocyanine increase the size of the π-electron system and diminish the D/hc constant; (3) the values of D/hc for the metal complexes are somewhat higher than those for the dications; this finding is probably associated with some contraction of the π-electron cloud by the metal atom towards the centre of the molecule; (4) on passing to porphyrin bases, the constants increase significantly. This anomalous effect may be attributed either to the orbital splitting of the lowest triplet level or to the fact that in the porphyrin molecule in an excited triplet state the electrons spend most time in the 18-membered small ring of the molecule (Fig. 4*f*). This leads to a marked decrease of D/hc, since this structure predominates over all others under conditions of dynamic equilibrium.

Table 3. Characteristics of the ESR spectra of the triplet state of porphyrins at 77° and 320°K (ν = 9260 MHz).

Porphyrin	H_{min}, G 77°K	H_{min}, G 320°K	ΔH 77° K	ΔH 320° K	D/hc, cm^{-1} 77°K	D/hc, cm^{-1} 320°K	Symmetry
Aetio-	1626	1631	11.5	11.0	0.047	0.042	D_{2h}
Mg-aetio-	1637	1639	9.5	10.5	0.036	0.033	D_{4h}
Meso-	1627	1632	11.5	10.0	0.046	0.041	D_{2h}
Proto-	1626	1629	11.0	11.0	0.047	0.044	D_{2h}
Zn-TPP	1640	1644	11.0	12.5	0.031	0.025	D_{2h}

The values of D^*/hc are almost insensitive to the solvent (ethanol, cyclohexanol, PMT, isopentane, and pyridine). However, pyridine, which is known to exhibit complex-forming properties, causes an appreciable broadening of the ESR line. The introduction of magnesium into the centre of the porphyrin molecule narrows the ESR line compared with the spectra of the bases and dications. When the temperature is raised from 77° to 320°K, the values of D^*/hc decrease by 7–19% for various porphyrins (Table 3), which is probably associated with an increase of the size of π-electron cloud owing to the population of high vibrational sublevels of the triplet state or to dynamic effects leading to the predominance of more symmetrical porphyrin structures [40].

As already mentioned in the introduction to the review, the main contribution to the canonical peaks of the ESR spectra of the $\Delta m = \pm 1$ transitions in a system of molecules oriented at random comes from molecules for which the principal axes of the spin–spin interaction tensor are oriented in the direction of the external magnetic field H_{const} or nearly so (±5°);[27, 28] other orientations give rise to an almost constant absorption background. Thus there is a selection of molecules with respect to canonical orientation—magnetoselection. When such a system is excited by polarised light (magnetophotoselection), only the canonical peaks for which the direction of the $S_0 \rightarrow S_1$ transition moment and the electric vector of the incident light waves (E and H_{const}) coincide appear in the spectrum [56, 57]. The authors of the review [58] investigated the variation of the line form of the ESR spectra ($\Delta m = \pm 1$ transitions) as a function of the polarisation of the exciting light relative to the direction of the external magnetic field. Fig. 5A presents the ESR spectra of Mg-aetioporphyrin and Zn-aetioporphyrin in the triplet state excited

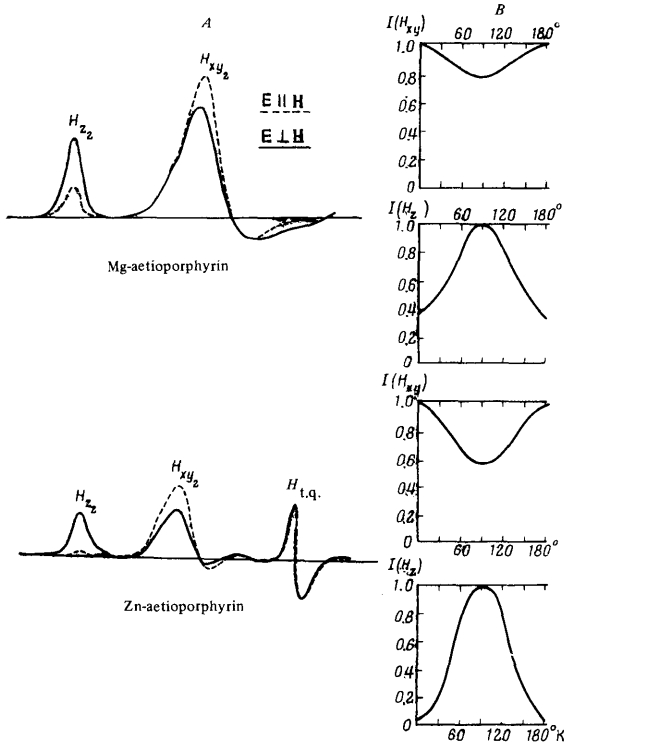

Figure 5. *A*) ESR spectra of Mg- and Zn-aetioporphyrins for different polarisations of the exciting light; *B*) variation of the height of the canonical peaks as a function of the angle between H_{const} and E.

by polarised light. On the right-hand side of the same figure, the amplitudes of the canonical peaks H_Z and H_{XY} are plotted against the angle between the directions of the polarised light vector E and of H_{const}. Evidently the limiting heights of different canonical peaks occur for parallel and perpendicular orientations. For the parallel orientation ($E \parallel H_{const.}$), the H_{XY} peak is a maximum and

the H_Z peak a minimum; for the perpendicular orientation, the situation is reversed. For intermediate orientations of E and H_{const}, the amplitude of the H_Z peak varies as $\sin^2 \alpha$ and that of the H_{xy} peak, as $1 + \cos^2 \alpha$. The amplitude of the $H_{t.q.}$ peak is independent of polarisation.

This behaviour of the canonical peaks can be readily explained if it is assumed that an oscillator oriented in the plane of the molecule is responsible for the triplet excited state. This conclusion is also consistent with optical data[53,59]. The line shape for porphyrin dications varies similarly on excitation with polarised light (Table 4).

Table 4. Effect of polarised light on the intensity of the canonical peaks in $\Delta m = \pm 1$ transitions.

Porphyrin	$\frac{I(H_z)_\parallel}{I(H_z)_\perp}$	$\frac{I(H_{xy})_\parallel}{I(H_{xy})_\perp}$
Mg-aetio-	0.23±0.05	1.44±0.1
Zn-aetio-	0.15±0.05	1.7±0.1
$2H^+$-aetio-	0.42±0.05	1.2±0.1
$2H^+$-meso-	0.7±0.1	1.5±0.2

Table 4 lists the ratios of the amplitudes of peaks 1 (H_1), for the parallel orientation of E and H_{const}, to the amplitude corresponding to the perpendicular orientation. Theoretically these ratios are given by the following formulae:

$$\frac{I(H_z)_\parallel}{I(H_z)_\perp} = 0; \quad \frac{I(H_{xy})_\parallel}{I(H_{xy})_\perp} = 2^{57}.$$

However, Table 4 shows that they do not hold exactly for porphyrins, or incidentally, for the other compounds investigated[56]. This deviation from theoretical values is associated with depolarisation effects of different types, which have been discussed in detail by Kottis and Lefevre[57].

2. Photosynthesising Pigments

The ESR signal of the triplet state of chlorophyll b was observed for the first time in a frozen ethanol solution[60]. The same investigators[61] succeeded in observing the ESR absorption of the excited triplet state using a spectrum accumulator with alcoholic and pyridine chlorophyll a, chlorophyll a + b, and phaeophytin a + b solutions at pigment concentrations of about 10^{-3} M. Transitions were observed in the range 1636–1640 G (ν = 9260 MHz) between the lowest and highest triplet sublevels ($\Delta m = \pm 2$). The amplitude of the ESR signal of the chlorophyll b triplet state is proportional to its concentration, but, starting with a 10^{-3} M pigment concentration, the amplitude falls owing to concentration-induced quenching[46,60]. When films of chlorophyll a + b, in which the pigment is in a highly aggregated state, were investigated, no ESR absorption was observed, which is also due to concentration-induced quenching[61]. The intensity of the ESR signal of the triplet state of chlorophyll *b* is two and a half times greater than that of the signal of chlorophyll **a**. This might have been expected, since τ_{phosph} for chlorophyll b is almost three times higher than for chlorophyll a.[59]

The ESR spectra of $\Delta m = \pm 2$ transitions consist of singlet slightly asymmetrical lines (Fig. 6*A*). At the temperature of liquid nitrogen, oxygen does not influence the signal intensity. Table 5 lists the ESR parameters of the triplet state of the pigments investigated.

Using a spectrum accumulator, Lhoste[34] observed the ESR signal of the triplet state of chlorophyll b in high fields ($\Delta m = \pm 1$ transitions). The ESR signal consists of seven peaks (Fig. 6*D*): H_{x_2}, H_{x_3}, H_{y_2}, H_{y_3}, H_{z_2}, H_{z_3}, and the $H_{t.q.}$ peak corresponding to the two-quantum transition. This spectrum corresponds to C_{2v} molecular symmetry. The zero-field splitting constants were estimated from the spectra: $D/hc = 0.0306 \pm 0.0010$ cm^{-1} and $E/hc = 0.0034 \pm 0.0006$ cm^{-1}. The additional peaks (IV and V) were not assigned by the authors (Fig. 6*D*), but they may be due to the presence of an admixture of chlorophyll a or phaeophytin.

Table 5. Characteristics of the ESR spectra of chlorophyll a and b in the triplet state (ν = 9260 MHz).

Pigment	H_{min}, G	ΔH, G	D^*/hc, cm^{-1}	Solvent
Chlorophyll a	1640	13	0.032	Ethanol
Chlorophyll b	1636	13	0.037	Ethanol
	1638	13	0.035	Pyridine

From the standpoint of the understanding of the role of the excited triplet state of chlorophyll in photosynthesis *in vivo*, its direct investigation in photosynthesising systems (chloroplasts, chromatophores, and leaves turning green) is of greatest interest. An attempt has been made[61] to observe the ESR signal due to photosynthesising pigments in chloroplast and "greening" leaf preparations. A study was made of pea chloroplasts. In native preparations, ESR absorption due to the triplet state was not observed. The light-induced ESR signals due to the triplet state of chlorophyll were observed in chloroplast preparations containing between 10 and 50 vol.% of pyridine (Fig. 6*C*). Pyridine is known to have a deaggregating effect on the pigment system of chloroplasts and in the given case there was a possibility of the extraction of chlorophyll into pyridine. As pointed out earlier, in studies on pigment films ESR signals of the triplet state were not observed either. Therefore one may suppose that at high pigment concentrations there is an effective transfer of excitation energy via triplet levels resulting in a sharp decrease of τ and hence also n_{st} for chlorophyll. In this connection one might have expected the appearance of an ESR signal in leaves during the process of acquisition of the green colour, which involves the formation of the monomeric components of the pigment system. A study has been made[61] of the ESR absorption of etiolated corn leaves subjected to illumination for different periods (between 1 and 30 h). However, the ESR signals due to the triplet state were not observed in these systems either. The extraction of the pigments from the leaves to a pyridine solution makes it possible to record the ESR absorption. Probably, during the first stages of the generation of the green colour in the leaves, the deactivation processes of the triplet molecules are already fairly effective. Such deactivation may be a consequence of an effective transfer and employment of the energy of the triplet excitation in the reaction centre, so that in native chloroplasts measurable steady-state concentrations of chlorophyll molecules in an excited triplet state are not observed.

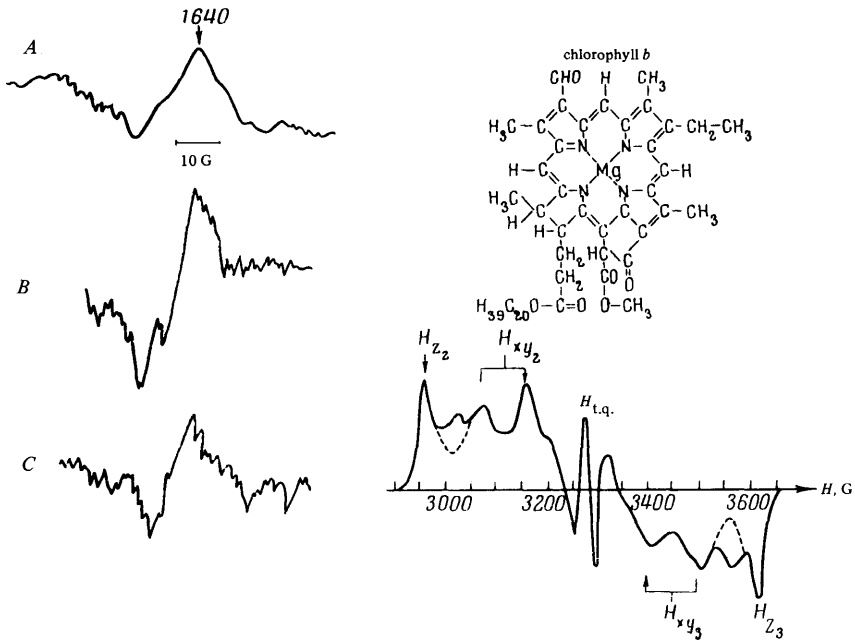

Figure 6. The structure and ESR signal of the excited triplet state of chlorophyll a (*A*), phaeophytin a + b (*B*) in ethanol and in chloroplasts treated with pyridine (*C*) ($\Delta m = \pm 2$ transitions, $\nu = 9260$ MHz), and of chlorophyll b (*D*) in ethanol ($\Delta m = \pm 1$ transition, $\nu =$ 9210 MHz). The spectrum *B* is probably the sum of two signals, due to phaeophytin a and phaeophytin b, as shown by the reproducible splitting of the line.

3. Aromatic Aminoacids, Di- and Poly-peptides, and Proteins

The observation of the excited triplet state of aromatic aminoacids by the ESR method has been reported by a number of workers, starting in 1963.[9,11,13,32,38,62-68] Ethanol and aqueous ethanol solutions of aromatic aminoacids (tyrosine, tryptophan, and phenylalanine) were excited by ultraviolet light at 77°K. $\Delta m = \pm 2$ transitions were recorded. The ESR signals consist of single asymmetric ESR lines (Fig. 7*A* and 7*B*) with the parameters listed in Table 6. After the illumination has been switched off, the ESR signal of tryptophan in ethanol decayed with the period $\tau = 2.4$ s (decrease of the initial ESR signal amplitude by a factor e), which is consistent with optical data[69]. When acetic acid was added to an ethanol solution of tryptophan, the signal intensity fell approximately by a factor of ten[32,42]. Ptak and Douzou[65] observed the ESR signals of the excited triplet state of aromatic aminoacids in methanol solutions and obtained results analogous to those of Gribova and coworkers[32,42], in particular they showed that the decay of the ESR signal is strictly parallel to the decay of phosphorescence (Fig. 7*B*). The times required for the decrease of the ESR signal by a factor of 2 ($\tau_{1/2}$) in a phosphate buffer are respectively 6.7 s for tryptophan, 6 s for phenylalanine, and 3 s for tyrosine. It is noteworthy that the ESR and luminescence characteristics of the triplet state of aromatic aminoacids depend on the nature of the matrix, the temperature, and the pH of the solution. In particular Shiga and Piette[66] noted that the nature of the solvent (water–methanol, phosphate buffer) does not influence the ESR signal line form, but significantly alters the signal decay time.

Among the three aromatic aminoacids, the highest ESR signal ($\Delta m = \pm 2$) was recorded for tryptophan and the lowest for phenylalanine in solutions at the same concentration. Shiga and Piette[66] noted that the yield of tyrosine molecules in an excited triplet state is one third of that for tryptophan. Zuclich[38] found that the intensity ratios of the ESR signals ($\Delta m = \pm 2$) for tryptophan, the tyrosinate ion, tyrosine, and phenylalanine are respectively 8 : 2 : 1 : 1. The characteristics of the ESR spectra determined from the $\Delta m = \pm 2$ transitions are listed in Table 6.

Hélène et al.[70] investigated the dependence of the parameters of the ESR spectra on the aggregation of aminoacids in solution. As for the variation of phosphorescence intensity, the authors observed an increase in the ESR signal on deaggregation when deaggregating additives (ethanol and sodium chloride) were added to the aqueous solutions of the aminoacids before freezing. They explained this effect by a change in the probability of an intersystem crossing and in the probability of energy transfer in the microcrystals.

Malig et al.[67] made a detailed study of the effect of the pH of the medium on the properties of the ESR signal of L-tyrosine in the crystalline state. They observed two ESR signals and the corresponding absorption bands of the

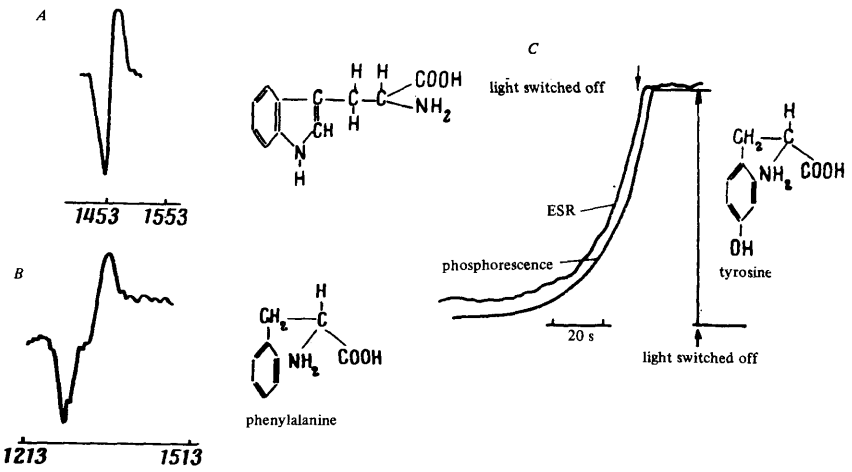

Figure 7. ESR spectrum of the triplet state of tryptophan (*A*) and phenylalanine (*B*) at 77°K in ethanol solutions ($\Delta m = \pm 2$ transitions). Curves *C* represented the decay of the ESR signal and phosphorescence of L-tyrosine under the same conditions.

two forms of tyrosine: unionised and ionised. The parameters of the spectra are presented in Table 6. The signal intensity depends on the pH of the medium. At pH 6.9 the ionic form is absent and a peak at 280 nm, due to the non-ionic form, is observed in the absorption spectrum together with the corresponding ESR signal at 1287 G ($\nu = 9138$ MHz). At pH 10 only the ESR signal at 1390 G and the corresponding absorption maximum of the ionic form at 295 nm (Fig. 8) persist. On raising the temperature from 77° to 295°K, the equilibrium is displaced towards the formation of the unionised form; $\tau_{1/2}$ for the decay of the ESR signal is about 2 s for the ionic form and about 3 s for the non-ionic form.

Table 6. Parameters of the ESR spectra of aromatic aminoacids in the triplet state ($\Delta m = \pm 2$ transitions; 77°K).

Compound	D^*/hc, cm^{-1}	ΔH, G	$\tau_{1/2}$, s	Solvent
Tryptophan	0.126	15	2.4	Ethanol (Ref.32)
	0.119	22	4.1	Methanol + 6 *N* HCl phosphate buffer (Ref.66)
Tyrosine	0.112	32	1.9	Ditto
Non-ionised L-tyrosine	0.161	32	3	H_2O + propylene glycol
Ionised L-tyrosine	0.141	47	2	H_2O + propylene glycol + HCl
Phenylalanine	0.161	63	6.4	Methanol + HCl phosphate buffer

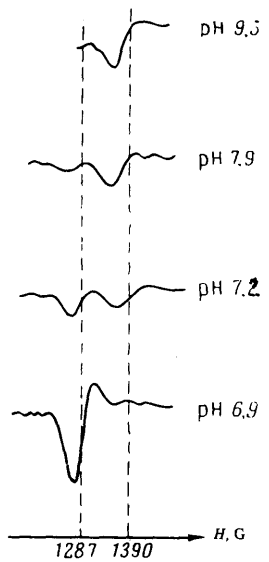

Figure 8. ESR spectrum of L-tyrosine in the triplet state as a function of pH (pH established with a tris buffer and HCl at 295°K).

Similar studies were made by Shiga et al.[68] for L-tryptophan, glycyl-L-tryptophan, and poly-L-tryptophan. The decay curves for the ESR signal and phosphorescence are identical. At an L-tryptophan concentration in excess of 2×10^{-4} M, concentration-dependent quenching is observed; we then have $\tau = 4.4$ s regardless of concentration. The intensity of the ESR signal depends non-linearly on the light intensity and saturation is attained at a fairly high intensity.

The ESR signal of the triplet state of poly-L-tryptophan is the same as that of L-tryptophan with $\tau_{1/2} = 4.2$ s, but the number of paramagnetic centres per unit optical density is smaller by a factor of 2. The authors explained the decrease of the yield by concentration-induced quenching.

$\Delta m = \pm 1$ transitions. $\Delta m = \pm 1$ transitions in tyrosine were observed for the first time by Bosch et al.[35] Recently Zuclich[38] reported the observation of the $\Delta m = \pm 1$ ESR spectra for three aminoacids. Tryptophan was

excited in pure ethanol, tyrosine in 0.1 M HCl solution in ethanol, and phenylalanine and tyrosinate in 0.25 M NaOH solution in ethanol. The zero-field splitting energies X_1, X_2, X_3 and the zero-field splitting constants ($D = -3/2$ and $Z = -\frac{3}{2}X_\perp$) are listed in Table 7. Zuclich[38] adopted X_1, X_2, and X_3 (instead of X, Y, and Z) as the symbols for the zero-field splitting energies because in a specimen with a random orientation they cannot be assigned to specific molecular axes. $X_\perp$ is the zero-field splitting energy associated with the direction perpendicular to the plane of the molecule. $X_\perp$ values were determined by studying the line form of the ESR spectrum in polarised light.

Table 7. Parameters of the zero-field splitting of aromatic acids (cm^{-1}).

Compound	$\Delta m=\pm1$						$\Delta m=\pm2$
	X_1/hc	X_2/hc	X_3/hc	D/hc	E/hc	D^*/hc	D^*/hc
Tryptophan	0.0082	0.0656	0.0738	0.0984	0.0410	0.1213	0.1210
Tyrosine	0.0124	0.0867	0.0991	0.1301	0.0558	0.1621	0.1635
Tyrosinate ion	0.0180	0.0720	0.0900	0.1080	0.0540	0.1429	0.1432
Phenylalanine	0.0053	0.0930	0.0983	0.1475	0.0439	0.1659	0.1652

The transfer of triplet excitation energy in mixtures of aminoacids. This made it possible to identify the ESR signal of the triplet state in proteins and to understand the mechanism of the interaction of photoexcited molecules *in vivo*. The transfer of triplet excitation energy in a mixture of tyrosine and tryptophan in 6 M HCl has been investigated[68,96]. During the first seconds of illumination, two ESR signals of tyrosine and tryptophan were recorded ($\Delta m = \pm2$ transitions). The intensity of the signal due to tryptophan increased with time and that due to tyrosine fell compared with the one-component system under continuous illumination. The behaviour of aromatic dipeptides in the presence of tryptophan is similar[68]. According to Tables 6 and 7, the zero-field splitting constants for various aromatic acids differ markedly and therefore the ESR signals can be identified readily and unambiguously. The ESR data for the triplet state of individual aromatic aminoacids and particularly di- and poly-peptides made it possible to identify the triplet state of proteins.

Shiga et al.[66,68] were the first to investigate the excited triplet state of proteins by the ESR method and the energy transfer in proteins was discussed by Lhoste[52] and Zuclich[38]. Bovine serum albumin, egg albumin, β-lactoglobulin, D-aminoacid oxidase (the apo- and holo-enzymes), and native oxy- and deoxy-haemocyanines were investigated. In order to record ESR signals of low intensity, a spectrum accumulator was employed. In all cases[66,68] $\Delta m = \pm2$ transitions were observed. For all the above proteins, ESR absorption gave rise to the same H_{min} and line form as for the ESR signal of L-tryptophan. Thus the triplet signal originates from the tryptophan residues. The behaviour of D-aminoacid oxidase proved to be somewhat different. It is suggested[68] that in this protein, containing flavin-adenine dinucleotide (FAD), the ESR signal is caused not only by the triplet excitation of the aromatic aminoacid but also by a considerable interaction between the aromatic aminoacid in the excited triplet state and FAD. The holoenzyme gives rise to two different signals with $H_{min} = 1450$ and 1560 G, which are respectively due to tryptophan and FAD. Proteins have a significant influence on the triplet state of FAD, but the converse effect is not shown. While the characteristics of the ESR spectra of proteins are similar, the decay time $\tau_{1/2}$ depends on the nature of the protein and on the composition of the solvent. The values of $\tau_{1/2}$ are compiled in Table 8 on the basis of the data of Shiga et al.[68]

Table 8. The $\tau_{1/2}$ values for the triplet state of proteins at 77°K.

Protein	$\tau_{1/2}, s^{-1}$					
	I	II	III	IV	V	VI
Egg albumin	3.3	4.1	4.3	4.4	—	—
Bovine serum albumin	3.7	4.6	4.0	4.7	—	—
β-Lactoglobulin	3.9	4.0	4.7	4.8	—	—
D-aminoacid oxidase						
apoenzyme	2.4	—	—	—	—	—
holoenzyme	2.8	—	—	—	—	—
Native haemocyanin						
oxy-	—	—	—	—	1.7	3.4
deoxy-	—	—	—	—	4.8	4.4
Apohaemocyanin						
deoxy-	—	—	—	—	4.8	3.8

The following notation is employed in the Table: solvent I—buffer (pH 7; 0.1 M); solvent II—1 : 1 glycerol–buffer; solvent III—buffer + 8 M urea; solvent IV—1 : 1 glycerol–buffer + 8 M urea; solvent V—tris buffer (pH 6.8; 0.05 M; containing 0.01 M Ca^{2+}); solvent VI—1 : 1 glycerol–tris buffer.

Table 8 shows that $\tau_{1/2}$ increases in the presence of urea and when glycerol is added. The authors suggest that the nature of the environment of the tryptophan residues in the protein has a significant influence on $\tau_{1/2}$. On denaturation the environment changes and some of the tryptophan residues may pass to the solution. The activity spectra and the intensities of the ESR signals of various proteins are also different. It is believed[68] that these differences are due to the following causes:
(a) different distances between the tryptophan residues and their different orientations in different proteins;
(b) different distribution of tyrosine and phenylalanine residues between the tryptophan residues; (c) different degrees of dissociation of the protons in the peptide chain relative to the tryptophan residues; (d) different environments of the tryptophan residues.

However, Zuclich's latest measurements[38] showed that in human and bovine serum albumin (in an ethylene glycol–phosphate buffer at pH 7) two ESR signals of the triplet state ($\Delta m = \pm2$ transitions) are observed. The signals undergo neither broadening, nor displacement, nor a change in the zero-field splitting constant. The relative intensities of the tryptophan signals in the three proteins investigated (human and bovine serum albumin and ovalbumin) were respectively 1 : 1 : 2. The tyrosine signal was four times more intense in human serum albumin than in bovine albumin and was completely absent from ovalbumin. This is consistent with the finding that the degree of tyrosine → tryptophan energy migration increases with the relative concentration of tryptophan. Since the tyrosine content in the albumins is the same, the author attributes the differences between the intensities to the differences between the contents of tryptophan residues

(one and two tryptophan molecules per molecule of human and bovine serum albumin respectively). In this case at least 75% of the tyrosine molecules in bovine albumin are quenched by the two tryptophan residues. The author [38] calculated the minimum radius R_0 of the region of energy transfer from tyrosine to tryptophan in bovine serum albumin and obtained $R_0 = 20$ Å. The $\Delta m = \pm 1$ ESR spectrum was observed only for ovalbumin [38] and proved to be wholly due to tryptophan residues.

4. Flavins and Their Derivatives

Flavosemiquinones are known as intermediate electron-transfer agents in the respiratory chain of mitochondria and chloroplasts. The study of the triplet state by the ESR method in solid solutions and the determination of the zero-field splitting constants made it possible to describe qualitatively the properties and distribution of electron density in the triplet state of these complex molecules [16,52,71].

Table 9. Characteristics of the ESR spectra of flavins and pteridines in the triplet state at 77°K ($\Delta m = \pm 2$ transitions; $\nu = 9210$ MHz).

Compound	H_{min}, G	D^*/hc, cm^{-1}	Solvent
Isoalloxazine compounds			
Riboflavin	1602	0.062	Ethanol
Lumiflavin	1602	0.062	ditto
Tetra-acetylriboflavin	1603	0.061	»
3-Benzyl-lumiflavin	1602	0.062	»
o-(2)-Methyl-lumiflavin	1596	0.066	»
2-Thiolumiflavin	1596	0.066	»
4-Phenyliminolumiflavin	1599	0.064	Ethanol + dimethylformamide
8-Morpholino-8-norlumiflavin	1585	0.072	Ditto
Neutral FMN	1602	0.062	Propylene glycol + H_2O
Anionic FMN	1602	0.062	Propylene glycol + NaOH
Cationic FMN	1582	0.074	Propylene glycol + HCl
Alloxazine compounds			
Lumichrome	1578	0.077	Ethanol
1,3-Dimethyl-lumichrome	1581	0.075	ditto
1,3-Dimethylalloxazine	1575	0.078	»
Pteridine derivatives			
Lumasine	1564	0.086	»
1,3-Dimethyl-lumasine	1569	0.083	»
8-Methyl-lumasine	1578	0.079	»
6,7-Dimethyl-4-oxopteridine	1535	0.098	Ethanol + dimethylformamide
2-Amino-6,7-dimethyl-4-hydroxypteridine	1559	0.088	ditto
2-Ethylthio-4-hydroxypteridine	1557	0.089	»
2,4-Diamino-6,7-dimethylpteridine	1537	0.097	»
2,4,7-Triamino-6-phenylpteridine	1538	0.097	»

The ESR spectra of the excited triplet state associated with the $\Delta m = \pm 1$ and $\Delta m = \pm 2$ transitions were recorded for substituted, tautomeric, and reduced forms of flavins and pteridines, including flavin mononucleotide (FMN), FAD, and riboflavin. The most complete data about the properties of the ESR spectra of the triplet states of flavins and peridines were obtained by Lhoste et al. [52] Table 9 gives the characteristics of the ESR spectra associated with the $\Delta m = \pm 2$ transitions. A typical ESR spectrum of the triplet state ($\Delta m = \pm 2$) for $H_{const} \perp H_{rj}$ is presented in Fig. 9*A*. The distribution of resonance fields in the region 1500–1700 G ($\nu = 9210$ MHz) is shown below (Fig. 9*B*).

At 77°K, $\Delta m = \pm 1$ transitions were observed in a concentrated ethanol solution or a propylene glycol—water-hydrochloric acid mixture. The spectrum of the FMN cations is presented in Fig. 9*A*. The parameters of the ESR spectra are listed in Table 10. The line shape of the triplet absorption in the region of $\Delta m = \pm 1$ is unusual and corresponds to equal energies of the two sublevels of the triplet level, which are comparable in absolute magnitude but have different signs. For this reason the corresponding ESR lines merge. The narrow $H_{t.q.}$ line in the spectrum corresponds to a two-quantum transition. The $\Delta m = \pm 1$ spectrum of the cation exhibits a low symmetry of the triplet state owing to the effect of the charge.

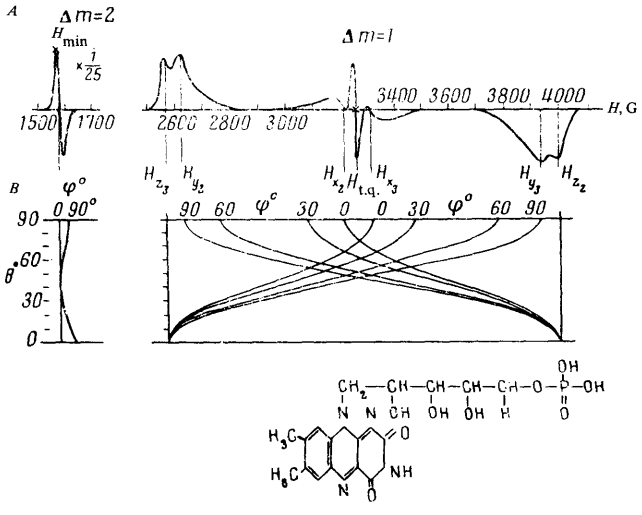

Figure 9. *A*) ESR spectrum of the triplet state ($\Delta m = \pm 2$, ± 1 transitions; $\nu = 9210$ MHz) of the cationic form of flavin mononucleotide in water–propylene glycol–6 *N* HCl solution at 77°K; *B*) distribution of resonance fields.

It is significant that the triplet state of the FMN anions does not differ from that of the neutral form either in the properties of its phosphorescence or in the parameters of its ESR spectrum. The triplet state of the cationic form is significantly different from the two preceding ones. In particular H_{min} is displaced by 20 G towards higher fields and the spin–spin interaction energy is higher (Tables 9 and 10).

Compared with other bicyclic (naphthalene, $D^* = 1.0030$ cm^{-1}) and polycyclic aromatic compounds [28], the zero-field splitting constants of pteridines and flavins are lower, which indicates a greater delocalisation of the excited-triplet electrons in the molecule. Another consequence of the lower values of the constants is that the triplet state is due to a $\pi-\pi^*$ transition and not $n-\pi^*$. For the $\pi-\pi^*$ triplet state, the energy of the molecule associated with the axis perpendicular to the molecular plane is negative. This highest value of the energy determines D/hc (Table 10). Two other values of the energy of the splitting of the triplet level in the absence of a field, associated with the axes in the molecular plane, determine E/hc. E/hc is small for pteridines and flavins.

Analysis of the data in Tables 9 and 10 leads to the following findings: (a) the nature of the substituent in the 10-position of flavins does not influence the zero-field

splitting constants, with the sole exception of tetraacetylriboflavin; (b) alkylation (3-benzyl-lumiflavin) or ionisation in the N_3 position (anionic form of FMN) do not alter the constants but alkylation in the 2-position, corresponding to the flavoquinone form, increases D^*/hc. The introduction of sulphur in the 2-position (2-thiolumiflavin) does not affect D^*/hc, but decreases the lifetime of the triplet state; (c) the alloxazine–isoalloxazine tautomerism decreases D^*/hc. A similar effect obtains with pteridine derivatives, compared with, for example, 1,3-dimethyllumazine and 8-methyl-lumazine; (d) the benzenoid ring plays a definite role in the delocalisation of electrons. D^*/hc for flavins is smaller by approximately 0.2 cm^{-1} than for pteridines. This shows that electrons in the triplet state are delocalised over the benzenoid ring.

Table 10. Characteristics of the ESR spectra of the triplet state of flavins and alloxazine compounds in concentrated solutions at 77°K ($\Delta m = \pm 1$ transitions; $\nu = 9210$ MHz).

Compound	X/hc	Y/hc	Z/hc	D/hc	E/hc	D^*/hc
	cm^{-1}					
3-Benzyl-lumiflavin	±0.0034	±0.0336	±0.0369	±0.0553	∓0.0150	0.0611
Cationic FMN	±0.0034	±0.0404	±0.0440	±0.0660	∓0.0185	0.0733
Tetra-acetylriboflavin	±0.067	±0.0309	±0.0376	±0.0564	∓0.0121	0.0602
Lumichrome	±0.0035	±0.0424	±0.0460	±0.0690	∓0.0194	0.0768
1,3-Dimethyl-lumichrome	±0.0026	±0.0415	±0.0440	±0.0660	∓0.0194	0.0741
1,3-Dimethylalloxazine	±0.075	±0.0406	±0.0481	±0.0721	∓0.0165	0.0776

Substituents in the 6- and 7-positions of the pteridine rings do not influence D^*/hc. The marked effect of various substituents in the 7- and 8-positions of the flavin ring (1,3-dimethyl-lumichrome has a smaller D^*/hc than 1,3-dimethylalloxazine) is evidence of an appreciable spin density in these positions. The introduction of CH_3 or Cl substituents in the 7- and 8-positions affects significantly the photochemical behaviour of flavins. Different substituents in the N_5 position quench the triplet state (5-acetyl-leucoflavin and 5-isopropyl-leucoflavin). A similar effect is observed for the 10-substituted derivatives Leucoflavins phosphoresce but do not give rise to ESR absorption. Reduced FMN does not show an ESR absorption either. According to Lhoste[52], the molecular skeleton of these species is non-planar in the lowest triplet state. This leads to a change in hybridisation of the N_5 orbitals. The triplet state can have a lower symmetry, which increases the spin–orbital coupling, reduces τ, and at the same time increases D^*/hc, making it impossible to observe the triplet absorption in the 3-cm range.

Thus the spin density of the triplet state of flavins is mainly localised in the quinoxaline part of the molecule. Characteristic features of these substances are a low spin density at the N_3 atom, a high density at N_5, N_1, and N_{10}, and the non-equivalence of the methyl groups in the 7- and 8-positions. These data are important in a consideration of the photochemical properties and biological functions of flavins.

5. Nucleic Acids, Purine and Pyrimidine Bases, and Nucleotides

Nucleic acids are high-molecular-weight compounds consisting of purine and pyrimidine bases, carbohydrate residues, and phosphate groups. Purine and pyrimidine bases enter into the composition of not only nucleic acids but also of a number of low-molecular-weight compounds which play an important role in vital processes, ranging from respiration to muscular contraction. Adenine play a special role in biology. In particular, adenine is a component of adenosine triphosphate (ATP), a kind of energy accumulator in a living system.

The ESR of the triplet state of nucleic acids and their constituent purine and pyrimidine bases, nucleotides, and nucleosides was investigated by Rahn, Shulman, Eisinger, and coworkers [35,36,72–77] and also by Hélène and coworkers [15; 78,79]. At a neutral pH in an ethylene glycol–water solution, adenine, adenosine, guanine, guanosine, and their monophosphates give rise to powerful ESR signals ($\Delta m = \pm 2$ transitions)[72]. Under these conditions, cytosine monophosphate gives rise to only a weak phosphorescence, while thymine monophosphate does not yield either phosphorescence or an ESR signal. The zero-field splitting constants and the values of τ are listed in Table 11.

Table 11. ESR characteristics of the triplet state of certain nucleic acid derivatives.

Compound	D/hc, cm^{-1} $\Delta m=\pm 1$	E/hc, cm^{-1} $\Delta m=\pm 1$	D^*/hc, cm^{-1} $\Delta m=\pm 2$	$\tau_{1/2}$, s
Adenine			0.126	2.6
Adenosine			0.126	2.6
Adenosine monophosphate, pH 7	0.121	0.027	0.126	2.5
Guanine			0.145	1.26
Guanosine			0.145	1.26
Guanine monophosphate	0.141	0.0127	0.145	1.25
pH 7				
pH 1			0.126	0.37
Thyminate ion, pH 12			0.198	0.50
Thymine monophosphate			0.198	0.45
Uridinate ion, pH 11			0.163	0.40
Orotic acid				
pH 7	0.176	0.016	0.184	0.30
pH 12			0.175	
Poly-dAT, pH 7			0.201	0.032
DNA			0.200	0.29

The triplet state ESR signal was not observed for native DNA at pH 7, although small signals due to the triplet state of guanine and adenine were recorded for denatured and degraded DNA [37,76]. At pH 12 (under these conditions thymine monophosphate ionises with a loss of a proton from the N_3 atom) the ESR signal of ionised thymine monophosphate (T^-) was observed at $H_{min} = 1067$ G for a decay time of 0.45 s, which is close to τ_{phosph} for DNA (0.3 s). The T^- signal is separated from the adenine signal by approximately 300 G and can be readily identified. A signal, analogous to that of thymine, was observed in poly-dAT at $H_{min} = 1046$ G ($\nu = 9104$ MHz) and with $\tau = 0.32$ s (see Table 11).[73]

A dilute mixture of guanine and cytosine monophosphate gives rise to an ESR signal of the triplet state of guanine monophosphate and a mixture of adenine and thymine monophosphates gives a triplet signal due to adenine monophosphate only. However in DNA there are no signals of the triplet state of the purine bases. Their triplet state is either not populated or it is populated and quenched. It is also possible that the energy of the triplet state is effectively transferred to thymine. An ESR signal was observed for native DNA from bovine thymus on ultraviolet irradiation in the same fields ($H_{min} = 1054$ G, $\Delta H = 50$ G, and $\tau = 0.29$ s) [37,72,73] as for the ionised form of thymine and poly-dAT.

$\Delta m = \pm 1$ transitions were observed together with $\Delta m = \pm 2$ transitions in frozen solutions of orotic acid and guanosine and adenosine monophosphates. The calculated constants are listed in Table 11, the analysis of the data of which shows that the zero-field splitting constants for purine and pyrimidine derivatives are significantly different. On the other hand, the constants also differ for the ionic and non-ionic forms of the bases. Rahn and coworkers [75,76] suggested that the DNA triplet is localised at a thymine residue, which is ionised when its labile proton is transferred via the hydrogen bond to adenine. The equality of the ESR absorption fields serves as an argument in favour of this hypothesis. The small difference between the values of τ is more likely to be due to a slight difference in the environment. That the DNA triplet originates from thymine was also confirmed by a detailed study of various synthetic nucleic acids and model polymers [72,73]—in all cases triplet absorption was shown by polymers containing thymine. Such unambiguous identification could not be made on the basis of spectroscopic data, since the phosphorescence of DNA is different from the phosphorescence of both individual nucleotides and their sum in solution.

6. Phenoxazine and Phenothiazine

Phenoxazine and phenothiazine belong to the class of photosynthesising dyes and also find wide application in pharmacology. They are tricyclic aromatic compounds with C_{2v} symmetry. Phenoxazine and phenothiazine readily form mixed single crystals with biphenyl; they have been investigated not only in solutions but also in single crystals.

Table 12. Parameters of the ESR spectra of the triplet state of phenoxazine and phenothiazine.

ESR constants	Phenoxazine		Phenothiazine	
	biphenyl crystal	ethanol glass	biphenyl crystal	ethanol glass
D/hc	± 0.0990	0.1249	± 0.1230	0.1237
E/hc	± 0.0154	0.0119	± 0.0142	0.0135
X/hc	± 0.0482	0.0535	± 0.0270	0.0278
I/hc	± 0.0175	0.0297	± 0.0553	0.0547
Z/hc	$+0.0659$	0.0833	± 0.0820	0.0825
g_{xx}	2.0037	—	2.0042	—
g_{yy}	2.0037	—	2.0045	—
g_{zz}	2.0020	—	2.0014	—

A study of the triplet state of phenoxazine and phenothiazine by the ESR method was made comparatively recently by Lhoste and coworkers [52,80]. The ESR spectra associated with the $\Delta m = \pm 1$ and $\Delta m = \pm 2$ transitions are presented in Fig. 2. As expected, the spectrum for a molecule with C_{2v} symmetry has six canonical peaks and an $H_{t.q.}$ line in the region of $\Delta m = \pm 1$. The line width of the H_X and H_Y canonical peaks is about 25–30 G, while that of the H_Y peak is about 15 G (measured between the points of maximum slope). They study of a single crystal of phenoxazine in biphenyl made it possible to assign the peaks unambiguously to the molecular system of axes, as shown in Fig. 2. In parallel fields, the canonical H_{X_1} and H_{Y_1} peaks observed were displaced from H_{min} (Fig. 2A). Owing to its low intensity, the H_{Z_1} peak was not recorded. The parameters of the ESR spectra are listed in Table 12. The signs of the constants given are arbitrary, but according to McLachlan [81], D/hc for the triplet $\pi-\pi^*$ state is positive.

The surprising difference between the zero-field splitting energies of phenoxazine in the biphenyl and ethanol matrices is noteworthy. It may be due to different polarities of the solvents, their capacity to form hydrogen bonds, and finally to small differences in their geometry in solid solutions. In particular, in a biphenyl crystal these molecules can remain planar, while in ethanol they may become slightly bent. The latter leads to a change in the geometry of the π-electron cloud and the corresponding values of the D^*/hc constants. Phenothiazine has a high tendency towards bending and therefore its zero-field splitting energy changes little on passing from one matrix to another (in a single crystal it is also bent) [52]. The bending of the benzene rings of the molecule is deduced in particular from calculations of the dipole moment and the electronic structure of phenothiazine free radicals [80].

The study of the hyperfine structure of the ESR spectrum of the triplet state of phenoxazine and phenothiazine single crystals made it possible to assign the H_X peak to the long molecular axis. Of the other two peaks, the peak with a lower energy (H_Y in Fig. 2) was assigned to the short molecular axis (y) passing through the O–N atoms and the peak with the highest energy (H_Z) was assigned to the z axis perpendicular to the molecular plane. Additional studies in polarised light showed [80] that in a concentrated solution the lowest triplet state of phenoxazine is populated via S_0-S_1 excitation, the transition moment of which is parallel to the y axis. However, since in solution the molecule can be bent, the magnetic y axis cannot coincide exactly with the direction of the N–O bond. This is also confirmed by studies of the hyperfine structure of the spectra of phenoxazine free radicals [52], since the hypothesis of the sp^3 hybridisation of the nitrogen atom gives a better explanation of the experimental results than the hypothesis of sp^2 hybridisation corresponding to a planar molecule.

7. Coumarin and its Derivatives

Coumarin and related compounds are known in biology as uncoupling agents for mitochondrial oxidative phosphorylation and as anticoagulants (dicoumarol). The triplet state of coumarin and its derivatives was observed for the first time by Graber et al. [82] The spectrum of coumarin in ethanol at 77°K is presented in Fig. 10 ($\Delta m = \pm 1$ transitions). The position of the H_{X_3} peak was calculated since its measurement is hindered by the superposition of the spectrum due to the ethanol radical. The narrow line at 3201 G corresponds to $H_{t.q.}$ The zero-field splitting energies and constants and the values of τ are listed in Table 13. Except for 6-substituted coumarins, the zero-field splitting energies are intermediate between the values for benzene and naphthalene [2]. This and also the high value of τ show that the triplet state of coumarin and its derivatives is of a $\pi-\pi^*$ type. Graber et al. [82] chose for coumarin the same designation of the axes (Fig. 10) as for naphthalene [1,2]. Qualitatively this is justified by the fact that the energy of the zero-field splitting of the triplet level for planar $\pi-\pi^*$ molecules, associated with the z axis, is negative [81]. Two other energies characterise the distribution of spin density in the molecular plane. Table 13 shows that the values of D^*/hc for coumarin and

its monosubstituted derivatives are higher than for polysubstituted derivatives. This is evidence of a greater delocalisation of spin density in the latter. On the other hand, chromanone and chromanol, which contain one unsaturated ring, have still higher values of D^*/hc, which are comparable with that of benzene (0.193 cm^{-1}).

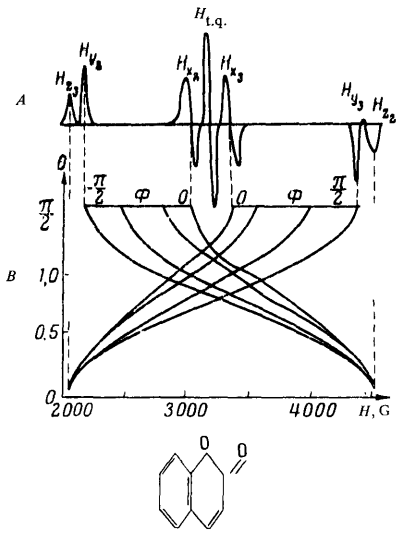

Figure 10. *A*) ESR spectrum of coumarin in the triplet state ($\Delta m = \pm 1$ transition) in ethanol at 77°K (ν = 9239 MHz); *B*) distribution of resonance fields.

Table 13. Parameters of the ESR spectra of the triplet state of coumarin and its derivatives.

Compound	X/hc	Y/hc	Z/hc	D^*/hc	τ, сек.
Coumarin	0.0094	0.0680	−0.0774	0.1244	0.54
4-Hydroxycoumarin	0.0137	0.0680	−0.0817	0.1301	1.5
7-Hydroxycoumarin	0.0147	0.0642	−0.0788	0.1177	1.1
6-Methylcoumarin	0.0026	0.0661	−0.0636	0.1124	0.6
Aesculine (6β-glucosido-7-hydroxycoumarin)	0.076	0.0600	−0.0524	0.0980	1.5
7-Nitro-3,4-benzocoumarin	—	—	—	0.0870	2.3
4-Chromanone	—	—	—	0.1584	1.8
4-Chromanol	—	—	—	0.1354	0.9
Dicoumarol	0.0172	0.0680	−0.0807	—	1.3

The excited triplet state of dicoumarol in low and high fields was observed by Gull et al.[83] in an ethanol–dimethylformamide mixture at 77°K. The $\Delta m = \pm 1$ ESR spectrum consists of six canonical peaks (molecular axes $x \neq y \neq z$). In the $\Delta m = \pm 2$ region a more intense peak with H_{min} = 1468 G (ν = 9239 MHz) was observed. The decay time τ of the ESR signal at H_{min} was 1.3 s after switching off the light (Table 10), which agrees with the phosphorescence decay time. The zero-field splitting energies calculated from the spectra are listed in Table 13.

Thus we have attempted to give as far as possible complete information about the characteristics of various classes of biologically active compounds in a triplet excited state. Summarising, we emphasise yet again that the ESR method yields the greatest amount of information, particularly in studies on large biological molecules, such as those of DNA and proteins, where the triplet states have been identified, and also for compounds which show weak phosphorescence. Next we shall discuss the role of the excited triplet state in the photochemistry of these molecules.

III. THE TRIPLET STATE IN THE PHOTOCHEMISTRY OF BIOLOGICALLY IMPORTANT MOLECULES. TWO-QUANTUM REACTIONS

1. Photochemistry of Porphyrins in Solid Solutions

When ethanol solutions of porphyrins are illuminated at 77°K with light corresponding to the long-wavelength absorption maxima of the pigments, a triplet state ESR signal arises, whose intensity persists during the period of irradiation. The formation of free-radical products is not observed. However, when solutions of porphyrins are irradiated with the unfiltered light of a mercury lamp, the intensity of the ESR signal of the triplet state falls and at the same time free-radical products accumulate[8,9,32]; they have been identified[11] as the radical products of the decomposition of ethanol ($CH_3\dot{C}HOH$, $\dot{C}H_3$, and $\dot{C}HO$) and the porphyrin radical. With increased concentration of the pigment, the yield of radicals rises. The use of calibrated photometric grids showed that the concentration of ethyl[8,32,42] and pigment[48,50] radicals varies with the square of the intensity of the incident light. Therefore it was suggested[32] that the process has a two-quantum mechanism and that free radicals are formed via a triplet state, the second quantum for porphyrins being greater than the exciting quantum.

Simultaneously with the accumulation of free radicals, the absorption spectrum of the pigment undergoes significant changes. In particular, in the spectrum of Mg-aetioporphyrin[8,42,84,85] the intensities of the initial absorption band at 542 and 578 nm and of the Soret band fall (virtually to zero in a dilute solution after prolonged illumination) and a new absorption arises at 450, 605, and 686 nm. When the temperature of an irradiated specimen is gradually raised, the 686 nm absorption vanishes, the 450 nm peak diminishes, and new bands arise between −150° and −125°C with maxima at 660 and 750 nm, the intensity of which also falls to zero on further heating and the spectrum is regenerated. In order to demonstrate that the photochemical reaction proceeds via a triplet state, the authors of the review investigated the effect of intermittent illumination (with light pulses of a duration shorter than that required for the establishment of phosphorescence) on the yield of free radicals in an ethanol solution of Mg-aetioporphyrin, Mg-mesoporphyrin, and Zn-tetraphenylporphyrin[19]. The dark intervals lasted 1–2 s, which, for an exponential phosphorescence decay law, corresponds to virtually complete decay of the glow. It was shown that, under interrupted illumination, the yield of radicals (the areas under the integral curves were compared) is lower by a factor of 15–25 (depending on the duration of the light pulse) then under continuous illumination of the same integral intensity (Fig. 11). This finding is satisfactorily consistent with calculated values[19].

In order to demonstrate directly that the process has a two-quantum mechanism, a method involving the illumination of the solution by two independent light sources was employed[7]. As already stated, the illumination of the solutions with yellow light did not result in the accumulation

of radical products at 77°K. Irradiation of the specimens with ultraviolet light (between 365 and 248 nm) also does not lead to the formation of free radicals in appreciable concentrations[16]. Under simultaneous illuminations by two independent sources, one of which excites the molecules to the triplet state and the light of the other ($\lambda \leq 320$ nm) is absorbed by the pigment molecule in the excited triplet state, free radicals of the porphyrins and the matrix accumulate (Fig. 12A). The yield of radicals increases with the energy of the second quantum. It was also shown that in this case the yield of radicals increases in direct proportion to the intensities of both the exciting (578 nm and the additional) light (302 and 248 nm). Analogous evidence for the two-quantum process mechanism was obtained in a study of the variation of the absorption spectrum of Mg-aetioporphyrin[86]. Initially the authors showed that, when an ethanol solution of Mg-aetioporphyrin is illuminated at 77°K with light having a wavelength of 578 nm, its absorption spectrum does not change. Also the authors did not observe measurable changes in the absorption spectrum of Mg-aetioporphyrin on illumination with ultraviolet light alone (λ_2 = 365, 320, and 313 nm).

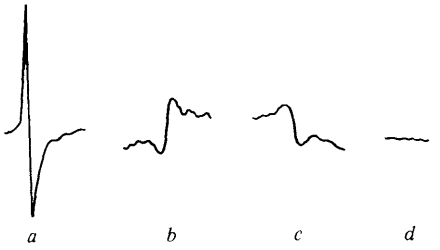

Figure 11. Yield of free radicals in alcoholic solution of Mg-aetioporphyrin as a function of illumination: *a*) with continuous light under steady-state excitation conditions for 30 s; *b*)–*d*) with intermittent illumination for 55 min with periods of exposure to light of 1.8×10^{-2} s, 9×10^{-3} s, and 6×10^{-3} s respectively.

Under simultaneous illumination by the total quanta ($h\nu_1 + h\nu_2$), the initial absorption bands of Mg-aetioporphyrins at 542 and 578 nm become less intense and a new absorption arises at 686 nm (Fig. 12*B*). The latter confirms that both radical products and the new 686 nm absorption arise by a two-quantum mechanism via the triplet state and that the product absorbing at 686 nm is a radical. Similar results were obtained for the dications of haematoporphyrin and protoporphyrin. When the temperature is raised to −165°C and above, yellow light is sufficient for the formation of Mg-aetioporphyrin radicals. The free radicals recorded give rise to only one chromophore line[11,42], the yield of radicals being again proportional to the square of the incident light intensity.

The kinetics of the formation of ethyl and pigment radicals have been investigated[48–50,93]. The logarithmic form of the kinetic curves for the destruction of triplet molecules and the accumulation of ethyl and porphyrin radicals can be fitted fairly satisfactorily by two intersecting lines. The observed photochemical process can be treated kinetically as the sum of two first-order reactions having rate constants k_1 and k_2 respectively, with $k_1 = 10k_2$. It was shown that the formation of one ethoxy-radical corresponds to one porphyrin radical[49,50] at a low light intensity. In order to demonstrate the reductive nature of the reaction, a study was made of the effect of electron-accepting additives (O_2, riboflavin) on the kinetics. It was found that electron-accepting impurities diminish the rate of destruction of molecules in the excited triplet state and the formation of radical products, the constant k_1 showing a much stronger dependence on O_2 and riboflavin than k_2.

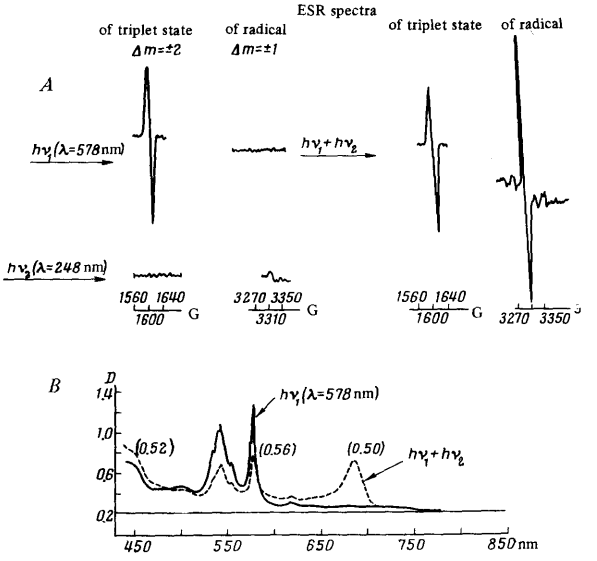

Figure 12. Effect of the two-quantum mechanism. Formation of free radicals in ethanol solution of Mg-aetioporphyrin on illumination by one ($h\nu_1$) and two ($h\nu_1 + h\nu_2$) light sources. *B*) formation of the 686 nm product under the same conditions.

It is noteworthy that, on illumination with visible light at 77°K, an appreciable change in the yield n_{st} of triplet molecules as a function of the oxygen content of the specimen was not observed. However, τ is also independent of the oxygen content of the specimen at 77°K[47]. Consequently the mechanism of the action of oxygen does not include direct quenching of the triplet state of porphyrins at 77°K. The observed inhibition of the formation of ethanol and porphyrin radicals in the presence of oxygen is consistent with the available data concerning the inhibition by oxygen of the photochemical reduction of tetrapyrrole pigments[59]. On the whole, the data permit the conclusion that the mechanism of the photochemical reaction of porphyrins in solid solutions at 77°K involves electron transfer from the alcohol to the porphyrin molecule in the excited triplet state. This results in the formation of a porphyrin radical-anion, which can then combine with a proton, forming a porphyrin radical—the semireduced form. The "686 nm" form of Mg-aetioporphyrin is a porphyrin radical-ion.

Thus the photochemical reduction reactions of porphyrins at 77°K in solid solutions proceed via the triplet state and involve a two-quantum mechanism. Although

the results have been obtained for model systems and low temperatures (the two-quantum reaction in PMT takes place at room temperature[48,49]), processes of this kind must be taken into account in a consideration of the mechanism of real photobiological processes, in particular photosynthesis.

2. Photochemical Properties of the Triplet State of Flavins

When ethanol solutions of flavins (riboflavin, lumichrome, lumazine) and pteridines are irradiated with ultraviolet light ($\lambda > 310$ nm) at 77°K, a complex ESR signal due to free radicals is observed, increasing with the duration of illumination[16]. Analysis of the contour of the signal formed in the ethanol flavin solution showed that it is due to ethyl radicals, $CH_3\dot{C}HOH$, and a species giving rise to a single line with a mixed g-factor. The shape of the single line and its g-factor resemble those of the ESR spectrum of the radical formed in aqueous solution of flavin mononucleotide. The relative intensities of the ESR lines of the ethyl and flavin radicals remain constant regardless of the duration of irradiation and light intensity. The rates of formation of the radicals are the same.

In order to elucidate the reaction mechanism, a study was made of the effect of light intensity on the kinetics of the accumulation of free radicals and the destruction of flavin molecules in an excited triplet state. It was found that the concentration of free radicals at any instant is proportional to the concentration of molecules in the excited triplet state for various light intensities and it was shown that the reaction has a two-quantum mechanism and proceeds via the higher triplet state of flavins and pteridines.

Similar behaviour of riboflavin was investigated by Azizova et al.[87] in the sensitised photochemical decomposition of ethanol and aliphatic aminoacids at 77°K. On illumination with visible light exciting riboflavin to a triplet state, sensitised deamination of aliphatic aminoacids, the spectra of which lie in the range 180–220 nm, was observed. It was demonstrated by the method of intermittent illumination that the reaction proceeds via the triplet state of riboflavin.

3. The Excited Triplet State in the Photochemistry of Nucleic Acids and Their Bases

In 1964 Pershan et al.[88] investigated the mechanism of the formation of thymine free radicals under the influence of ultraviolet light. In particular, it was shown that the concentration of free radicals formed in DNA on ultraviolet irradiation falls when cobalt(II) ions are added. On the other hand, Bersohn and Esenberg[89] showed that the ions of bivalent paramagnetic metals cause marked quenching of the phosphorescence of nucleotides and nucleosides. Later Rahn et al.[75] showed that bivalent metals quench vigorously the triplet state of DNA. In particular, at a fairly high concentration of manganese ions, the ESR signal of the triplet state falls almost to zero. Under these conditions, the DNA fluorescence is not quenched. It was also shown that the number of DNA free radicals formed is comparable to the concentration of the molecules in the excited triplet state. Since the quenching of the DNA triplet state entails a decrease of the yield of thymine radicals in the same proportion, one may assume that the thymine triplet state precedes the formation of free radicals. Thus the formation of thymine free-radical products in DNA proceeds via the excited triplet state.

In a study of quenching of the triplet state of thymine and of uracil in acetonitrile solution, Lamola and Mittel[90] showed that the photodimerisation of thymine takes place wholely via its triplet state. The photodimerisation of uracil proceeds via two mechanisms, one of which also involves the triplet state.

Finally, we shall consider in somewhat greater detail the two-photon reactions of nucleic acid derivatives: purine, adenosine, and guanosine in alkaline aqueous and ethanol solutions at 77°K. These reactions were investigated for the first time by Hélène and coworkers[15,79], who showed that, when the compounds are irradiated with ultraviolet light ($\lambda > 250$ nm) in alcoholic and aqueous solutions, the intensity of the phosphorescence and the ESR signal of the triplet state falls, but the fluorescence intensity remains unchanged. The rate of quenching of phosphorescence is proportional to the square of the incident light intensity. This relation remains unchanged within the concentration range 10^{-4}–10^{-3} M. After unfreezing and subsequently refreezing the specimen, the intensity of its phosphorescence is restored to the extent of 90%. When the phosphorescence is almost completely quenched, the optical absorption spectra remain unchanged. Very large irradiation doses result in the appearance of a new absorption in the range 300–350 nm, which is particularly distinct for purine.

At the same time, when aqueous solutions of purine bases are irradiated with ultraviolet light, a single ESR signal is observed with a g-factor close to 2. On subsequent irradiation with visible light, the signal amplitude falls by 15–20%. In 2% ethanol solution, the ESR spectrum of ethyl radicals is observed together with the singlet spectrum. The rate of formation of the radicals is higher by a factor of 30 than in pure ethanol. Subsequent illumination with visible light leads to a decrease of the singlet ESR signal. The authors showed that the rate of formation of ethyl radicals at any time after the start of illumination is proportional to the instantaneous concentration of the excited triplet molecules and to the square of the incident light intensity.

Thus in aqueous solutions purine bases are ionised with formation of a purine cation and an electron. Under the influence of visible light, the solvated electrons are bleached, liberated from traps, and undergo secondary interactions with cations and neutral purine and solvent molecules. In ethanol solutions two competing reactions develop—photosensitation and light-induced removal of an electron, the first predominating. According to the authors, photosensitation takes place at a high excited triplet level and does not involve the decomposition of the purine, since the absorption and fluorescence spectra remain unchanged. The base is ionised by a two-quantum mechanism. Since the sum of the energies of the triplet level (3.4 eV) (purine, adenosine, guanosine) and of the second quantum ($\lambda = 250$ nm; 5 eV) corresponds to an energy of 8.4 eV, it is sufficient to ionise the molecule in the solid phase (the ionisation potential in the gas phase is known to be about 9 eV).[79] The behaviour of pyrimidine bases and their nucleosides (cytosine, cytidine, thymine) is analogous, but the rate of accumulation of radicals is lower by a factor of 5–6 than for purine bases. Visible light does not affect the ESR signal. In the presence of ethanol, only the radicals of pyrimidine bases are formed and even after prolonged illumination ethyl radicals are

absent. Evidently pyrimidine bases are less sensitive to short-wave radiation and, when account is taken of energy transfer from purine to pyrimidine bases, this fact may help our understanding of the characteristics of the photochemistry of nucleic acids and their metabolism.

4. Two-Quantum Reactions of Aromatic Aminoacids

The first communication about the decomposition of aliphatic compounds photosensitised by aromatic aminoacids appeared in 1963.[32] The mechanism of the photochemical reaction was then investigated in detail by the same workers[11,42,85]. When ethanol solutions of aromatic aminoacids were illuminated at 77°K with the unfiltered light from a mercury lamp, the ESR signal of the excited triplet state fell and rapid accumulation of free-radical products was observed. The rate of accumulation was proportional to the concentration of aminoacids in solution, the square of the incident light intensity, and the intensity of the ESR triplet absorption. Ptak, Douzou, and coworkers[14,15] recorded the formation of free-radical products under analogous conditions.

Analysis of the ESR spectra showed[11,42] that the radicals formed are decomposition products of ethanol (ĊHO, $\dot{C}H_3$, $CH_3\dot{C}HOH$) and an aromatic aminoacid (a single line with a g-factor close to that of the free electron). The characteristics of the latter product (the radical is stable up to −143°C) are analogous to those of the radicals formed on irradiation of aqueous solutions of aromatic acids with ultraviolet light[91]. Since a correlation was observed between the kinetic curves for the destruction of the aminoacid molecules in an excited triplet state and the formation of $CH_3\dot{C}HOH$ and the aminoacid radicals (the slopes of the curves on a logarithmic scale are the same, but after prolonged irradiation the concentration of ethyl radicals increases faster owing to secondary processes), Gribova[32] suggested that the triplet state of the aminoacid is involved in the photochemical reaction (a similar process occurs in methanol and in EPA). This was demonstrated unambiguously by the method of interrupted illumination[8,9]. Santus and coworkers[15,79] observed two-quantum ionisation of aromatic aminoacids in boric acid. The two-quantum ionisation and two-quantum photosensitised decomposition of aliphatic aminoacids in the presence of aromatic aminoacids was demonstrated in a number of studies by Fesenko using the method of flash photolysis[12]. Here it is important to emphasise that, in the presence of aromatic aminoacids or dyes, which are excited by an energy much lower than the ionisation energy of aliphatic aminoacids, the latter are decomposed when the quanta are added together at the triplet level of the sensitiser.

Thus it is evident from the foregoing that the ESR method has been successfully employed in the study of complex biologically important molecules in an excited triplet state. It is also clear that the triplet state is important in chemical reactions and in the accumulation and transfer of energy in model systems *in vitro*. It is difficult to arrive at a direct conclusion concerning the involvement of the excited triplet state in photochemical processes *in vivo* on the basis of data obtained for model systems, owing to the extreme complexity of real biological structures and processes. However, the structural organisation of molecules, resembling the DNA double spiral, the close packing of protein molecules, or the structure of chloroplasts, is similar to the molecular arrangement in solid solutions. Therefore we believe that the study of the mechanism of reactions at a molecular level in simplified model systems (solutions of biologically important compounds) will permit a deeper understanding of the physical and chemical processes occurring in real biological systems.

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Determination of the Thermodynamic Functions of Solutions by Gas-liquid Chromatography

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This review of the latest progress in gas-liquid chromatography is devoted to a description of the methodologi experimental technique for the gas-chromatographic determination of the thermodynamic properties of soluti are given for the calculation of the chief thermodynamic functions—the distribution constant, activity coeffi entropy, and free energy of the solution. The bibliography contains 152 references.

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I. INTRODUCTION

The method of gas-liquid chromatography (GLC), discovered in 1952 by Martin and Synge, has been widely accepted as a means of analysing complex mixtures of substances[1-3]. Although in their first paper the discoverers of the method pointed out not only its possible analytical applications but also methods for studying the physicochemical properties of substances, the application of GLC in physical chemistry has been extremely limited. Since 1955, papers on the study of the properties of solutions using gas-chromatographic methods have been published[4], but up to the present the number of such papers has been measured in tens (the number of papers on the analytical applications of gas chromatography is more than 14 000), although the potential promise of the GLC method for making physicochemical measurements have been pointed out in a number of reviews[5,6].

In GLC, the components of a mixture are separated as a consequence of their different solubilities in the stationary liquid phase, so that it is quite natural to use this method primarily for the study of the resulting dilute solutions of a volatile solute in a non-volatile solvent (coefficients of mass transfer and diffusion, the thermodynamic functions of the solutions, etc.). GLC provides a unique method for the experimental study of the properties of infinitely dilute solutions of volatile substances in non-volatile solvents; a convenient and rapid method for determining the equilibrium composition of solutions is obtained if the components are analysed by gas chromatography. The measurement of solubility by a static method requires several days if the results are to be obtained over a given temperature range, whereas when GLC is used, these measurements can be made in 40–60 min. Before the development of the GLC method, there were only about ten pieces of data characterising quantitatively the solubility of volatile substances in non-volatile solvents at infinitely low concentrations of the solution; now, by means of GLC, such data are numbered in thousands.

II. CLASSIFICATION OF CHROMATOGRAPHIC METHODS FOR DETERMINING THE THERMODYNAMIC PROPERTIES OF SOLUTIONS

All chromatographic methods for determining the thermodynamic functions of solutions can be divided into three groups.

1. Determination of Solubility in a Chromatographic Column by the Development Method

In this instance a study is made of the properties of the solution formed when the solute is passed through a chromatographic column filled with a solid carrier on which is deposited the stationary liquid phase (solvent). The solute is introduced at the start of the chromatographic column in the form of vapour or liquid, and is moved along the column by a stream of carrier gas. Along the column, equilibrium is established between the concentrations of solute in the gaseous and liquid phases. The method of development gas chromatography is suitable for the study of the solubility of volatile substances in non-volatile solvents at low concentrations of the solutions (not greater than 1%) and is technically simple; however careful account must be taken of the experimental conditions. The Henry coefficient should not change with change in the concentration of the solution. The time required for the measurements and their subsequent analysis is not great.

2. Methods Using Frontal Chromatography

These methods are applicable in the study of the thermodynamic properties of solutions at any concentration. They include vacancy chromatographic methods for studying the thermodynamics of solutions. The values of the solubility at different solute concentrations are determined from the parameters of the sorption or desorption wave in the frontal method. In one experiment it is possible to obtain data on the solubility of one component at any concentration of the solution, but the calculation of the thermodynamic quantities from the parameters of the experiment requires some time and skill.

3. Methods in which the Chromatograph is Used as an Instrument for the Quantitative Analysis of the Composition of an Equilibrium Mixture

An advantage of these methods over classical static methods is the small volume of the equilibrium systems studied, since a specimen weighing less than 0.01 mg is sufficient for analysis by gas chromatography. The removal of such a small specimen produces almost no displacement of equilibrium in the system, and the decreased volume of the saturator in which the system being studied is placed facilitates the attainment of equilibrium between the phases in a shorter time. The time required to obtain the experimental data by these methods is greater than the time required for determination by the methods of the first group, but here there are no restrictions on the concentration of the solution and the volatility of the components of the mixture.

A necessary condition for carrying out an experiment by the third group of methods is that it be possible to analyse one or more of the components of the given mixture by gas chromatography. In principle, gas chromatography can be used to analyse any system, the components of which boil without decomposition at any temperature at a pressure of not less than 0.1 torr. Pyrolytic gas chromatography also makes it possible to analyse solid compounds which decompose when distillation is attempted. The apparatus required for methods of the third group is extremely simple for pressures equal to atmospheric pressures; higher or lower pressures require special attachments for the removal of the specimen.

The methods of the second group are used chiefly for the study of two-component systems, whereas this restriction does not apply to the methods in the other groups. An important advantage of chromatographic methods for studying equilibrium is the decreased requirements as to purity of the components of the solution. In the study of equilibrium by the static method from the vapour pressure, any impurities distort the experimental results, whereas gas chromatography makes it possible to determine each component of the solution with a high degree of selectivity. Moreover, if the solution contains several components, their simultaneous determination is always possible in principle, and this increases considerably the efficiency of chromatographic methods of studying solutions. For example, the chromatographic method makes it possible to study equilibria in systems containing up to 20–30 components.

The high sensitivity of gas-chromatographic instruments makes it possible to analyse extremely dilute solutions down to concentrations of $10^{-3}-10^{-4}\%$, and hence to obtain valuable experimental data for the development of the theory of infinitely dilute solutions, where it is possible to neglect concentration effects in solubility.

Thus gas chromatography not only makes it possible to obtain thermodynamic data on the properties of solutions with minimal effort but also in a number of instances provides a unique method for determining solubility in infinitely dilute solutions.

III. CALCULATION OF DISTRIBUTION CONSTANTS FROM RETENTION VOLUMES

We can consider the determination of this thermodynamic quantity using the first group of methods, that is in a chromatographic column. When the component being separated moves along a layer of sorbent, thermodynamic equilibrium is effectively established between the liquid and gaseous phases, since as a consequence of the extensively developed surface of the solid carrier the thickness of the film of stationary phase is negligibly small.

The ratio of the quantities of solute in unit volume of the liquid and gaseous phases is defined as the chromatographic distribution constant K: [6]

$$K = \frac{n_l/v_l}{n_g/v_g}, \tag{1}$$

where n_l, n_g, v_l, and v_g represent respectively the number of moles of solute in the liquid and gaseous phases and the volumes of liquid and gas in the chromatographic column.

Subsequently, for the sake of brevity, the chromatographic distribution constant will be referred to as the distribution constant. We can examine how this quantity is related to the characteristics of a sufficiently small section of the chromatographic column, in which the pressure drop of the carrier-gas approaches zero, and the average pressure is 1 atm. The rate of travel of the solute along a given section of the column (u_1) is given by Eqn. (2), [1] since only that fraction of the substance which is in the gaseous phase can be transported by the carrier gas

$$u_1 = \bar{u}f, \tag{2}$$

where f is the fraction of time for which the substance is in the gaseous phase, and $\bar{u}$ the linear velocity of the carrier gas.

We then have

$$f = \frac{n_g}{n_1}. \tag{3}$$

Combination of Eqns. (1) and (3) gives

$$\frac{n_g}{n_1} = \frac{n_g}{n_g + n_l} = \frac{n_g}{n_g + n_g \cdot Kv_l/v_g} = \frac{v_g}{v_g + Kv_l}. \tag{4}$$

If the linear velocity of the carrier gas is defined as

$$\bar{u} = \frac{u}{v_g/\Delta L},$$

where u is the volume rate of flow of gas and ΔL the length of the section of the column, we have

$$u_1 = \frac{u}{v_g/\Delta L}\frac{v_g}{v_g + Kv_l} = \frac{u\,\Delta L}{v_g + Kv_l}. \tag{5}$$

The retention volume of the solute is defined [1-3] as

$$V_R = \tau_R u, \tag{6}$$

where τ_R is the time for which the component is in the column.

Since

$$\tau_R = \frac{\Delta L}{u_1},$$

we have

$$V_R = \frac{\Delta L}{u_1} u.$$

We thus obtain the fundamental static equation in GLC:

$$V_R = v_g + K v_l. \quad (7)$$

Eqn. (7) can be used only for those systems where the pressure drop of the carrier gas in the chromatographic column can be neglected, and the total pressure in the column is equal to 760 torr. Under real conditions of chromatographic column operation, this is not attained, so that it is necessary to consider the corrections made to the retention volume to take account of the change in the pressure of the carrier gas along the column. We can consider the elution of a component from a column of finite length, divided into equal sections ΔL.[7] For a non-compressible gas we obtain

$$V_r = K \cdot v_l \cdot \Delta L,$$

where $V_r = V_R - v_0$.

If N is the number of parts into which the column is divided, we have

$$\tau_r = \frac{V_l}{N} \sum_{i=0}^{i=N} \frac{K_i}{u_i}, \quad (8)$$

where $V_l = Lv_l$.

From the equation of state for an almost perfect gas

$$p = \frac{n_g \cdot RT}{V} + \frac{RT}{V^2} \sum_{ij} B_{ij} x_i x_j,$$

where x_i and x_j are the mole fractions of the components in the gas, and B_{ij} the second virial coefficients for the components of the system, Everett[8] found that at infinite dilution of the solute in the gaseous phase

$$\tilde{v}_g = \frac{RT}{p} + B_{33}, \quad (9)$$

where $\tilde{v}_g$ is the molar volume of the gaseous phase, and B_{33} the second virial coefficient of the pure gas.

We can thus write the following expression for the distribution constant

$$K = \lim_{x_l \to 0} \left\{ \frac{x_l n_l}{x_g V_l} \left[\frac{RT}{p} + B_{33} \right] \right\}. \quad (10)$$

Everett also showed that at a pressure at the inlet to the chromatographic column $p_i < 20$ atm and a ratio $p_i/p_0 < 5$ (p_0 is the pressure at the outlet from the chromatographic column) it is possible, with sufficient accuracy, to write

$$V_R = KV_l [1 + \beta p_0 J_3^4], \quad (11)$$

where

$$J_3^4 = \frac{3}{4} \frac{(p_i/p_0)^4 - 1}{(p_i/p_0)^3 - 1},$$

$$\beta = \frac{2B_{13} - \tilde{v}_1^{\infty}}{RT},$$

B_{13} is the second virial coefficient taking account of the interaction between the solute and the carrier gas, and $\tilde{v}_1^{\infty}$ the partial molar volume of the solute at infinite dilution.

For an ideal gas, the pressure at each point of the column (p) is given by the equation

$$p = \sqrt{p_i^2 - \frac{l}{L}(p_i^2 - p_0^2)}, \quad (12)$$

where l is the distance from the column inlet to the given point.

If however the gas does not obey the laws for ideal systems, it is necessary to take account of the corrections involving the virial coefficient B_{33}:[8]

$$p = \left[p_i^2 - \frac{l}{L}(p_i^4 - p_0^2) - \frac{2B_{33}}{3RT} \left\{ \frac{p_i^3 - p^3}{p_i^2 - p_0^2} + \frac{p_i^3 - p_0^3}{p_i^2 - p_0^2}(p_i^2 - p^2) \right\} \right]^{1/2}$$

$$u = \frac{p_0 u_0}{p} \left[1 - \frac{B_{33}(p_0 - p)}{RT} \right].$$

Overall allowance for the change in the distribution constant with the carrier gas pressure, the effect of the viscosity of the gas, and its effective pressure, makes it possible to write the following equation[7]:

$$V_r = \frac{\frac{KV_l J_3^4}{p_0} \left[\frac{e^{i\beta p}}{\beta^2} \left(\beta^2 p^2 - 2\beta p + 2 \right) \right]_{p_l}^{p_0}}{0.5\,[p^2]_{p_l}^{p}}. \quad (13)$$

From this equation, using the experimentally determined values of the retention volumes of the solutes studied, it is possible to determine the chromatographic distribution constant under standard conditions and the magnitude of the second virial coefficient B_{13}. Eqn. (13) is usually solved graphically, but for analytical calculations an approximate version of this equation is usually employed[9]:

$$\ln V_R = \ln KV_l + \beta p_0 J_3^4. \quad (14)$$

For systems where the carrier gas dissolves in the stationary phase, this effect was taken into account[10] using the derived overall equation

$$\ln V_r = \ln KV_l + \beta' p_0 J_3^4 + \zeta (p_0 J_3^4)^2, \quad (15)$$

where

$$\beta' = \beta + \lambda \left[1 - \frac{\partial \ln \gamma_1^{\infty}}{\partial x_3} \right],$$

$$\zeta = \frac{3C_{133} - 4B_{13}B_{33}}{2RT} + \varphi \left[1 - \frac{\partial \ln \gamma_1^{\infty}}{\partial x_3} \right] + \frac{\lambda^2}{2} \left[1 - \frac{\partial^2 \ln \gamma_1^{\infty}}{\partial x_3^2} \right] + \frac{KV_l}{RT}.$$

The quantities λ and φ characterise the solubility of the gas in the stationary phase. In the expression for ζ the penultimate term characterises the compressibility of the stationary phase. For most systems, however, particularly if the work is carried out at temperatures up to 100°C with common carrier gases, the influence of the solubility of the carrier gas in the stationary phase on the retention volume can be neglected. A number of experiments specially carried out to study the influence of the nature of the carrier gas on the distribution constant[11-15] showed that the solubility of the carrier gas in the liquid need be taken into account only for gases such as carbon dioxide, ethane, and the heavier hydrocarbons.

Thus theoretical allowance for the various possible effects of the experimental conditions on the magnitude of the distribution constant being calculated shows that for its sufficiently accurate determination from a chromatographic experiment, the following data are required: the retention volume V_r, the volume of the stationary phase in the column, and the pressure at the inlet and outlet of the column; to introduce corrections for the non-ideal nature of the gaseous phase in the column it is necessary to take account of the molar volume of the solute at infinite dilution and the second virial coefficient. The last two corrections are rarely used, chiefly to obtain results with an extremely high accuracy, of about 0.5%. In order to introduce the minimal number of corrections in the calculation of the distribution constant from chromatographic data, it is recommended that the studies be carried out with very short columns and a solid carrier with large particle size, to ensure the minimum pressure drop along the column.

IV. EXPERIMENTAL DETERMINATION OF RETENTION DATA FOR THE CALCULATION OF THE THERMODYNAMIC PROPERTIES OF SOLUTIONS

To obtain the true values of the distribution constant, characterising the gas–liquid equilibrium, it is necessary to observe certain precautions, dictated by the nature of the processes occurring in the chromatographic column during the movement of the zone of solute.

For solutions with low concentrations the retention data of a component are independent of the presence of other compounds in the mixture, with the condition that the components of the mixture do not react with one another. Thus it has been shown[16] that in a mixture of benzene, cyclohexane, and methylcyclohexane, no mutual influence of the components of the solution on their retention volumes is observed. The interaction of solutes is observed experimentally only at solute concentrations which are so high that the solution must be regarded as a mixture of components in approximately equal concentrations. When a mixture of substances is introduced into the inlet section of a chromatographic column, all the components of the mixture move in a single zone only in the first sections of the column, after which they separate into zones containing only binary solutions. Thus the mutual influence of the components in a mixture on their retention times is shown most strongly for those substances for which the rates of movement of the zones along the column are similar. In general it is better to carry out the solubility determination with specimens of individual substances or substances with markedly different solubilities.

The stationary phase is applied to the surface of the solid carrier in a very thin film. There naturally arises doubt as to whether the nature of the dissolution is the same in these thin layers in the chromatographic column and in static experiments. The vapour pressure above a pure liquid and a layer of liquid deposited on a chromatographic carrier of the celite type has been measured[17–19] and it has been shown that the results of the static and chromatographic experiments are identical. These conclusions are applicable for fairly large quantities of stationary phase on the carrier—more than 0.03 volumes of liquid per volume of solid carrier.

The stationary phase is present on the surface of the solid carrier in two energetically different states—as an absorption layer and as capillary liquid[20]. The adsorption layer of liquid has a low entropy of solution compared with the pure liquid, whereas the properties of the capillary liquid and the pure liquid are identical. With small quantities of stationary phase on the carrier, due to the effect of the adsorption layer of liquid, the solvent power of the stationary phase is lower than that of the pure liquid[21]. With increase in the quantity of stationary phase on the carrier, the solubility increases exponentially, since the relative quantity of capillary liquid in the stationary phase increases.

When a solute passes through a chromatographic column, the maximum concentration in the solution in the zone decreases, as a consequence of spreading by diffusion[1]. If the experiment is carried out under conditions where the concentration in solution in the first sections of the column is extremely high, concentration distortion of the value of the distribution constant is observed. To decrease the influence of concentration effects it is desirable to use columns with a large quantity of stationary phase on the carrier.

The size of the specimen placed on the chromatographic column also influences the concentration of the gas-chromatographic solution. It is desirable to have a specimen which is sufficiently small, at the concentrations of the solutions formed in the stationary phase, for the values of the distribution constant to remain constant, that is for Henry's law to apply. At a ratio of the quantities of stationary phase and carrier greater than 0.01 : 1, an activity coefficient in the range 0.5–1.5, and size of specimen up to 2 μmole (column with internal diameter 4 mm), distortions of the experimentally observed values of the distribution constants were not observed for non-polar systems[17].

As the chromatographic zone moves along a column, processes of condensation and volatilisation lead to a change in the temperature of the solution. It was calculated[17] that these micro-changes in temperature under the real conditions indicated above do not exceed 0.1 deg, and this has almost no influence on the experimentally determined retention data.

When a solute passes through a chromatographic column the viscosity of the carrier gas changes as a consequence of the formation of a gaseous zone of mixed solute and carrier gas, and this produces pressure surges along the column. According to published data[5], these surges are negligibly small if the specimen size is less than 1 μmole, the activity coefficients between 0.2 and 5, and the retention volume of the solute, corrected for the dead volume, not less than 500 ml. It has been shown[17,22] that the nature of the carrier gas has no influence on the magnitude of the distribution constant (the following gases were studied: helium, hydrogen, nitrogen, oxygen, argon, carbon dioxide, and methane). On the other hand, results obtained by capillary chromatography show that the retention data depend on the nature of the carrier gas[23], although it is possible that with the large pressure drops encountered in capillary columns, the authors cited were unable to calculate the distribution constant with sufficient accuracy.

As the chromatographic zone passes through the column, its rate of movement depends on three factors: the solubility in the stationary phase (K), the adsorption at the gas–liquid interface, and the adsorption at the solid–liquid interface[24–27]:

$$V_r = Kv_l + K_{gl}s_l + K_{ls}s_s, \qquad (16)$$

where s_l and s_s represent respectively the surface areas of the liquid and solid in the chromatographic column, and K_{gl} and K_{ls} the adsorption coefficients at the gas–liquid and solid–liquid interfaces respectively. These phenomena were first observed for systems formed by a non-polar solute and a polar solvent[25,28].

To calculate the constant of this equation it is necessary to determine experimentally the dependence of the retention volume on the quantity of stationary phase in the column and the surface area of the stationary phase. The calculations are then carried out by means of the equations[27,29]:

$$\frac{V_r - \bar{V}_r}{v_l - \bar{v}_l} = K + \frac{s_l - \bar{s}_s}{v_l - \bar{v}_l}, \qquad (17)$$

$$\frac{V_r - \bar{V}_r}{m - \bar{m}} = V_g + K_{gl}\frac{s_l - \bar{s}_l}{m - \bar{m}}, \qquad (18)$$

where $\bar{V}_r$ is a selected value of the retention volume for the sorbent, characterised by the quantities $\bar{m}$ and $\bar{s}$, and V_g the specific retention volume.

Eqns. (16)–(18) are applicable for sufficiently large quantities of stationary phase on the carrier—greater than 1% of the weight of sorbent. The characteristics of adsorption at the boundaries between the phases in GLC have been calculated by a number of authors[24–30].

The adsorption of solutes on the surface of the stationary phase is most marked in the chromatography of non-polar substances on a polar stationary phase, but even when a non-polar stationary phase is used, allowance must be made for this effect[30].

A number of authors[29,31-36] have made detailed studies of the effects associated with the adsorption of a solute at the interface between the solid and the stationary liquid phase. These effects are least marked when the gas-chromatographic method is used to study non-polar systems. Polar solutes are usually readily sorbed by the surface of the diatomites used as carrier in GLC. This leads to a change in the retention time with the size of the specimen, and the effect is greatest with small quantities of stationary phase on the carrier[37,38]. Particular care in the thermodynamic treatment of chromatographic data is required for solutions of polar substances in non-polar solvents, where various concentration distortions can affect the determination of retention volumes[39]. Polar stationary phases to some extent modify the carrier surface, decreasing its adsorption activity with respect to polar compounds. The best results in decreasing the adsorption power of the carrier surface are achieved by treating the diatomites with silane; it is always best to do this when non-polar stationary phases are used. In some instances, satisfactory results have been obtained on solid carriers with a non-polar surface—Teflon[30] or polyethylene[40]. Interfacial adsorption produces particularly marked distortion of retention volume values in those instances where the substances being separated have small distribution constants. For $K > 100$ and correctly chosen experimental conditions, the fraction of interphase adsorption does not exceed 2–3% of the total retention volume[26,28].

When the first portions of stationary phase are deposited on a solid carrier, an adsorption layer of liquid is formed; the total surface area of the liquid increases until the solid carrier is completely covered. With further addition of liquid, the pores of the carrier are filled, so that the total surface area of liquid decreases exponentially towards a limiting value. The addition of liquid also increases the concentration of capillary liquid in the stationary phase, so that the total solvent power of the stationary phase increases. As a result, the curve giving the dependence of the distribution constant, calculated with allowance for adsorption at the solid–liquid interface, on the quantity of stationary phase on the carrier shows a maximum for very small quantities of stationary phase, and a minimum when the volume of staionary phase is about 2% of that of the diatomite carrier[21]. At ratios of stationary phase to solid carrier greater than 0.03 : 1, the values of the distribution constant are stabilised. The heats of dissolution remain constant for proportions of stationary phase greater than 0.01 : 1.

In general, it is best to use capillary columns to obtain information on the thermodynamics of solutions. Thus in the determination of retention data for polar compounds in non-polar stationary phases[41], marked discrepancies were observed between the results obtained on packed and capillary columns. For polar stationary phases, the retention characteristics are similar for the two types of column. The calculation of the specific retention volume of *n*-heptane in squalane on a capillary column[27] gave the values 1550 ml g^{-1} without allowance for interphase adsorption, and 416 ml g^{-1} after the necessary corrections. Littlewood[42] used packed micro-columns with a small quantity of stationary phase on a solid carrier, and this was the main reason for the difference between the experimental results and static data. Martire and Pollara[43] calculated the retention volume not from the apex of the peak, as is usually done in GLC, but from the start of the emergence of the peak, which explains the distortion of the results.

A correctly chosen procedure for the determination of the thermodynamic functions of solutions from gas-chromatographic data makes it possible to obtain reliable values for the distribution constants, agreeing with the results of static experiments[17,44-48]. According to these results, the discrepancy between the results obtained by gas-chromatographic and static methods did not exceed 1%.

To obtain precise experimental data on the thermodynamics of solutions it is necessary to take account of all the parameters of the gas-chromatographic process appearing in Eqn. (14). The procedure has been described in sufficient detail by a number of authors[16,49,50]. For the experiment, the substance being studied is introduced into the chromatographic column in the form of liquid or vapour, and the time taken for the apex of the peak for the component to emerge is measured with a stopwatch. The time correspond to the emergence of the peak for air or methane (τ_0) is then subtracted from the measured time, the carrier gas flow rate is measured with a bubble flowmeter, and all the other necessary parameters of the process are noted. The total time taken for the experiment is usually not more than half an hour per component. Use of the correct experimental procedure in the gas-chromatographic method makes it possible to obtain thermodynamic values of the distribution constant with a small error of the order of 1%.[22] In some instances this error has been halved[17,51]. A number of structural changes in chromatographic instruments, particularly improved methods for controlling the carrier gas flow, made it possible to achieve an accuracy of the order of 0.2% in the determination of the specific retention volume[52,53] or 0.02% in the calculation of the relative retention volume[54]. In the work cited[54], a chromatograph with automatically controlled carrier gas flow rate was used. When it is remembered that the results refer to solutions at limiting dilution, it is clear that such high experimental accuracy cannot be achieved by any other method.

High accuracy in the determination of solubility characteristics by GLC is realised only for components present in the mixture in medium concentrations. In the study of retention data for substances with a high concentration in the mixture it is necessary to introduce a number of corrections[55]. It has been found[56] that with change in the concentration of a trace component from 0.03% to 2% the value of the retention volume of this component changes by 2–3%.

V. CALCULATION OF ACTIVITY COEFFICIENTS

Thus experimental retention data obtained by development GLC can be used to calculate the chromatographic distribution constant K. For more universal application of this parameter it is necessary to relate it to the thermodynamic distribution constant $\bar{K}$, given by the equation

$$\bar{K} = a_l/a_g, \qquad (19)$$

where a is the activity, equal to γc (γ is the activity coefficient†, and c the concentration).

† In GLC, the standard state of the solute in the calculation of the activity coefficient is usually taken as the pure solute under normal conditions, so that for infinitely dilute solutions $\gamma \neq 1$. The quantity γ shows the departure of the solute vapour pressure from the value which would be observed for an ideal solution.

Warnings against confusion of the thermodynamic and chromatographic distribution constants have been published[57,58]. In the latter work the following relationship was derived for converting the chromatographic distribution constant into the thermodynamic constant:

$$\overline{K} = \frac{c_l/n_l}{pc_g/n_g} = \frac{K}{N_l RT} \qquad (20)$$

N_l is the number of moles per unit volume of the stationary phase. From this we can readily calculate the molar free energy of dissolution

$$\Delta G_s = -RT \ln \overline{K}. \qquad (21)$$

We can establish the relationship between the distribution constant and the activity coefficient for dilute solutions[6,59,60]. For non-ideal solutions, Raoult's law is written as

$$yp = \gamma_p^{\infty} x p^0,$$

where x and y represent respectively the mole fractions of the solute in the liquid and solid phases.

Since

$$K = \frac{xN_l}{yN_g} = \frac{xpN_l}{\gamma_p^{\infty} x p^0 N_g}$$

and

$$p/N_g = RT,$$

we obtain

$$\gamma_p^{\infty} = \frac{N_l RT}{Kp^0}. \qquad (22)$$

To take account of the non-ideal nature of the gaseous phase, we can use the equation derived by Everett[8] making the same assumptions as when correcting the distribution constant

$$\ln \gamma^{\infty} = \ln \frac{N_l RT}{Kp^0} - \frac{(B_{11} - \tilde{v}_1^0)p^0}{RT} + \frac{(2B_{12} - \tilde{v}_1^{\infty})p}{RT}, \qquad (23)$$

where $\tilde{v}_1^0$ is the partial molar volume of the solute, and p^0 the vapour pressure of the solute at the temperature of the experiment.

A similar type of equation was derived by Cruickshank and coworkers[9]. The chief difference between Eqns. (22) and (23) is that in the former, the activity coefficient is calculated with the assumption that the gaseous phase is non-ideal, and the vapour pressure of the pure solvent obeys the laws for ideal gases; the second equation takes account of all the deviations from ideal behaviour which can arise in a chromatographic experiment. Thus Eqn. (23) gives a more accurate value for the activity coefficient.

If data on the fugacity of the substance being studied are available, the activity coefficient is calculated from the equation

$$\gamma^{\infty} = \frac{N_l RT}{Kf^0}, \qquad (24)$$

where f^0 is the fugacity of the vapour of the pure solute at the temperature of the experiment.

A somewhat inconvenient feature of the above equations is the need to determine the density of the stationary phase (solvent) at all temperatures of the experiment, since the volume of the stationary phase appears in the equation for the calculation of the chromatographic distribution constant. It is therefore preferable to use the specific retention volume (V_g), where the retention volume of the component is related to unit mass of the stationary phase in the column. The last quantity is independent of temperature:

$$V_g = \frac{273.2 \cdot V_r}{m \cdot T}, \qquad (25)$$

where m is the quantity of stationary phase in the column, g. The retention volume in Eqn. (25) is also corrected for the non-ideal nature of the gaseous phase, as with the distribution constant. The activity coefficient is calculated with allowance for the specific retention volume by means of the equation

$$\gamma^{\infty} = \frac{273.2R}{MV_g f^0}. \qquad (26)$$

In estimating the selectivity of the stationary phase in gas-liquid chromatography, considerable use has been made of relative values of the activity coefficients, for which some readily available compound is taken as standard (for example benzene, carbon tetrachloride, n-alkanes). The relative activity coefficient is calculated from the minimum in the experimental data

$$\gamma_{xr}^0 = \gamma_x/\gamma_r = \frac{f_r^2}{f_x^0 V_r^0} = 1/f_{xr}^{00} V_r^0, \qquad (27)$$

where v_r^0 is the relative retention volume, and f_{xr}^{00} the relative volatility of the substances being compared.

If the activity coefficients of a large number of compounds are being determined, it is usual, for convenience, to choose one of them as standard and to calculate relative values of the activity coefficients for the others. The absolute value of the activity coefficient is measured for the standard component. The accuracy of the determination of the relative activity is then greatest, and reaches 0.05%, indicating that the extensive use of the relative values is appropriate.

GLC provides the experimentalist with extensive possibilities for studying systems with multicomponent solvents[61]. The composition of the stationary phase in the chromatographic column may be altered arbitrarily. In such instances it is necessary to make allowance for purely gas-chromatographic effects associated with the use of small quantities of added polar substances, which may be sorbed by the surface of the solid carrier and hence influence not so much the solubility of the substances in the mixed stationary phase as the degree of chemical modification of the surface of the solid carrier[49].

If the stationary phase volatilises from the column under the conditions of the experiment, it is possible in the measurements to weigh the column before and after the experiment in order to make allowance for the loss of liquid and to make a corresponding correction to the retention data[62,63]. In a number of experiments[6,48,64] with volatile stationary phases, use has been made of saturators placed in front of the chromatographic column. The saturator contains solid carrier, impregnated with a large quantity of the stationary phase. Carrier gas at the temperature of the column passes through the saturator and is saturated by the vapour of the stationary phase. The loss of stationary phase from the column is compensated by the introduction of fresh portions of material from the saturator. This method has two important advantages over weighing the column before and after the experiment; firstly, the quantity of stationary phase remains unchanged during the experiment, and secondly, the stationary phase is distributed uniformly along the entire length of the column, whereas when the method of weighing is used, the liquid volatilises primarily from the start of the column. This last feature may lead to marked distortion of the results, due to the marked concentration dependence at

the low concentration of stationary phase in the first sections of the column.

The activity coefficients in systems containing benzene, toluene, *n*-propanol, dichloroethane, and carbon tetrachloride have been determined[50]. Allowance was made for the non-ideal nature of the gaseous phase, resulting from the presence of the vapour of the volatile solvent.

The use of circulation arrangements also makes it possible to carry out the determinations in systems with a volatile stationary phase. For example, the activity coefficients of methanol and ethanol (solvent benzene) were determined at 25° on a circulation apparatus[65].

Methods for the determination of activity coefficients by GLC have been reviewed[66], and the influence of departure of the behaviour of the gaseous phase from ideal behaviour on the values of the thermodynamic quantities has been discussed[67].

VI. DETERMINATION OF THE THERMODYNAMIC PROPERTIES OF SOLUTIONS WITH MEDIUM AND HIGH CONCENTRATIONS

The above material relates to the determination of thermodynamic data at infinite dilution, that is in the very dilute solutions existing in the chromatographic column. For the theory and practical utilisation of solutions it is of interest to study solutions of substances at finite concentrations. Static methods for obtaining these results require considerable expenditure of effort and complicated experimental technique[68,69]; the chromatographic method is free from these disadvantages.

A method for determining solubility over a wide range of solution concentrations by frontal gas chromatography has been described[70]. A stream of carrier gas passes through an ordinary gas-chromatographic assembly, the column of which contains a measured quantity of stationary phase on a solid carrier. At a selected moment, the stream of carrier gas is passed through a saturator containing the solute. The temperature of the saturator is chosen to create the required vapour pressure of solute in the carrier gas. The chromatograph records the appearance of a concentration wave at the outlet from the column. When the concentrations of the substance added to the carrier gas have become the same at the inlet and outlet, pure carrier gas is passed through the column, and the chromatograph records the desorption concentration wave. The assembly is calibrated with respect to the concentration of the saturated vapour of the substance being studied in the carrier gas. The solubility is calculated from an arbitrarily selected number of points on the sorption or desorption curve. The quantity of substance sorbed is calculated from the equation

$$q = \frac{cV - q_1}{m}, \qquad (28)$$

where q_1 is the quantity of substance eluted from the column at the moment of emergence of the point of the curve corresponding to the concentration c, and v the volume of carrier gas which has left the column up to the moment when the concentration c of solute appears at its outlet.

The quantity of substance which has left the column (q_1) is determined directly from the chromatogram by planimetry. This method makes it possible to determine the distribution constants over a wide range of concentrations in one experiment.

A similar method for determining solubility by frontal chromatography was described by Condér and Purnell[71], but in this instance allowance was made for the non-ideal nature of the gaseous phase. An equation was derived[71-73] for determining the activity coefficient at finite concentrations of the solution

$$\ln\gamma = \ln\frac{RT(c_l v_l + n_l)}{p^0 K v_1} + \frac{p_0 J_3^4}{RT}[2xB_{11}J_3^4 + 2(1 - xJ_3^4)B_{13} - \tilde{v}_1^0] - p^0/RT\,[B_{33} - \tilde{v}_1], \qquad (29)$$

where n_1 is the total number of molecules of solvent in the column, and $\tilde{v}_1^0$ the partial molar volume of the solute.

The determination of the distribution constants at finite concentrations of the solutions from chromatographic data is based on the equation[71]

$$V_R = V_0 + m(1 - J_3^4 x)\partial q/\partial c. \qquad (30)$$

In practical measurements, the stream of carrier gas, saturated with the vapour of the component being studied at a definite concentration, is passed through a short column with a small pressure drop. Thus an equilibrium mixture of carrier gas and solute is passed constantly through the column, and the concentration of the solution in the column is known and constant along the entire length of the column. A small specimen of the substance being studied is introduced into the column; this gives a positive peak on the chromatogram. The retention time of this peak is used to calculate the quantity $\partial q/\partial c$ from Eqn. (30). The work cited gives equations which make it possible to make corrections for the non-ideal nature of the gaseous phase when the frontal method is used.

The methods for determining the thermodynamics of concentrated solutions, described in the works cited[70,71], differ in the time taken for the experiment. In the first, the experiment takes a comparatively short time compared with the time required for the calculation of the distribution constants. In the second method, the experiment takes more time than the calculations. The time required for the determination of the solubility isotherm by means of a McBain balance is approximately the same as that for the chromatographic method, if the solvent in the static method is deposited on a solid carrier of the diatomic type. If however the static experiment is carried out with pure liquid, the time taken for the determination of the dissolution isotherm is not less than 3 d. The chromatographic determination and calculations take 3–6 h.

The accuracies of the chromatographic and static methods for determining the solubility in concentrated solutions have been compared[17,71,74]. It has been shown that when a McBain balance is used in a purely static experiment the error in the determination of the activity coefficient is 0.1% at a mole fraction of the solute $x = 0.4$, and 0.4% at $x = 0.2$. If in the static determinations the solvent is deposited on a solid carrier[18], however, the error is 1.5% at $x = 0.4$, and 4% at $x = 0.2$. The error obtained when chromatographic methods are used to determine the distribution constants in these systems is not greater than 0.2%.[71] Thus for the same expenditure of time on the experiments and the treatment of the results, the accuracy of the static method is much less than that of the chromatographic method; for equal accuracies in the determination, the measurement of solubility by the static method requires much more time.

Some authors[75-78] have proposed a method for determining sorption isotherms from the trailing edge of the chromatographic zone (peak) leaving the column in development chromatography. In actual fact, the form of the peak depends on the sorption isotherm, but this is by no means the only factor influencing the form of the peak.

Various diffusion processes also distort the form of the peak, so that it is extremely difficult to separate the contribution of the sorption isotherm in the formation of the trailing edge of the zone in a real chromatographic experiment. Thus these methods for determining the sorption isotherms are extremely approximate, so that they can be used only in gas-adsorption chromatography for substances with a high adsorption capacity. It is more rational to determine the dependence of the time of emergence of the apex of the chromatographic peak on the height of this peak, that is on the maximal concentration of the component in the chromatographic zone. For these determinations, short columns with a small pressure drop are used, but in these instances account must be taken of the fact that the concentration of the solution changes along the length of the chromatographic column.

An original method for determining solubility (V_g) was proposed by Zhukhovitskii and coworkers [79-83]. These methods are suitable for determining the solubility of substances in solutions at concentrations as high as required. A version of chromatography without carrier gas is used for the determinations; the mixture being studied, with or without an inert gas, is passed through the chromatographic column until equilibrium is established along the entire column. Some perturbation to the flow is then created, or a small specimen of air or any substance being studied is introduced, after which the time of emergence of the peaks, the number of which is smaller by one than the number of components in the gaseous phase, is determined. The retention volume of the component, obtained in this way, is related to the distribution constant by the equation

$$V_g = n_g(\partial q_3/\partial n_3 - \partial q_3/\partial n_g) + n_3(\partial q_1/\partial n_g - \partial q_1/\partial n_3), \qquad (31)$$

where the subscripts 1 and 3 refer respectively to the solute and the diluent gas or second component of the mixture. For multi-component systems, similar equations are compiled and solved on electronic computers.

An experimental assembly for the determination of solubility for solutions with concentrations up to 12% has been described [83]. The required concentration is established by adding a sufficiently large specimen of the substance being studied to a column, and the solubility is determined by vacancy chromatography. The distribution constants and activity coefficients for non-polar systems in the concentration range 0–10% have been determined by vacancy chromatography [84]. Comparison of data obtained by the static and vacancy-chromatographic methods for the *n*-hexane–1,2,4-trichlorobenzene system [83] shows that for solution concentrations $x \leq 0.2$ the results agree satisfactorily, but differences are observed at higher concentrations. An important advantage of vacancy-chromatographic methods over frontal methods is that it is possible to study multi-component systems.

The accurate establishment of the quantity of stationary phase in a chromatographic column presents a difficult experimental problem. The accuracy of the results obtained in a gas-chromatographic experiment depends to a large extent on the solution of this problem. Thus a number of authors have tried to combine the advantages of the static method, where an accurately measured quantity of pure stationary phase (solvent) is used, with the chromatographic determination of the equilibrium composition of the gaseous or liquid phase of the system. The design of an apparatus in which the gaseous phase from the static system passes through heated connections into the inlet compartment of a gas chromatograph has been described [85]. The chromatograph is used to determine quantitatively the concentration of the component being studied in the gaseous phase. This method can be used to study multi-component systems, and the calculation requires little time [85,86]. A slightly different modification of the flow system, in which the carrier gas was saturated with vapour from a solution and passed to the inlet chamber of the chromatograph, has been described [87], but in this instance the calculation of the results is extremely complicated.

For the periodic gas-chromatographic analysis of the phase composition of equilibrium systems it is possible to use saturators of small volume with a thin layer of solvent; this makes it possible to establish thermodynamic equilibrium fairly rapidly in the system [49]. A specimen of the gaseous phase from the saturator at constant temperature is removed with a gas syringe with piston stop or with a special micro-column, and introduced into the inlet chamber of a chromatograph with a flame-ionisation detector. The design of these systems is very simple only when the total pressure in the system is equal to atmospheric; otherwise, special attachments are required for the removal of the specimen. A disadvantage of this method is the appeciable time—about 0.5 h—taken for equilibrium to be established in the system, but the calculation of the results is extremely simple.

An important advantage of combined static–chromatographic methods is that it is possible to study systems in which all the components are volatile at the temperature of the experiment. Thus this method has been used to measure the solubility of inorganic gases in electrolytes [88] and the solubility of organic gases in various solvents [89-92]. In these last experiments, the solvent was added to a vessel containing the gas being studied, after which the gas was blown from the vessel to the inlet chamber of the chromatograph and its concentration was measured.

Comparison of different methods for the chromatographic determination of the thermodynamic functions of solutions shows that at low concentrations it is best to use the purely chromatographic method of determining the distribution constants. When it is necessary to measure the solubility at finite fixed concentrations of the solutions, it is rational to use special frontal development methods and chromatography without carrier gas, and also to combine static and gas-chromatographic methods. The use of gas chromatography makes it possible to study the properties of infinitely dilute solutions, to increase the accuracy of experimental thermodynamic data for dilute solutions, and to save time in experiments in the study of concentrated solutions.

VII. CALCULATION OF THE MOLAR HEAT OF DISSOLUTION

Eqn. (22) can be written in the logarithmic form [59]:

$$\ln K = \ln N_1 RT - \ln \gamma - \ln p^0 \quad .$$

According to the basic principles of thermodynamics

$$RT \ln \gamma = \Delta\bar{H}_s - T\Delta\bar{S}_s$$

(the bar above the symbol for a function denotes that the function is an excess function, i.e. it expresses the difference between a property of the pure substance being studied and the same property of the solution), so that we can write

$$\ln K = \ln N_1 R - \Delta H_s/RT - \Delta\bar{S}_s/R + \Delta H_v/RT - \ln(1/T) \qquad (32)$$

where N_1 is the number of moles in unit volume of the stationary phase, and ΔH_V the molar heat of volatilisation. Differentiating this equation with respect to $1/T$ and multiplying by R, we obtain

$$\Delta H_s = R\partial \ln K/\partial (1/T) - RT + R \ln R\partial \ln N_l/\partial (1/T) . \quad (33)$$

This equation makes it possible to calculate the molar heat of dissolution from the experimentally determined chromatographic distribution constants[4,59]. The need to determine the specific gravity of the solvent at different temperatures of the experiment introduces some inconvenience. This can be avoided by using the specific retention volumes for the calculation of the molar heats of dissolution[93]. According to the definition of the specific retention volume,

$$K = \frac{V_g mT}{273.2 v_l} .$$

Substituting this expression in Eqn. (33) and differentiating with respect to $1/T$, we obtain

$$\Delta H_s = R\partial \ln V_g/\partial (1/T) . \quad (34)$$

This equation shows that there is no need to determine the specific gravity of the stationary phase.

The heats of dissolution can be determined experimentally using activity coefficients. The equation relating the activity coefficient and the excess enthalpy of dissolution can be written

$$\Delta \overline{H}_s/T = -\Delta \overline{S}_s - R \ln \gamma .$$

Differentiation with respect to $1/T$ gives

$$\Delta H_s = R\partial \ln \gamma/\partial (1/T) . \quad (35)$$

Since this last equation contains the activity coefficient, the calculation of which requires data on the volatility of the substances being studied, the use of these equations in physicochemical determinations is limited.

The chromatographic determination of the heat of dissolution can be simplified further by eliminating from the necessary experimental data the mass of liquid in the column. The specific retention volume can be written as

$$V_g = \frac{273.2 u \tau_r}{mT} = k' \frac{\tau_r}{\tau_0 T} .$$

Since $u = k''/\tau_0$,

$$\ln V_g = \ln V_{g1} - \ln V_{g2} = \ln \frac{\tau_{r1}\tau_{02}}{\tau_{r2}\tau_{01}} + \ln \frac{T_1}{T_2}$$

so that

$$\Delta H_s = 4.58 \frac{\lg \frac{\tau_{r1}\tau_{02}}{\tau_{r2}\tau_{01}}}{1/T_1 - 1/T_2} + 4.58 \frac{\lg T_2/T_1}{1/T_1 - 1/T_2} , \quad (36)$$

where τ_0 is the time of emergence of the non-sorbed gas (dead volume of the system) and τ_r the actual time of emergence of the solute.

By selecting from the plot of $\lg \tau_r/\tau_0$ against $1/T$ the temperature range in which $1/T_1 - 1/T_2 = 4.58 \times 10^{-4}$, we obtain the final equation for these conditions:

$$\Delta H_s \cdot 10^4 = \lg \tau_{r1}/\tau_{01} - \lg \tau_{r2}/\tau_{02} + \lg (1 + 4.58 \cdot 10^{-4} T_2) \quad (37)$$

where the heat of dissolution is expressed in calories.

Thus the use of the last equation makes it unnecessary to determine the quantity of stationary phase in the column.

In the calculation of the heat of dissolution, allowance must be made for the difference between the enthalpy and heat of dissolution. The enthalpy of dissolution in most instances is negative, whereas the heat of dissolution has the opposite sign. The heat and enthalpy of dissolution are calculated by means of the same equations, and the quantities differ only in their signs. In most papers on gas chromatography, the heat of dissolution is denoted by H, and this may sometimes lead to confusion between thermodynamic and chromatographic data, since in chemical thermodynamics, heat is denoted by Q, and enthalpy by H.

A quantity used extensively in GLC is the relative heat of dissolution $\Delta H^0_{sx} = \Delta H_{sx} - \Delta H_{st}$, where ΔH_{sx} and ΔH_{st} are respectively the molar heats of dissolution of the substance being studied and a standard substance.

By carrying out the same steps used to derive Eqn. (37), we obtain a working equation for calculating the relative heat of dissolution from the difference in the logarithms of the retention volumes for $\Delta(1/T) = 4.58 \times 10^{-4}$:

$$\Delta H^0_s \cdot 10^4 = \lg V^0_{r1} - \lg V^0_{r2} . \quad (38)$$

It can be seen from Eqn. (38) that the calculation of the relative heat of dissolution from the relative retention volumes requires a minimum of experimental data.

Heats of dissolution can also be determined from data obtained for solutions with different concentrations by frontal, development, vacancy-chromatographic, and static-chromatographic methods. In these instances the isosteric heat of dissolution is usually calculated.

Many workers have determined heats of dissolution experimentally from retention data, and the experimental procedure has been described in detail[49,59,93-97].

Since in GLC practice extensive use is made of the so-called retention index, an attempt was made[98] to calculate the enthalpy of dissolution from the temperature dependence of the retention index

$$\Delta H_s = \frac{\delta I_n}{100} (\Delta H_{sr+1} - \Delta H_{sr}) + \Delta H_{sr} \quad (39)$$

where $\delta I_n = I_1 - IT_1/\Delta T$; $\Delta I = I_1 - I_2$; $\Delta T = T_2 - T_1$; I is the retention index of the substance being studied, and ΔH_{sr} the molar heat of dissolution of the n-alkane with the same number of carbon atoms in the molecule as the substance being studied, and ΔH_{sr+1} the molar heat of dissolution of the n-alkane with one carbon atom more in the molecule than the molecule of the substance being studied. The standard deviation which can be allowed when Eqn. (39) is used to calculate heats of dissolution is about 0.1 kcal mole^{-1}; in some instances, however, the discrepancy between the values of the heats calculated from the retention indices and from the retention volumes can reach 0.4 kcal mole^{-1}.

With precision measurement of the retention volumes, the reproducibility of the experimentally determined relative heats of dissolution is 0.02 kcal mole^{-1}, and that for the absolute heats 0.05 kcal mole^{-1}. Although the values of the heats of dissolution determined chromatographically agree to within an order of magnitude with the calorimetric values, there are as yet no sufficiently accurate calorimetric data on heats of dissolution for infinitely dilute solutions, so that a quantitative comparison of the chromatographic and calorimetric values cannot be made. Thus GLC makes it possible to determine heats of dissolution for solutions with any concentration, including infinitely dilute solutions; this last feature is particularly important.

VIII. CALCULATION OF THE MOLAR ENTROPY OF DISSOLUTION

The excess molar entropy of dissolution is calculated from the equation

$$RT\ln\gamma = \Delta\bar{H}_s - T\Delta\bar{S}_s \ . \qquad (40)$$

On the other hand, we can write the following equation containing the thermodynamic distribution constant:

$$-RT\ln\bar{K} = \Delta H_s - T\Delta S_s \ . \qquad (41)$$

In the last equation, in place of the thermodynamic distribution constant, it is possible to substitute the chromatographic distribution constant or specific retention volume

$$-RT\ln\frac{K}{RTN_1} = \Delta H_s - T\Delta S_s \ . \qquad (42)$$

To calculate the relative molar entropies of dissolution it is necessary to substitute in Eqn. (40) the value of the relative activity coefficient. By expressing the last quantity in terms of the relative retention volume and relative vapour pressure of the pure substances being compared at the temperature of the experiment (p^{00}) we obtain the relationships:

$$-RT\ln p^{00}V_r^0 = \Delta H_s^0 - T\Delta S_s^0 \ ,$$

$$-RT\ln V_r^0 = \Delta H_s^0 - T\Delta S_s^0 \ .$$

The error in the determination of the entropy of dissolution by gas-chromatographic methods is made up of the errors of the determination of the activity coefficient and the heats of dissolution. For relative molar entropies of dissolution the mean error is 0.4 e.u. Examples of the calculation of molar entropies of dissolution can be found in many papers [49,99,100].

IX. CALCULATION OF THE MOLAR FREE ENERGY OF A SOLUTION

This quantity is calculated from classical thermodynamic relationships using the distribution constant or activity coefficient

$$\Delta G = -RT\ln\bar{K} \ , \qquad (44)$$

$$\Delta\bar{G} = -RT\ln\gamma \ . \qquad (45)$$

Finally, a number of points may be made regarding the interpretation of the thermodynamic quantities obtained by gas-chromatographic measurements [57]. In the treatment of data on the thermodynamics of solutions of non-electrolytes, two standard states can be used: the pure solute (the distribution constant in this instance is denoted K_3, and an infinitely dilute solution of the same substance (for this standard state the corresponding symbol is K_2). For the gaseous phase, the standard state is usually taken as the ideal gas at a pressure of 1 atm. In the first instance the activity coefficient shows the departure of the properties of the solution from the ideal: the extent to which the vapour pressure of the solute in the solution is less than or greater than the value which would be observed for an ideal system. In GLC it is this standard state which is used in the calculation of the activity coefficient. The activity coefficient for the second standard state characterises the departure of the properties of the solution from Henry's law. These two standard states lead to different quantitative expressions for the thermodynamic functions of the solutions. Thus if the subscripts 2 and 3 are used to denote the heats and entropies of dissolution obtained from K_2 and K_3, we obtain the relationships:

$$\Delta H_{s3} - \Delta H_{s2} = -RT(Td\ln\rho/dT + 1) \ , \qquad (46)$$

$$\Delta S_{s3} - \Delta S_{s2} = R\ln\frac{M}{\rho TR} - R(Td\ln\rho/dT + 1) \ , \qquad (47)$$

where ρ is the density of the stationary phase. For example, when silicone 702 with M = 530 is used as stationary phase, the difference in the heats of dissolution according to Eqn. (46) is 0.5 kcal mole^{-1}, and the difference in the entropies of dissolution 10 e.u.

List of examples where GLC has been used to determine the thermodynamic functions of solutions.

Solutes	Solvents	Refs.
C_4–C_5 alkanes	Liquid paraffin	97
Iso-alkanes, fluorine-containing compounds	Octadecane	10
C_{4-6} iso-alkanes	Dinonyl phthalate, squalane	17
C_{5-6} alkanes	Squalane	8
C_{5-12} alkanes	C_{18-36} alkanes	101
C_{5-8} alkanes	Alkanes	102
n-Alkanes	Apiezon	99
Alkanes	Solar oil	103
C_5 alkanes	Amides	104
C_5 alkenes	Nitrobenzene, dodecane	105
Aliphatic hydrocarbons	Various	93
Alkenes	Polar liquids	106
C_{2-6} alkenes	Various	107-110
Alkenes	Silver nitrate solutions	111
Methylcyclohexanes	Various	112
Benzene	Polyethylene glycol cresyl ether	96
Benzene	C_{16-28} alkanes	113
Benzene	Polyphenyls	114
Aromatic hydrocarbons	Various	100
Aromatic hydrocarbons	Various	115-120
C_{6-10} aromatic hydrocarbons	Various	121
Aromatic hydrocarbons	*n*-Decanol	122
Aromatic hydrocarbons	Various	123
Hydrocarbons	Dinonyl phthalate	51
Hydrocarbons	*n*-Heptadecane	124
Hydrocarbons: butane, butenes	Furfural, *n*-dodecane	125
Hydrocarbons	Various	94
n-Hexane, cyclohexane, benzene	Various	126
Benzene, cyclohexane, methylcyclohexane	PEG ethers	16
Hydrocarbons	Various	23
Aliphatic hydrocarbons	Aromatic hydrocarbons	127
Hydrocarbons	Various	128
Hydrocarbons	Squalane	129
Hydrocarbons	Phthalates	130
Aromatic amines	2,4,7-Trinitrofluorenone	131
Alcohols	Squalane	132
Furan and its derivatives	Various	133
Halogenated hydrocarbons	Various	134
Halogenated hydrocarbons	Alkanes	135
Nitrogen-containing compounds	Aromatic hydrocarbons	136
Diphenyl methyl phosphates	Various	137
Chloroacetones	Various	138
Organic peroxides	Various	139
Oxygen-containing substances	Alkanes	140
Oxygen, hydrogen	Electrolytes	88
Hydrocarbons, nitrogen-containing substances	Squalane, octadecane, dinonyl phthalate	23
Alkanes, acetone, alcohols	Squalane, polyethylene glycol, water	87
Aromatic hydrocarbons, heterocyclic compounds	2,4,7-Trinitrofluorenone	141
Ditto	Various	142,143
Hydrocarbons, alcohols, ketones	Squalane, didecyl phthalate, triol	144
Benzene, cyclohexane, alcohol	Various	145
Hydrocarbons and other classes of compound	Water	146
Hydrocarbons	Water	147
Dichloroethane, propanol	Benzene, toluene	148
Glycols, aminoethanols	Polyethylene glycol, Apiezon	95
Ethanol, carbon tetrachloride	Dinonyl phthalate	149
Hydrocarbons, oxygen-containing compounds	Hydrocarbons	48
Hydrocarbons, halogenated hydrocarbons	Squalane, polyglycols	150
Review	Various	49,151 152

In a number of instances in gas chromatography, however, two different standard states are used in the same equation. For example, the departure of the properties of the solution from Raoult's law is taken into account by the expression $p_1 = \gamma p^0 x_1$, where p^0 is the vapour pressure of the pure solute. Since $K_2 = x/p$, we have

$$\Delta G_2 = -RT \ln \gamma p^0 .$$

In this equation the activity coefficient has the standard state corresponding to K_3, and the free energy that corresponding to K_2. Allowance must be made for the fact that in the determination of the chromatographic values of the distribution constants and specific retention volumes, an infinitely dilute solution is taken as standard state. From this it is clear that, for example, the values of the heats of dissolution obtained from the temperature dependence of the specific retention volumes and activity coefficients may differ. In the calculation of the entropy of solutions it is preferable to use an equation containing the distribution constant or the specific retention volume, if the heat of dissolution is calculated from these quantities. In a number of instances, change in the standard state has little influence on the numerical values of the quantities obtained, but in the treatment of thermodynamic quantities for the study of intermolecular interaction the choice of standard state is extremely important.

Thus examination of gas-chromatographic methods for determining the thermodynamics of solutions shows that these methods can give unique data for infinitely dilute solutions, and for solutions with finite concentrations the experimental data obtained by gas chromatography are distinguished by their high accuracy and by the low expenditure of time in the experiment. In the near future the use of gas-chromatographic methods in the study of solutions will apparently give results as fruitful as those obtained in analytical chemistry.

To conclude we are listing examples of work in which GLC has been used for the determination of the thermodynamic properties of solutions (see Table on p. 183).

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Biological Activity of Quinolinium Salts

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The review deals with problems in the study and applications of quinolinium salts as biologically active preparations; the relation between the structure of quinolinium salts and their activity is discussed.
The bibliography includes 393 references.

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I. INTRODUCTION

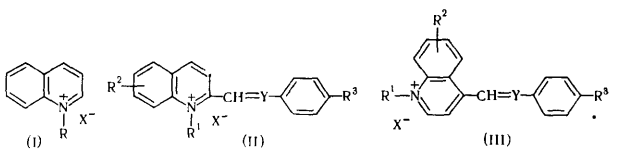
Quinolinium salts (I) have a number of very valuable physiological properties, among which the antimicrobial and antihelminthic properties have been investigated comparatively most thoroughly (although by no means completely). In the middle 1940's the antitumour properties of certain quinolinium compounds were discovered. There are data concerning the hypotensive, ganglion-blocking, carcinogenic, and mutagenic activity of various quinolinium salts. Certain quinolinium derivatives function as plant growth regulators.

During recent years, considerable advances have been achieved in the study of the physiological activity of quinolinium salts; at the present times, many such compounds have found practical application.

The methods of synthesis and chemical properties of quinolinium salts have already been reviewed [1].

II. ANTIMICROBIAL ACTIVITY OF QUINOLINIUM SALTS

In the 1920's Browning and coworkers [2] discovered the antimicrobial properties of certain quinolinium salts. The antiseptic and trypanocidal properties of styryl derivatives [(II), Y = CH] and anils [(II), Y = N], of quinaldinium were investigated in comparative detail [3-8]:



(I) (II) (III)

The analogous lepidinium (III) derivatives exhibited a very low antimicrobial activity at the beginning of the investigations, as a result of which they were not subsequently studied by this particular group of workers.

Examination of the relation between the structure and antiseptic activity revealed that even the simplest styrylquinolinium compounds [for example, II, Y = CH, R^1 = CH_3, R^2 = 6-CH_3, and R^3 = H] are active against *Staphylococcus aureus*. The presence of an amino- and particularly of a dimethylamino-group in the *para*-position of the benzene ring of the styryl substituent in compounds (IV) [II, Y = CH and R^3 = NH_2 or $N(CH_3)_2$] enhances the antiseptic activity. The displacement of these groups to the *meta*- or *ortho*-position is accompanied by a shortening of the conjugation chain involving the amino-group with a positively charged nitrogen atom and leads to a weakening of the antiseptic properties. Acylation of the aminogroup has a similar effect. When the aminogroup is shifted from the 6-position to the 4-position of the quinolinium ring, the activity against *E. coli* diminishes. However, the 4-dimethyl- or 4-diethyl-aminostyrylquinolinium salts have a very marked antiseptic activity in relation to staphylococci [9]. It is interesting that the pyridinium analogue has a lower antiseptic activity while benzoquinolinium derivatives are somewhat more active than the quinolinium salts [10].

Styrylquinolinium salts and anil derivatives of quinolinium salts are in most cases comparatively weak trypanocidal agents (against *T. brucei*) [11-14]. However, 1-methyl-2-(*p*-acetamidostyryl)-6-(aminobenzamido)-quinolinium acetate ("styryl 245") exhibits both therapeutic [15,16] and prophylactic [17] activity in relation to *T. brucei* (in mice). In addition, this compound has a synergistic effect when employed together with tryparsamide [15]. The activity of 2-(*p*-acetamidostyryl)-1-methyl-6-dimethylaminoquinolinium sulphate ("styryl 314") [18] against *T. brucei* was also investigated experimentally in mice.

It is noteworthy that the investigators were unable to discover a direct relation between the antiseptic and trypanocidal activities of the styryl and anil derivatives of the quinolinium salts investigated.

It was also established that certain styryl and anil derivatives of quinolinium salts are active against *Spirillum minus* which causes ratbite fever. 1-Methyl-2-(*p*-dimethylaminophenyliminomethyl)-6-acetamidoquinolinium chloride and sulphate show the most pronounced activity [19]. The corresponding 2-styrylquinolinium salts proved to be inactive in this respect. "Styryl 314" chloride has a very weak activity in relation to spirilla.

The work of Browning and coworkers on the above antimicrobial properties of the styryl and anil derivatives of quinolinium salts attracted the attention of scientists from many countries to these compounds. Österlin [20], who studied the relation between the trypanocidal activity of styrylquinolinium salts and their fluorescence in concentrated sulphuric acid, found that all active preparations exhibit green fluorescence. The absorption and fluorescence spectra were described in detail by Bandow [21]. Curd

and Ellingworth[22] suggested 2-styrylquinolinium compounds with amino-groups in the quinoline ring and in the styryl substituent are trypanocidal agents. Indian workers[23] investigated the effects of certain styryl and anil derivatives of quinolinium salts on paramecia. Petroff and Gump[24] studied the bacteriostatic activity of these compounds on gram-positive and gram-negative bacteria. The anils of 5,6-benzoquinolinium showed a more pronounced bacteriostatic activity: they are more active in relation to cocci but have no effect whatever on *E. coli*.

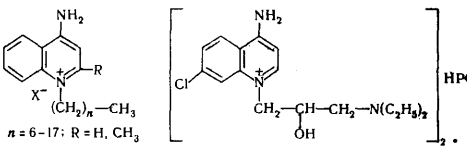
In 1941–1945 extensive studies were carried out in the U. S. A. on the antimalarial properties of many inorganic and organic substances. Various quaternary quinolinium salts were investigated among other organic compounds[25]. The activity of the compounds investigated was compared to that of quinine.

Among styrylquinolinium salts, the most active (when introduced intra-abdominally) proved to be compounds (IV) [II, $R^1 = CH_3$, $R^2 = 6\text{-}CH_3$, $R^3 = N(C_3H_7)_2$] (6 times more active than quinine), (V) [II, $R^1 = CH_3$, $R^2 = 6\text{-}CH_3$, $R^3 = N(\text{iso-}C_3H_7)_2$], and (VI) [II, $R^1 = CH_3$, $R^2 = 7\text{-}CH_3$, $R^3 = N(C_2H_5)_2$] (3 times more active than quinine). The antimalarial activity of the remaining styryl and anil derivatives of quinolinium salts did not exceed 30% of the activity of quinine. Some of them were quite inactive. It is interesting that the quinolinium salt with a phenyl group at the nitrogen atom of the quinolinium ring—compound (VII) [II, $R^1 = C_6H_5$, $R^2 = H$, $R^3 = N(CH_3)_2$, X = Cl] were described for the first time in connection with these studies. It proved to be twice as active as its *N*-methyl analogue.

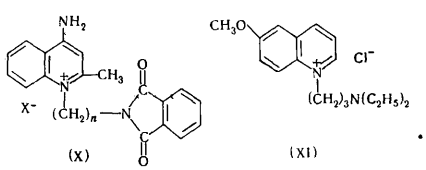
In connection with the study of chemotherapeutic properties, Rubtsov and Bunina synthesised[26] in 1943 quinolinium salts with sulphonamido-groups. The antitubercular activity of some of its compounds was tested[27].

In 1957 Japanese investigators[28] described the antibiotic activity of the "NK-458" preparation [II, $R^1 = C_2H_5$, $R^2 = 6\text{-}N(CH_3)_2$, $R^3 = N(CH_3)_2$, X = I] against trichomonads and pathogenic fungi. Taylor and coworkers[29] showed that 2-(*p*-acetamidostyryl)-1-methyl-6-methylaminoquinolinium methosulphate, an analogue of the preceding preparation, suppressed the development of pyroplasmosis in experiments on white mice. Berg[30] published a study on the synthesis and the trypanocidal properties of styrylquinolinium salts with a *m*-amidinophenyldiazoamino-group in the *para*-position of the styryl substituent. The above compounds proved to be active against *Trypanosoma rhodesiense*, *Trypanosoma congolense*, and also *Babesia rodhaini*. It was also found[31] that 1-ethyl-2-(*p*-dimethylaminostyryl)quinolinium sulphate has some fungistatic activity in relation to *Trychophyton gypseum*, *Trychothecium roseum*, *Achorion quinqueanum*, and *Epidermophyton* Kaufmann-Wolf, but is inactive against *Penicillium simplicissimum*, *Aspergillus niger*, and *Candida albicans*.

Among quaternary quinolinium salts without styryl groups in the 2- and 4-positions of the quinolinium ring, compounds containing amido- and sulphonamido-groups in the 6-position exhibit antimicrobial properties. These salts are recommended as preparations against blood parasites[32]. At the beginning of the 1930's Domagk[33] found that quaternary ammonium salts, including quinolinium salts with long-chain aliphatic substituents, have a high germicidal activity. This discovery promoted a successful search for a new antibacterial preparations. Similar compounds were suggested as disinfectants for surgical instruments, since their high antimicrobial activity is combined with a low toxicity. Shelton and coworkers[34,35] investigated the relation between the structure and germicidal activity of these salts. Some of them are produced commercially. For example, 1-laurylquinolinium bromide is used in practice as a disinfectant[36] under the name "Isotan Q-14". Tetrahydroquinolinium salts containing a long-chain hydrocarbon substituent at the nitrogen atom have antiseptic properties and their toxicity is low[37]. The fungistatic properties of certain quinolinium salts with a long chain hydrocarbon substituent at the nitrogen atom (n-hexyl, n-octyl, n-decyl, and n-dodecyl) were investigated by Zsolnai[31]. All the compounds studied proved to be inactive against *Aspergillus niger*. The last two compounds proved to be active against *Penicillium simplicissimum* and *Candida albicans*. 4-Aminoquinolinium and quinaldinium (VIII) salts with long-chain aliphatic substituents containing between 7 and 18 carbon atoms at the nitrogen heteroatom[38–41] have marked bacteriostatic and bactericidal activity:



The most effective compound in this series is 4-amino-1-dodecylquinaldinium acetate (laurolinium acetate)[42,43], which exhibits antibiotic activity *in vitro* against 32 species of gram-positive and gram-negative bacteria, pathogenic fungi, and certain protozoa. In relation to plasmodia, such salts are apparently relatively ineffective. Thus the activity of preparation (IX) amounts to 40% of that of quinine[25]:



Taylor and Austin[44] developed a method of synthesis of 4-aminoquinaldinium salts of type (X), which are intermediates in the synthesis of medicinal preparations. When the amino- or alkylamino-group is in the 2- rather than the 4-position of the quinolinium ring, the preparation loses its activity. Thus 2-alkylaminoquinolinium and 2-arylaminoquinolinium salts do not exhibit appreciable antiseptic, trypanocidal, and antimalarial activities[45].

Since 8-hydroxyquinoline has a fairly pronounced bactericidal and bacteriostatic activity, numerous quaternary derivatives of hydroxyquinolines were investigated. Müller[46] studied the toxicity and bacteriostatic activity of 8-hydroxy-1-methylquinolinium salts against cocci, *E. coli*, and brucellae. The salts containing high-molecular-weight anions (benzoates and stearates) showed a more pronounced specific bacteriostatic activity, while the corresponding sulphate does not exhibit an appreciable antibacterial activity[47]. However, it was found that salts of 1-alkyl- and 1-arylalkyl-8-hydroxyquinolinium, containing an acyl or nitro-group in the 5-position and an alkyl group in the 7-position, show an appreciable antifungal and bactericidal activity[48]. Various hydroxyquinolinium esters have been suggested as disinfectants[49–51]. Vogt[52] made a detailed study of esters of 8-hydroxyquinolinium and showed that, with increase of the chain in the aliphatic acid group (forming part of the ester group) up to 16 carbon atoms, the activity of the compound rises. The introduction of a thiocyanato-group into the quinoline ring of these compounds leads to a considerable enhancement

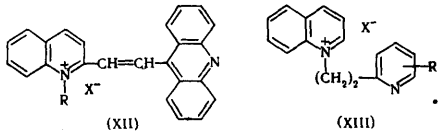
of their bactericidal activity [53,54]. One of the most active compounds of this group is 8-n-butoxy-1-methyl-5-thiocyanatoquinolinium sulphate. Its bactericidal activity against *E. coli* is still apparent at a dilution of 1 : 100 000. Buchmann [55,56] studied the activity of the methyl and ethyl ethers of 4-hydroxy-1,6-dimethyl quinolinium iodide against *Aspergillus niger*, *E. coli*, and *Staphyllococcus aureus*. Although the activity of the preparations was low, it is interesting to note that the ethyl ether proved to be 20 times more active than the methyl ether in relation to *E. coli* and almost twice as active against *Staphyllococcus aureus*. In a study of the antimalarial activity of hydroxyquinolinium derivatives, it was established[25] that, whereas 6-methoxy-1-methylquinolinium iodide exhibits 15% of the activity of quinine, its 1-benzyl analogue is twice as active and preparation (XI) is 10 times as active as quinine. It is also interesting to note that the betaine of 2-hydroxy-1-methylquinolinium has a considerable prophylactic activity against *P. gallinaceum* in chicks (it is almost 8 times as active as sulphadiazine). The antibacterial properties of certain 8-alkoxyquinolinium salts, among which the most active proved to be the 1-methyl-8-octyloxyquinolinium salt, were investigated recently [57].

Among other quinolinium salts with antimicrobial activity, mention should be made of the 1-aryloxymethyl [58], 1-alkylnaphthyl [59], and 1-β-halogenophenoxymethyl derivatives [60]. The latter also exhibit antifungal activity and are more active than the analogous pyridinium salts.

Quinolinium salts containing as the anion a sulphonic acid residue with a long aliphatic chain were also synthesised. They proved to be highly effective bactericidal and fungicidal agents [61]. Sparingly soluble quinolinium salts containing anions of heavy-metal complex acids have been recommended as antifungal and antibacterial preparations (including preparations effective against plant pests) [62].

As a rule quaternary quinolinium salts are more active than the tertiary quinoline bases. However, 4-(2′-nitrovinyl)quinolinium salts proved to be inactive against *Trichomonas vaginalis* and *Candida albicans*, while the corresponding tertiary bases are very effective in this respect [63].

The antimicrobial properties of quinolinium salts with a further heterocyclic ring have also been investigated:

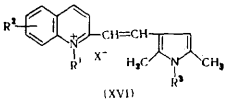


(XII)

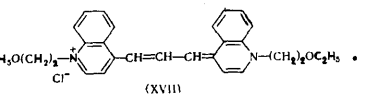
(XIII)

Compounds of type (XII) appreciably suppress the growth of staphylococci at a dilution of 1 : 40 000 in water, but are inactive against trypanosomas [64,65]. 7-Chloro-4-[1′-methyl-4′-1(1″-pyrrolidinyl)butylamino]quinolinium salts have been recommended as antimalarial preparations [66]. However, it is interesting to note that quinine ethiodide shows only 8% of the activity of the tertiary base [25]. 1-[2′-(2″-Pyridyl)ethyl]quinolinium salts (XIII) show fungicidal activity [67].

Quinocyanine dyes, the molecules of which consist of two and more heterocyclic rings (not less than one of which is a quinoline ring) joined by a polymethine chain, are interesting derivatives of quinolinium salts. The first studies on the antimicrobial activity of cyanine dyes with quinolinium rings were carried out by Browning et al. [68] Sensitol red (Pinacyanol), violet, and green were tested against *E. coli* and *Staphylococcus aureus*. Among these sensitol green [Ethyl Red, (XIV)] proved to be the most effective suppressing the growth of *Staphylococcus aureus* at a dilution of 1 : 100 000 in serum and of *E. coli* at a dilution of 1 : 10 000.



(XVI)



(XVII)

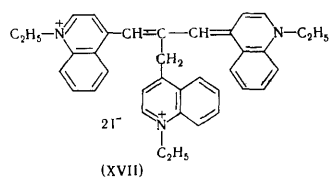
Somewhat later the same investigators[69] published the results of studies on the antiseptic properties of apocyanines, isocyanines, and carbocyanines of the quinolinium series. They did not find among these cyanine dyes compounds meriting attention. At almost the same time Karwacki and Biernacki [70] discovered that a cyanine dye has a slight effect on the micro-organisms responsible for tuberculosis. Petroff and Gump [24] studied the effect of quinolinium dyes (XIV), ethylcyanine T, orthochrome T, and Pinacyanol on gram-positive and gram-negative micro-organisms. The study of the antimalarial activity of cyanine dyes during the second World War [25] showed that the simplest cyanine dyes with two quinoline rings in the molecule exhibit as a rule a low antimalarial activity (15–30% of that of quinine). Carbocyanine (XV) proved to be more active, showing 80% of the activity of quinine. It is interesting that its isomer, 2,2′-trimethinecyanine, is almost 3 times less active (30% of the activity of quinine). Certain quinocyanine dyes—pseudocyanine, isocyanine, and dicyanine in the form of methochlorides—exhibited less than 20% of the activity of quinine in the treatment of chicks infected with *P. gallinaceum*; the activity of Pinacyanol and cryptocyanine was less than 15% than that of quinine. The data from the Rockefeller Institute of Medical Research [25] also indicate that the methochlorides of cyanine, isocyanine, Pinacyanol, dicyanine, 6,6′-dimethylcyanine, and carbocyanine are inactive in relation to these parasites. The activity of Quinolinium Blue is less than 3% of that of quinine against *P. lophurae* in ducks. Among asymmetric quinocyanine dyes, the dimethines with the general formula (XVI) were investigated in greater details. The effect of the substituents R^1, R^2, and R^3 on the antimalarial activity of the compounds was studied.

In 1947 Brooker and Sweet [71] published a short report on the results of chemotherapeutic studies on cyanine dyes. They note that preparation (XVI) ($R^1 = CH_3$, $R^2 =$ 6-CH_2, and $R^3 =$ n-C_5H_{11}) completely suppresses the growth of *L. casei*, *L. arabinosus*, *Streptococcus faecalis*, and *E. coli* at concentrations of the order of $(2–4) \times 10^{-6}$ M. Individual representatives of various classes of cyanine dyes were tested *in vivo* against *Streptococcus haemolyticus*, *Streptococcus viridans*, *Staphylococcus aureus*, *Diplococcus pneumoniae*, *Trypanosoma equiperdum*, and *Treponema pallidum*, which are responsible for encephalitis, influenza, typhus, and a group of interstinal parasites, and also *in vitro* against *Entamoeba histolytica*. Although individual compounds showed a distinct activity against the above micro-organisms, the authors believe that the activity is not high enough to be of therapeutic value. However, Silverman [72,73] reported that 1,1′-dimethyl-2,2′-cyanine iodide suppresses the growth of *E. coli*, although the Ca^{2+} cation behaves as an antagonist. It was also found [74,75] that Quinolinium Blue (1,1′-dipentyl-4,4′-cyanine iodide) is extremely active *in vitro* against the organism responsible for diphtheria and against gram-positive cocci, including *Staphylococcus aureus*. In view of its low toxicity, the preparation was recommended as a therapeutic agent. However, the compound is inactive in relation to pathogenic fungi [31]. Ryzhikov et al. [76] reported that Quinolinium Blue is a moderately strong inactivator of the

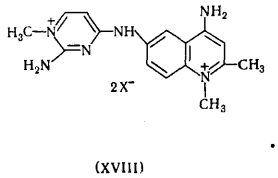
tobacco mosaic virus, suppressing its activity to the extent of 63%. However, later studies by Bobir [77] showed that the preparation is completely indifferent in relation to the above virus.

In 1951, almost 30 years after the studies of Browning [68], it was found that Pinacyanol shows a high bactericidal and bacteriostatic activity against cocci and the organism responsible for diphtheria, whilst its toxicity is very low [78].

A study was also made of the physiological properties of quinocyanine dyes with 3 ring systems. The interaction of 1-ethyl-lepidinium iodide with triethyl orthoformate in acetic anhydride or in dry pyridine are known to give a mixture of polymethine dye, called Lumin (or the Cryptocyanine OA complex). Somewhat later this mixture was separated into components, which were called cryptocyanines 1, 2, 3, 4, and 5 respectively. Cryptocyanine 1 proved to be identical with the so called neocyanine or Koha No. 1 (XVII):



(XVII)



(XVIII)

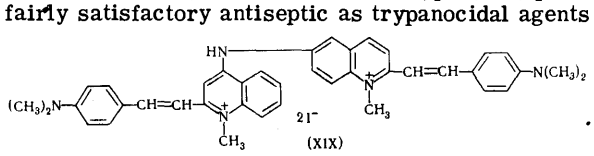
The physiological activity of both the non-purified dye (Lumin), with about 92% of Koha No. 1, as well as that of the individual components, mainly pure Koha No. 1, were investigated by Japanese workers. A detailed study was made of the optimum conditions for the formation of compound (XVII). [79] Hatano [80] found that compound (XVII) exhibits antitubercular activity. Miyazaki [81] reported that Lumin has an appreciable effect in the treatment of human leprosy, 81.9% of 371 patients showing some improvement and only 1.6% deteriorating after a 10 month course of treatment by this preparation. At the same time pure Koha No. 1 has undesirable side effects. However, investigations by other workers showed that this preparation is not quite so effective in the treatment of both experimental and human leprosy [83,84]. Sato and Chida [85] made a more detailed study of the effect of the non-purified product and pure Koha No. 1 on organisms responsible for tuberculosis and for human and experimental rat leprosy. The preparations showed tuberculostatic activity against the Aoyama strain in a dilution of 1 : 100 000–1 : 50 000. However, in relation to the natural organism responsible for tuberculosis, the activity of these compounds was shown only at a dilution of 1 : 10 000. The preparations had no effect on experimental leprosy and did not exhibit a promising therapeutic activity on human leprosy. A study was also made of the antiviral activity of Koha No. 1 in relation to coliphage [86] and of its bactericidal activity against certain pathogenic bacteria [87]. The compound has an appreciable bactericidal activity against *Staphylococcus albus*. Partial suppression is also observed in the case of *E. coli*, *Salmonella typhosa*, and *Shigella dysenteriae*. In all cases the activity increases with the alkalinity of the medium (up to pH 10).

The effect of cyanine dyes on the respiration of *Staphylococcus aureus* and *S. typhi* was investigated [88].

Diquaternary salts with one or two quinolinium rings have very interesting antibiotic properties.

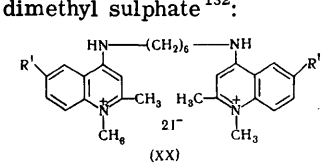
In 1949 a new very effective trypanocidal agent was described [89]; it is a diquaternary quinolinium salt called antrycide (XVIII) (synonyms: quinapyramine, pyraldine). It is active against various trypanosoma species [*T. congolense*, *T. brucei*, *T. evansi* (India and the Sudan), *T. equiperdum*, *T. equinum*, and *T. vivax*]. Veterinary field tests in Africa showed that antrycide salts are effective in both prophylactic and therapeutic treatment [90–93]. Antrycide has been used as the dichloride, the dimethosulphate, or in the form of a mixture of these two salts, the so called "pro-salt". This discovery stimulated the study of similar compounds and in recent years a number of publications dealing with the methods of synthesis of the isomers and analogues of antrycide have appeared [94–107]. New methods have also been developed for the determination of antrycide [108] in biological objects. The chemotherapeutic properties of antrycide were investigated in greater detail by workers in various countries [109–116]. Moreover, studies were performed both with a view to finding more effective therapeutic forms of antrycide in the treatment of trypanosomiases and in order to investigate the effects of antrycide on micro-organisms responsible for other diseases. Tests on mixtures of antrycide with other trypanocidal preparations led to the discovery that a complex of antrycide with suramin is less toxic than antrycide itself [117,118]. The complex also exhibits prophylactic and therapeutic effects in diseases of swine caused by *T. simiae* [119–121]. In tests of antrycide against other pathogenic agents, it was found that the preparation is active against the European trypanosomiasis of horses [122–124], su-auru [125], and the trichomoniasis of cattle [126]. The compound also effects a complete cure in mice infected with *Babesia rodhaini* [29]. Among the reviews in which antrycide is discussed, mention should be made of Williamson's review [127] dealing with the chemotherapy and chemoprophylaxis of African trypanosomiasis and also the review on the mechanism of the action of trypanocidal agents [128]. Babesicidal properties of an analogue of antrycide with a phenyl group in the 2-position of the quinoline ring have also been described [129].

Bisquinolinium salts are effective antimicrobial preparations. Jensch [130] suggested that azo-compounds in which the azo-group is joined to two quinolinium rings be employed as therapeutic preparations against blood parasites. Bis-styrylquinolinium salts of type (XIX) proved to be fairly satisfactory antiseptic as trypanocidal agents [13]:

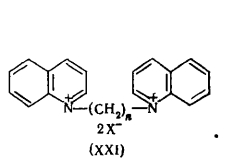


(XIX)

When two moles of 4-methoxy-1-methyl- or 6-amino-(dimethylamino- or methoxy)-4-chloro-quinaldinium iodide react with one mole of hexamethylenediamine, bisquinaldinium salts (XX), which exhibits trypanocidal properties, particularly against *T. rhodesiense*, are formed [132]. These preparations can also be obtained by the methylation of the corresponding tertiary base at the nitrogen heteroatom with dimethyl sulphate [132]:



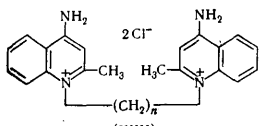
(XX)



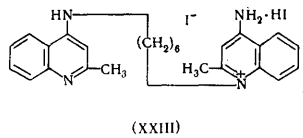
(XXI)

Collier et al. [133] tested the antifungal activity of bisquinolinium salts (XXI) in which both nitrogen atoms are joined by a polymethylene chain. The activity of these compounds, containing between 10 and 20 CH_2 groups, increases with increase of the number of methylene groups to 14–16, after which it falls again. The most active of these (XXI, $n = 14$, 16) inhibits the growth of many pathogenic fungi at a concentration of 0.3–10 μ g ml^{-1}. At the same time the preparations are relatively non-toxic for

warm-blooded animals. Subsequently, in a study of analogues of these compounds, Babs, Collier, and coworkers[134] described in 1956 a new highly effective antibacterial and antifungal agent, which they called Dequadin-1,1′-decamethylenebis-(4-aminoquinaldinium chloride) (XXII, $n = 10$). The preparation is also known as Dequalinium, Decatylene, and Decamine.



(XXII)



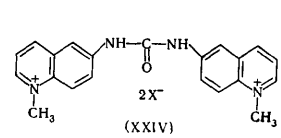
(XXIII)

The preparation is very effective *in vitro* against various gram-positive (cocci, corynebacteria) and gram-negative (intestinal bacteria, salmonellae, proteus, and cholera vibrio) micro-organisms and also against pathogenic fungi[134-136]. In addition Dequadin exhibits a synergistic activity when employed together with antibiotics. However, cases are known of an allergic response in Dequadin therapy after prolonged administration of antibiotics[137]. It is also active against certain pathogenic protozoa, in particular *Trypanosoma congolense*[138], but it is only slightly effective *iv vivo* against *Entamoeba histolytica*[139]. It is noteworthy that the isoquinolinium analogue of Dequadin showed a low trypanocidal activity. Dequadin has also been used as a disinfectant in dental practice[140] and in the surgery of the oral cavity[141], for the local treatment of wounds in humans and animals[142], for the treatment of vaginites caused by *Trychomonas* and *Candida*[143-146], trichophytosis of cattle[147], fungal affections of the skin[148-150], diseases of the throat and respiratory organs[151-153], including those of young children[154,155], and also other diseases[156-158]. Under the name Decamine, this preparation was adopted by the Soviet Pharmacopoeia as a therapeutic agent; various therapeutic forms of the substance have been developed[159-161].

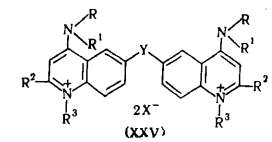
In connection with the very high antibiotic activity of Dequadin, a detailed study was made of its homologues, isomers, and analogues[134,162,163]. A number of patents have been taken out, both for the methods of preparation of Dequadin and analogues and also for its various therapeutic forms[164-170]. In many reviews dealing with new chemical preparations, a fair amount of attention has been devoted to this compound[139,148,171-173].

Homologues of Dequadin containing a smaller number of methylene groups ($n = 6$ and 8) show a considerable activity against *Trypanosoma rhodesiense*[162,174]. Buchmann[56] found that 1,1′-hexamethylenebis(7-methylquinolinium iodide), a Dequadin analogue, is active against *Staphylococcus aureus* and *E. coli*. A report was published in 1967 that certain analogues of Dequadin in the form of acetates with a secondary amino-group in the 4-position of the quinaldinium ring exhibit a higher antimicrobial activity than the unsubstituted preparation. The maximum activity is shown by substances with C_3–C_6 alkyl substituents. However, the toxicity of the preparations is also enhanced. When 4-aminoquinaldine reacts with 1,6-di-iodohexane, 6-(4-quinaldinyl)aminohexyl-4-aminoquinaldinium hydriodide iodide, called tozocide (XXIII), is formed together with the symmetrical compound (XXII, $n = 6$). The preparation is highly active against *Trypanosoma congolense* and *Trypanosoma vivax*, and is more active than both symmetrical isomers[174,176].

Among other bisquinolinium salts with antibacterial properties, mention should be made of bis-1-(6-methylquinolinium)urea salts [Babesan, Pyroplasmin, Acaprin (XXIV)][177,178] which have been recommended for the treatment of pyroplasmosis and taylorosis of domestic animals[179-182]. In addition, Babesan also exhibits an antimalarial activity[25]. The disadvantages of Babesan include the short duration of its action[181] and toxicity[183,184].



(XXIV)



(XXV)

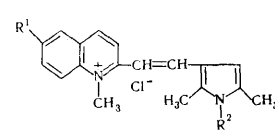
where Y = NH, O, S, or CH_2, R, R^1 = H or alkyl, and R^2, R^3 = alkyl.

Babesan analogues of type (XXV) have also been recommended as preparations for the treatment of piroplasmosis and taylorosis of animals[129,185].

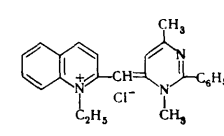
III. ANTIHELMINTHIC ACTIVITY OF QUINOLINIUM COMPOUNDS

Helminthic diseases in man, animals, and birds are very common. About 40% of the earth's population and a large number of animals are infected by pathogenic worms[186]. According to Stoll's data[187], more than 800 million people are affected by helminthiases. The losses in animal husbandry in the USSR due to helminthiases in 1960 amounted to approximately 58 million roubles per annum[188]. Therefore much attention has been devoted to the development of means of combating helminthic infestations. Thus at an SEV [significance of Russian abbreviations obscure (Ed. of Translation)] session in May, 1963 it was resolved that particular attention should be paid to the manufacture of antihelminthic preparations[188].

Among antihelminthic agents, quinolinium derivatives occupy a major place. The study of quinoline derivatives as antihelminthic agents was begun by the work of Brooker and Sweet[71], who synthesised in 1947 a number of quinocyanine dyes with pronounced antihelminthic properties[189]. Studies on a large number of similar compounds showed that two nitrogen atoms separated by an even number of conjugated bonds constitute an essential group for antihelminthic activity. Among all the compounds investigated, compounds (XXV), (XXVII), and (XXVIII) proved to be the most effective.



(XXVI, $R^1 = CH_3$; $R^2 = C_6H_{11}$)
(XXVII, $R^1 = N(CH_3)_2$; $R^2 = C_6H_5$)



(XXVIII)

The first of these, compound (XXVI), has been recommended as a therapeutic agent against *Litomosoides carinii*. Clinical tests on compound (XVIII) against *Wuchereria bancrofti* showed that the preparation is effective against microfilaria but not against the adult parasites[190]. However, when organisms responsible for onchocerciasis are acted upon, the compound kills adult filaria but does not affect the microfilaria[191]. The investigators note an undesirable[191] albeit non-systematic[189] side effect of this preparation. The mechanism of the action of compound (XXVII) on helminthes[192] and on the development of the embryos of *Litomosoides carinii* has been investigated[193]. Pyrimidoquinocyanine dyes of

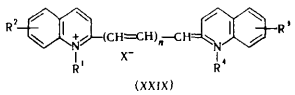
type (XXVIII) have been patented as antihelmintic preparations [194].

Compound (XVIII) has a very satisfactory therapeutic activity. It has been patented under the names Poquil, Vanquin, Povan, Moleac, Pyrvinium, and Pyrroviniquinium [195,196]. Poquil chloride has a high antihelminthic activity in the chemotherapy of enterobiasis and strongylidosis [197-203]. Apart from the chloride, the products of the interaction of phenolphthalein with Poquil is also recommended [204]. Recently reports have been published about the successful application of Poquil pamoate. This preparation is less toxic, since it is sparingly soluble in water and is not absorbed from the gastrointestinal tract in appreciable amounts [205,206] and it does not have a bitter taste [207].

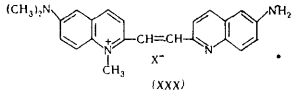
Poquil pamoate has been successfully employed in the treatment of animals and children both as an individual preparation [208-223] and in combination with piperazine [224,225] (preparation Cl-578). The antihelminthic activity of Poquil embonate in enterobiasis has also been investigated [226-228]. However, this preparation is less effective than the pamoate [sic!, embonate and pamoate are trivial names of the same anion (Ed. of Translation)].

The effect of pyrimido- and pyrrolo-quinocyanines of type (XXVI)-(XXVIII) on the metabolic processes in parasites [229-232] and also their side effects and toxicity [189-191,198,205,208,209,233-236] have been investigated.

At the beginning of the 1960's a number of patents for the application of trimethine (XXIX, $n = 1$) and pentamethine (XXIX, $n = 2$) quinocyanine dyes with symmetrical and asymmetric structures, dyes of type (XVII) with three ring systems [237], and also 2-styrylquinolinium salts (II) [238,239] were published.



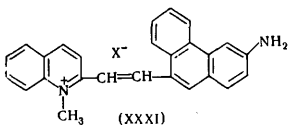
(XXIX)



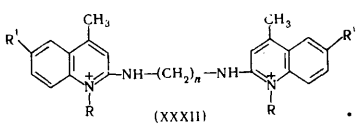
(XXX)

Pentamethine quinocyanines (XXIX, $n = 2$) are very effective antihelminthic agents with a wide spectrum of activity and are recommended for the treatment of helminthiases in man, animals, and birds. Together with a high therapeutic index, they are characterised by a low toxicity, which distinguishes them favourably from their extremely toxic benzothiazole analogue (Dithiazanine). *p*-Dimethylaminostyrylquinolinium salts show a high activity against the larvae of *Ascaris suum*, the larvae and adult forms of tapeworms and also in certain sheep helminthiases caused by *Trichostrongylus colubriformis* [238,239].

In addition the antihelminthic properties of compounds of type (XXX) and (XXXI) [240] and also of bisquinolinium, bis-4-aminoquinaldinium [241], and bis-2-aminolepidinium salts (XXXII) [242] have been investigated.



(XXXI)



(XXXII)

The latter are recommended for the treatment of animals infected with *Syphacia obvelata*, *Hymenolepis nana*, *Dypilidium caninum* and *Taenia pisiformis*.

In conclusion it should be noted that in many reviews dealing with antihelminthic agents considerable attention has been recently devoted to quinolinium derivatives [139,187,188,243-250].

IV. RADIOMIMETIC ACTIVITY OF QUINOLINIUM SALTS

The action of chemical agents on living organisms resembling the effect of radioactive ionising radiation is called radiomimetic [251]. For example, it is known that small doses of radioactive emission have an antiblastic activity, which is used in the treatment of malignant tumours. However, more prolonged action of such radiation causes the appearance of malignant neoplasms (oncogenic activity). In addition, they all have a mutagenic activity.

Certain quinolinium salts have a complete set of the above properties, but some of these have been investigated quite inadequately.

a. Oncogenic Activity of Quinolinium Salts

The oncogenic properties of certain styrylquinolinium salts were first reported by Browning [252,253], who observed that a single subcutaneous administration of 6-acetamido-2-(*p*-aminostyryl)-1-methylquinolinium acetate [Styryl 430, (XXXIII)] results in the appearance of a sarcoma at the site of administration after a certain period. This property has been used for the induction in white mice of an experimental sarcoma [254], the cell chromosomes of which were investigated by Arroyo and Murcia [255]. Another dye [(II, $R^1 = CH_3$, $R^2 = H$, $R^3 = N(CH_3)_2$, Y = CH, and X = SO_4CH_3)] causes malignant affections of the intestinal tract after systematic administration to rats in food over a period of one year (at a dose of 800 mg kg^{-1}) [256]. In connection with the oncogenic activity of compound (XXIII), its effects on the respiration of live cells [257] and on the ability of rats to swim [258] were investigated. Like other carcinogenic agents, the preparation suppresses cell respiration and reduces the capacity of rats for work.

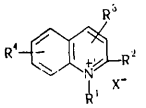
b. The Antitumour Activity of Quinolinium Salts

In recent years the search for effective antitumour agents has been considerably intensified. Among other compounds, numerous quinolinium derivatives were investigated. Shear et al. [259] noted that certain quaternary pyridinium and quinolinium salts decompose sarcoma cells, which attracted much attention to them. However, in a more systematic study it was found that *N*-alkylquinolinium salts unsubstituted in the 2- and 4-positions do not show any activity against sarcoma 180, adenocarcinoma 755, and leukaemia L1210 [260-266] (see Table).

Compounds (XXXIV) and (XXXV) (see Table) are an exception, showing a weak activity against carcinoma and the latter also against sarcoma. At the same time many quinolinium salts containing phenylethyl [(XXXVI) and (XXXVII)], phenylacyl [(XXXVIII)-(XLVI)], and β-naphthoylmethyl [(XLVII) and (XLVIII)] groups at the nitrogen heteroatom are active against sarcoma and some also against adenocarcinoma.

It is interesting to note that, while the simplest quinolinium salts are inactive against sarcoma and carcinoma, the analogous quinaldinium salts containing a methyl group in the 2-position of the quinoline ring exhibit a distinct albeit slight activity in relation to sarcoma [(XLIX)-(LI)]. A similar activity is shown by 2-phenyl-substituted [(LIV)-(LVI)] and 2-styryl-substituted [(LVII)-(LXVI)] quinolinium salts. Some of these are active also in relation to adenocarcinoma (see Table). Quinolinium salts (LVII) with an azomethine group in the 3-position also show

Quinolinium salts active against sarcoma 180 (Sa) and adenocarsinoma 755 (Ca).



Quinolinium salt	R^1	R^2	R^3	R^4	X	Inhibition, %		References
						Sa	Ca	
XXXIV	CH_2COOH	H	H	H	Cl	—	26	266
XXXV	CH_3	H	4-$NH(CH_2)_5CN$	6-OCH_3	I	29	23	267
XXXVI	$CH_2CH_2C_6H_5$	H	H	H	Br	—	55; 32	268
XXXVII	$CH_2CH_2C_6H_5$	H	H	6-Cl	Br	50; 38	56; 45	265
XXXVIII	$CH_2COC_6H_5$	H	H	6-OCH_3	Br	45	21	263
XXXIX	$CH_2COC_6H_4OCH_3$-*p*	3-Br	H	H	Br	46		263
XL	$CH_2COC_6H_4Br$-*p*	H	H	H	I	28	27	263
XLI	$CH_2COC_6H_4Cl$-*p*	H	H	6-Cl	Br	43	—	263
XLII	$CH_2COC_6H_4Br$-*p*	H	H	6-Cl	Br	27	—	269
XLIII	$CH_2COC_6H_4C(CH_3)_2$-*p*	H	H	6-Cl	Br	27		269
XLIV	$CH_2COC_6H_4Br$-*p*	H	3-Br	H	Br	49; 38	35	263
XLV	$CH_2COC_6H_4Cl$-*p*	H	3-Br	H	Br	19	19	263
XLVI	$CH_2COC_6H_4SCH_3$-*p*	H	H	6-OCH_3	I	49; 27	—	265
XLVII	CH_2CO-β-naphthyl	H	H	6-Cl	Br	29	—	265
XLVIII	CH_2CO-β-naphthyl	H	H	8-OH	Br	—	31	265
XLIX	C_2H_5	CH_3	H	6-CH_3	I	32	38	270
L	C_2H_5	CH_3	4-CH_3	H	I	27	—	269
LI	C_2H_5	CH_3	H	H	I	44	—	262
LII	CH_3	CH_3	H	H	I	—	23	271
LIII	$COOC_2H_5$	CH_3	H	H	Cl	37	—	266
LIV	CH_3	C_6H_4Cl-*o*	3-OCH_3	H	I	25	57; 25	264
LV	CH_3	C_6H_4F-*o*	H	H	I	25	22	264
LVI	CH_3	C_6H_4F-*o*	3-CH_3	H	I	33	62; 33	264
LVII	CH_3	CH=CH—C_6H_4OH-*o*	H	8-OH	SO_4CH_3	33	22	272
LVIII	CH_3	CH=CH—C_6H_3OH-*p*-(OCH_3)-*m*	H	8-OH	SO_4CH_3	24	—	272
LIX	CH_3	CH=CH=(1)-naphthyl-2-OH	H	8-OH	SO_4CH_3	38	—	272
LX	CH_3	CH=CH—C_6H_4Cl-*o*	H	H	I	24	28	264
LXI	CH_3	CH=CH—$C_6H_4NO_2$-*p*	H	H	I	59; 17	29	264
LXII	CH_3	CH=CH—C_6H_5	H	H	I	14	43	264
LXIII	CH_3	CH=CH—C_6H_4Cl-*p*	H	H	I	38	—	264
LXIV	CH_3	CH=CH—$C_6H_4NO_2$-*m*	H	H	I	37	—	264
LXV	CH_3	CH=CHC$_6$H$_3$OH-*p*-(OCH_3)-*m*	H	H	I	16	—	264
LXVI	CH_3	CH=CH—$C_6H_4NH_2$-*p*	H	6-$NHCOC_6H_4$— —$NHCOCH_3$-*p*	CH_3CO	62	—	265
LXVII	CH_3	CH=N—$C_6H_4N(CH_3)_2$-*p*	4-Cl	6-OCH_3	Cl	21	43	273
LXVIII	C_2H_5	CH=CH—$C_6H_4(CH_3)_2$-*p*	H	H	I	43	—	265

a slight activity. However, it is noteworthy that many styryl-substituted quinolinium salts proved to be virtually inactive against these types of tumours [260,263,271,274-276]. Certain 2- and 4-*p*-dimethyl(diethyl)aminostyrylquinolinium salts also proved to be inactive against leukaemia and Ehrlich ascites carcinoma when administered in combination with irradiation by X-rays [277].

In a study of the activity of styrylquinolinium salts against other malignant tumours, it was found that 1-methyl-4-(*p*-dimethylaminostyryl)quinolinium iodide (LXIX) and chloride (LXX) are exceptionally active against lymphoma 8, [278,279] suppressing completely the tumours in rats. It is interesting to note that, whereas compound (LXX) is active only when administered orally, compound (LXIX) is also active when injected subcutaneously. Slight changes in the structure of styrylquinolinium have a very marked influence on its antitumour activity. The replacement of the *p*-dimethylamino-group by the *p*-diethylamino group greatly reduces the activity of the preparation [280].

The migration of the *p*-dimethylaminostyryl group from the 4-position in the quinoline ring to the 2-position involves a complete loss of antilymphoma activity. In a study of the effect of preparations of type (LXIX) and (LXX) on other types of tumours, it was found that adenocarcinoma 11 also regressed in the majority of animals, but the effect of the preparations on this tumour is somewhat weaker. However, in experiments on mice, both in the case of spontaneously generated carcinoma of mammary glands and the transplanted carcinoma, preparation (LXIX) proved to be inactive.

In a study of the activity of this preparation and 4-styrylquinolinium against the Walker tumour [250], the tertiary base proved to be more active [281-283]. Preparation (LXIX) was found to be inactive against Nelson mouse ascites tumour [284] and against leukaemia L1210. [285,286] Compounds (LXIX) and (LXX) and also an isomer of the former, containing the *p*-dimethylaminostyryl group in the 2-position of the quinoline ring (LXXI), exhibited a cytotoxic activity to an extent proportional to their antitumour activity [287-289].

Compound (LXXI) and its 1-ethyl homologue are inactive against lymphoma 8 [280] and leukaemia [285,286,290], but they do suppress the growth of Walker carcinoma 256. [291] In addition, the activity of (LXXI) was investigated *in vitro* on cells of sarcoma 180 of mice and on four human tissue cultures [292]. A study was also made of the suppression of glycolysis by these preparations [293].

Various derivatives and analogues of compounds (LXIX)–(LXXI) were also investigated in order to elucidate the relation between structure and antitumour activity [294,295]. It was found that the vinylogue of compound (LXIX) is completely inactive against lymphoma 8. [296] The replacement of the quinoline ring by the isoquinoline ring reduces the antilymphoma activity [297] and the replacement of the *p*-$N(CH_3)$ group by F causes a complete loss of activity [298].

In an examination of the mechanism of the action of styrylquinolinium salts on normal and neoplastic cells, it was suggested that the antitumour activity of these compounds is determined by the quinoline part of the molecule, while the aminostyryl group is involved in the attachment

of the molecule to important sections of the tumour cell[295]. According to Bahner et al.[299], the above salts interact with sulphydryl groups in cysteine. The fate of styrylquinolinium compounds in the animal organism was investigated[300] and a highly sensitive method for the detection of these compounds was developed. Certain of the styrylquinolinium salts and anil derivatives of quinolinium salts containing the mustard gas group in the benzene ring of the styryl substituent have been patented as effective anticancer preparations[301].

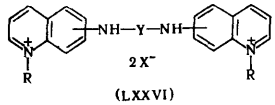
In 1963 Hirschberg[302] published a very brief compilation of the literature on the antitumour properties of certain styrylquinolinium salts.

Cyanine dyes with quinoline rings have also been tested for anticancer activity. It was found that compounds of type (XVI) are very weak carcinostatic agents or inactive. Thus compound (LXXIII) [XVI, $R^1 = CH_3$, $R^2 = 6\text{-}N(CH_3)_2$, $R^3 = C_6H_5$, and X = Cl] does not suppress sarcoma 180,[275] while its analogue with $R^1 = CH_2CH_2OH$ and $R^2 = 6\text{-}CH_3$ is inactive against carcinoma and leukaemia L1210, suppressing sarcoma very slightly (to the extent of 27%)[303]; compound (LXXI) [XVI, $R^1 = CH_3$, $R^2 = 6\text{-}CH_3$, $R^3 = C_5H_{11}$, and X = Cl] prolongs the life of animals suffering from leukaemia almost by a factor of 2.[304] 1-Methyl-4-[2′(4″-pyridyl)vinyl] quinolinium iodide is inactive against all three tumours[305]. Among symmetric quinocyanine dyes, cryptocyanine was tested for its activity against leukaemia. It proved to be inactive[306], although it suppresses the growth of a KB tissue culture to the extent of 50% at a concentration of 1.4×10^{-1} μg ml^{-1}.[268] Orthochrome T [bis-(1-ethyl-6-methylquinoline-2-yl)trimethinecyanine iodide] is also inactive against sarcoma 180, carcinoma, and leukaemia L2110.[265]

At the same time Quinolinium Blue at a dilution of 1 : 2000 proved to be very active against Ehrlich carcinoma[75,307]. The action of quinocyanine dyes with three rings against malignant tumours was also studied. Neocyanine (LXXV) suppresses sarcoma 180 to the extent of 21–51%.[265] Japanese investigators reported that it is also active against cancer tumours and its effectiveness is higher when administered orally than in local administration[308]. The use of compound (LXXV) in the treatment of Hodgkin's disease has been reported[309]. Mizuno[310] notes that cyanine dyes (the formulae and names are not quoted) suppress *in vitro* the growth of a tissue culture of Erlich carcinoma, sarcoma 180, and Yoshida sarcoma.

In a study of bisquinolinium salts of type (XXI) (X = Br), it was found that, when $n = 2$, the compound suppresses carcinoma to the extent of 45%, but the degree of suppression is only 24% when $n = 3$,[263] and when $n = 4$ the compound is inactive. The decamethylene derivative ($n = 10$) is also inactive against carcinoma but suppresses to the extent of 30% Erlich ascitices tumours[263]. A study was also made of the activity of compounds (XX) against sarcoma and carcinoma[267].

Bisquinolinium salts with a general formula (LXXVI) have recently attracted attention owing to their activity against leukaemia:



(LXXVI)

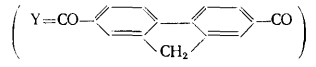
(LXXVII, Y = OC–C_6H_4–CO).

The activity of 6-substituted derivatives of quinoline is more pronounced with R = C_3H_7 and C_4H_9, falling rapidly in the case of higher homologues.

It has been found[311] that the physiological activity of compounds (LXXVI) is directly related to their lypophilic and hydrophilic properties. The replacement of the terephthaloyl residue by that of pyridine-2,5-dicarboxylic acid leads to some decrease of activity and its replacement by the isophthaloyl residue or the residue of an aliphatic dicarboxylic acid causes a loss of activity. A similar result is obtained when the –NHCOC_6H_4CONH– group joins the quinoline rings in the 5- and 7-position. A slight activity is also shown by derivatives of *p*-carboxyphenoxyacetic acid (LXXVI, Y = CO–C_6H_4–OCH_2CO).[311]

When the Y = COC_6H_4NHCONHC_6H_4CO group is introduced into (LXXVII), its antileukaemic activity is enhanced; the replacement of one of the quinoline rings by a pyridine ring has a similar effect[312].

When the phenyl group is Y = COC_6H_4CO is replaced by the biphenylyl group (Y = CO$C_6H_4C_6H_4$CO), the activity is retained; it is also retained when the Y group is in the 7-position[313]. This is believed[314] to be an indication that the minimum distance between the nitrogen atoms required for antileukaemic activity must be about 18 Å. When the benzene rings in the biphenylene group are fixed by a methylene bridge



the activity disappears[313].

The study of the activity of the most effective preparations of the type under consideration against various cancer tumours showed that they do not suppress carcinoma 180 and the spontaneous cancer of mammary glands. However, a distinct suppression of the tumour was observed in the case of lymphosarcoma induced by methylcholanthrene[311].

The activity of many quinolinium salts was studied by the method involving the suppression of the growth of a KB tissue culture[265,266,268,269,272,273,288,314,315].

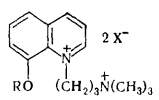
c. Other Radiomimetic Properties

Other radiomimetic properties of quinolinium salts have been investigated very little. There are reports of a mutagenic activity by compound (XXXIII), which is also known to be carcinogenic. It induces the mutation of strain B of *E. coli*[316] and *Saccharomyces cerevisiae*[317-319]. When the embryos of *Tritonia alpestris* and *Caenopus laevis* are treated in an early stage of development with preparation (XXXIII) at concentrations in the range 0.001 to 0.0001%, an abnormal course of development takes place (deformations, proliferation of tissues, and high mitotic activity), similar to the effect of X-rays at a dose of 120 to 500 roentgens[320].

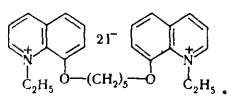
V. EFFECT OF QUINOLINIUM SALTS ON THE NEUROMUSCULAR SYSTEM AND ENZYMES

The effect of monoquaternary quinolinium salts on the neuromuscular system has been known for a long time. For example, Bamberger[321] reported in 1887 that *N*-phenylacylquinolinium bromide has a curare-like activity. However, these properties were investigated in greater detail much later. Schneider[322] and Denys and Levy[323] showed that 1-methyl-5,6-benzoquinolinium iodide is twice as active as eserine in suppressing the effect of acetylcholinesterase, but is slightly less active than Prostigmine;

it inhibits pseudocholinesterase more than the specific enzyme. The isomeric 1-methyl-7,8-benzoquinolinium iodide inhibits equally both acetylcholinesterases. High concentrations of the first preparation suppress the effect of acetylcholine on muscles. 1-(2'-Phenylcarbamoyloxyethyl)quinolinium iodide[324], 3-(diethoxyphosphinyloxy)-1-methylquinolinium methosulphate[325], and acetoxyquinolinium salts[326] also exhibit an antiacetylcholinesterase activity, 3-acetyl-1-methylquinolinium iodide being more active than the isomer containing the acetoxy-group in the 8-position of the quinoline ring. In a study of the effect of various quaternary ammonium salts on the rectus abdominis muscle, Iordache[327] found that 1-allylquinolinium bromide sensitises it with respect to acetylcholine. Quaternary salts of 8-alkoxyquinolinium have an analgesic effect[328]. In experiments on animals, 1-allyl-8-ethoxy- and 1-allyl-8-propoxy-quinolinium bromides showed a very satisfactory activity. 8-Hydroxy-1-methylquinolinium methosulphate has an analgesic effect in the treatment of the eye, associated with its ganglion-blocking activity[329]. Austin et al.[162] studied the curare-like activity of compound (X). It proved to be only twice as weak as (+)-curarine. Werner[330] suggested the use of quaternary quinolinium salts with a dioxanylalkyl residue at the nitrogen heteroatom as sympathomimetic preparations. Surrey and coworkers[331,332] synthesised mono- and di-quaternary salts of 4-dialkylaminoalkylquinolinium with hypotensive activity. Among other diquaternary quinolinium salts with hypotensive activity, mention should be made of the trypanocidal preparation antrycide (XVIII), which reduces blood pressure when administered in doses considerably below the therapeutic amount[333] and also causes the secretion of histamine[334]. The effect of compound (XVIII) on the cardiac activity of healthy cattle and cattle suffering from piroplasmosis has also been studied[335]. Gray and coworkers[336,337] synthesised and investigated diquaternary salts of type (LXXVIII).



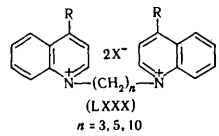
(LXXVIII)
(R = H, CH_3)



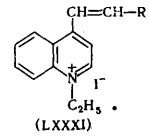
(LXXIX)

Many of these also exhibit a hypotensive activity. Quininebis(allyl bromide), which is also a diquaternary quinolinium salt, has an antiacetylcholine activity of the type of curare[337].

Bovet and coworkers[338,339] began an intensive study of the pharmacodynamic properties of bisquinolinium salts and in 1946 published data on the curare-like activity of compound (LXXIX) (RP-3381). Eserine and Prostigmine are antagonists of this preparation. Apart from the curare-like activity, compound (LXXIX) exhibits only physostigmine-like activity[340-342], inhibits pseudocholinesterase (but not the specific enzyme)[343,344], causes the contraction of the bronchi in guinea-pigs[345], and lowers the blood pressure in dogs[346]. Huidobro and Ugarte[347,348] studied the mechanism of the curare-like activity of the preparation. A number of patents have been obtained for preparations similar to compound (LXXIX)[349,350]. Barlow and coworkers[351,352] studied the curare-like activity of bisquinolinium salts of type (LXXX, R = H) with 3, 5, and 10 ethylene groups.



(LXXX)
n = 3, 5, 10



(LXXXI)

All three homologues exhibit a moderate curare-like activity and the highest member of the group shows in addition a considerable antiacetylcholinesterase activity. Reduction of the quinoline ring and the introduction of more than one OCH_3 group enhance the curare-like activity of the preparation[353-355]. Bhattacharya and Sen[356] studied compound (LXXX) with 20 methylene groups (n = 20). The preparation is antigonistic to acetylcholine but does not eliminate the effect of histamine and nicotine. Vyrbanova and Ivanov[357] studied the curare-like and anticholinesterase activity of compounds of type (LXXX, R = CH_3, n = 3–6, 8, or 10, X = Br). It was established that at a concentration of 10^{-6} M the anticholinesterase activity increases with the length of the polymethylene chain, but members with an odd number of CH_2 groups (n = 3 or 5) are somewhat more active. At the same time the curare-like activity is most pronounced in compounds with n = 4 and 6, i.e. those with the lowest anticholinesterase activity[358].

In a study of the effects of these compounds on the control of movement in rabbits, it was found that at a dose of 1 mg kg^{-1}, compounds with n = 3 and n = 10 enhance the control, while all other homologues lower it. The maximum decrease is observed with n = 5.[359]

The toxicity of polymethylenebislepidinium bromides (LXXX, R = CH_3, X = Br) is insignificant[360] and varies in parallel with their effect on subordination, reaching a maximum at n = 5. The compounds do not exhibit a local irritant activity when introduced into the conjunctival sac and also on subcutaneous and intramuscular administration.

Tarakhovs'kii and coworkers[361,362] showed that pentamethylenebisquinolinium bromide (pentaquinomethonium) (LXXX, R = H, n = 5, X = Br) lowers the blood pressure in experiments on cats and dogs in doses of 1–10 mg kg^{-1} and blocks the transmission of nerve impulses both via the sympathetic and parasympathetic ganglia of the vegetative nervous system. The preparation also exhibits a central cholinolytic activity. Kimenis[363,364] studied the effect of the quinolinium analogue of ditilin (preparation DS-3) on the neuromuscular system of warm-blooded animals. In its curare-like activity the compound is inferior to ditilin, but the duration of its action is longer. The antiacetylcholinesterase activity of compound DS-3 exceeds by severalfold that of proserene and is less toxic by a factor of 8.

At attempt has been made to establish a relation between the curare-like activity and the magnitude of the cationic charge of the nitrogen atoms. The ability of conjugated system to distribute the charge associated with the nitrogen atom leads to a decrease of the curare-like activity[365]. Maximum curare-like activity is observed with compounds in which the distance between the two positively charged nitrogen atoms is 15 Å.[366]

Certain quinolinium dyes also exhibit an appreciable activity. Although Brooker and Sweet[71] reported that cyanine dyes do not have an appreciable effect on α-amino-acid oxidase, cytochrome oxidase, succinate dehydrogenase glucosedehydrogenase, and glyoxalase and Ciaccio et al.[367] found that (LXX) and (LXX) are inactive in relation to lactate dehydrogenase and α-glycerolphosphate dehydrogenase and do not inhibit glycolysis, Hase and coworkers[368,369] showed that many cyanine and styryl dyes of the quinolinium series inhibit acetylcholinesterase.

It has also been established that the non-purified preparation (XVII) (the so called Lumin) has a marked influence on the respiration of animals[370-372]. Fuzimoto[373] investigated quinolinium dyes of type [LXXXI, R = piperidyl, $N(CH_3)_2$, $N(CH_3)C_6H_5$]. The preparations cause a dilatation of blood vessels and accelerate the peristalsis of the intestine. Many quinocyanine and quinostyryl dyes inhibit aerobic glycolysis[293,374]. Ogura et al.[375] made a kinetic study of the mechanism of the inhibition of catalase by compound (XVII).

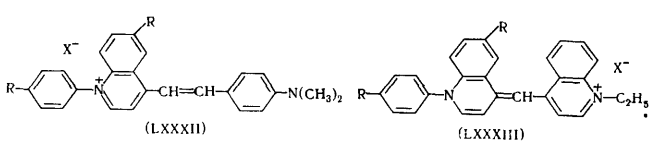
Recently styrylquinolinium compounds have also been investigated as inhibitors of choline acetyltransferase[376] and monoamine oxidase[377].

Among the numerous reviews dealing with the effect of quaternary ammonium salts on the neuromuscular system, only two[378,379] consider briefly bisquinolinium salts in this respect, on the basis of the literature between 1946 and 1951.

VI. QUINOLINIUM SALTS AS REGULATORS OF PLANT GROWTH AND DEVELOPMENT

The properties of quinolinium salts as regulators of plant growth began to be studied only 20 years ago by Japanese investigators. In 1949 Fujisawa and Ohba[380,381] made patent applications for the use of monomethinecyanine dyes, and particularly bis-(1-ethylquinolin-2-yl)-monomethinecyanine iodide, as stimulators of seed germination; Ogata and Shingu[382] studied the activity of a number of quaternary heterocyclic salts and cyanine dyes synthesised from them in tests on peas. The trinuclear quinocyanine dye (XVII) was investigated as a regulator of fungal growth[383]. The growth of fungi is stimulated when the preparation is diluted to 1 : 100 000–1 : 10 000 000 and is inhibited at a dilution of 1 : 10 000. The stimulation of the growth of certain medicinal plants by purified compound (XVII) was also investigated[384]. In the middle 1960's the work of Soviet scientists in this field was published. A method was proposed for increasing the crop of peas (to the extent of 117%) by soaking the seeds before sowing in 0.001% aqueous solution of (1,2-diphenylquinolin-4-yl). (1'-ethylquinolin-4'-yl)monomethinecyanine perchlorate[385]. Wheat grains treated with 0.001% solution of 4-*p*-dimethylaminostyryl-1,2-diphenylquinolinium perchlorate resulted in an increase of the growth of the green mass of wheat by the hydroponic method by 124%,[386] and treatment with a solution of 4-*p*-dimethylaminostyryl-1-β-naphthyl-5,6-benzoquinolinium perchlorate gave an increase of 117%.[387]

In a study of the activity of monomethinecyanine and styryl dyes derived from *N*-aryl-lepidinium on the growth of cucumbers and hemp[388], it was found that the dyes at a concentration of 0.01% inhibit the germination of the seeds or do not have an appreciable effect. The optimum concentrations proved to be 0.0001 and 0.00001% for cucumbers and 0.00001% for hemp. Experiments showed that lepidinium derivatives have unequal effects on the growth of various plant species.



(LXXXII) (LXXXIII)

Here R = H (a), CH_3 (b), OH (c), $OCOCH_3$ (d), or OCH_3 (e).

Thus in the case of cucumber seeds the best growth stimulating activity was shown by compounds (LXXXII, e), and (LXXXIII, b) and satisfactory activity was also shown by compounds (LXXXII, a, d) and (LXXXIII, a, c, e). In an identical experiment with hemp, the best stimulators proved to be (LXXXII, c, d) and (LXXXIII, a, c, d,). It is interesting to note that in experiments with cucumbers the preparations showed a somewhat lower activity than potassium heteroauxinate. However, in experiments with hemp, the latter proved less active than the lepidinium derivatives. Field tests on hemp showed that certain preparations increase the length of the internodal sections, enhance the saturation of tissues with water, and promote the accumulation of protein[388,389].

Preparations of type (LXXXII) and (LXXXIII) were also tested in the growth of tree seedlings, in particular fir seedlings[390]. Compounds (LXXXII, a, c, e,), (LXXXIII, a, c,), certain styryl derivatives, and monomethines synthesised from 1-aryl-5,6-benzolepidinium salts, and also Pinacyanol iodide [bis-(1-ethylquinolin-2-yl)trimethylcyanine iodide] proved to be the most active. It is interesting that, in order to stimulate the growth of tree seedlings, it is necessary to employ more concentrated solutions (0.005 and 0.001%). More water-soluble preparations (LXXX, LXXXII, a, X = Cl) and Pinacyanol chloride were tested *in vitro* on Belotserkovskaya 23 and Meris Widgen [spelling uncertain (Ed. of Translation)] wheat grains. The experiments showed that the activity of the preparations is almost equal to that of (LXXXIV) as regards the enhancement of the growth of the part of the plant above ground but is somewhat inferior as regards the stimulation of root growth[391]. The growth stimulating activity of compound (LXXXV) was also tested on leguminous plants[392]. In field tests the preparation increased the content of chlorophylls, reducing sugars, and the dry matter in the plant leaves during the flowering phase. The preparation is somewhat more active than (XXXIV). It increased the crop of broad beans by 108% and that of French beans by 114.6%.

In studies of the growth stimulating activity of dyes synthesised from 6-hydroxy-1-methyllepidinium chloride[393] in the initial phase of the growth of Belotserkovskaya 23 wheat and Nadezhnyi oats, a high activity of 1-methyl-4-*p*-dimethylaminostyryl- and 4-*p*-hydroxy-*m*-methoxystyryl-1-methyl-substituted 6-hydroxylepidinium chlorides was noted, being equal to that of compound (XXXIV).

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Determination of the Number of Active Centres and Growth Rate Constants in the Catalytic Polymerisation of α-Alkenes

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The reliability of different methods for determining the number of active centres (n) and calculating the growth rate constants (k_g) in the catalytic polymerisation of α-alkenes is discussed. The values of n and k_g obtained for different catalytic systems are given. Information on the dependence of the number of growth centres and the rate constants of the separate steps (primarily the growth rate constants) on the composition of the catalyst, its method of preparation, and the conditions of polymerisation can yield important conclusions regarding the mechanism of polymerisation and the composition of the active centres. The bibliography contains 113 references.

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I. INTRODUCTION

In the study of radical polymerisation, the rate constants of the elementary steps are now being measured. The problem of determining the kinetic characteristics of the elementary steps of catalytic polymerisation is only just being tackled. The complexity of the study of the elementary steps in this instance is associated with the fact that the separate reactions involved in catalytic polymerisation are not in general elementary steps in the sense in which this term is used in the theory of absolute reaction rates, but consist of many elementary steps. The study of the kinetics of polymerisation in the presence of homogeneous and heterogeneous catalysts is still at the stage where the rate constants of the separate reactions making up the overall process (chain growth, chain transfer, etc.) are being determined.

Since in the description of catalytic polymerisation, slight differences are noted in the interpretation of a number of terms, it is appropriate to explain the terminology used in the present paper.

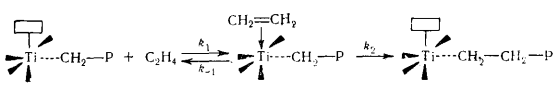
Catalytic polymerisation can be defined as a process in which a catalyst takes part in the formation of the activated complexes for the elementary steps of growth. The growth centre in catalytic polymerisation can be defined as the active bond between the catalyst and the growing polymer molecule, through which the monomer molecule is brought into the chain growth reaction, together with those atoms of the catalyst which take part in the formation of the activated complexes during growth. In heterogeneous catalysts, the growth centre is a surface compound.

In contrast to the situation in heterogeneous-catalytic reactions involving the production of non-polymeric products, the concept of active centres acquires particular

importance in heterogeneous catalytic polymerisation. All stages in the polymerisation involve the participation of localised growth centres; the rates of the elementary steps should thus be influenced primarily by the local properties of the growth centre—the properties of the active bond and the atom or group of atoms joined to the terminal atom of the growing polymer chain and the properties of the immediate environment of the growth centre. Early suggestions[1,2] regarding the mechanism of heterogeneous catalytic polymerisation, in which it was assumed that the end of the growing polymer chain is able, during growth, to move over the surface, which was assumed to have a regular structure, were not confirmed by detailed study of the mechanism of polymerisation on heterogeneous catalysts.

For homogeneous polymerisation, in some instances it is difficult to draw a clear distinction between a catalytic process and a process taking place by an ionic polymerisation mechanism. In general, the reactivity of the growth centre and the structure of the polymer are influenced by the composition of the catalytic complex; a free-ion mechanism may be realised in polymerisation in polar media[3].

A characteristic feature of catalytic polymerisation, which distinguishes it from radical polymerisation, is that the individual reactions are generally complex and consist of several successive elementary steps (in other words, more than one activated complex is formed in the reaction). For example, it is usually postulated that in the catalytic polymerisation of alkenes, growth takes place in two stages: in the first, an unstable π-complex of the alkene with a metal with variable valency is formed, and in the second a *cis*-insertion reaction takes place; for the polymerisation of ethylene on Ziegler–Natta catalysts, this scheme can be represented as follows (the rectangle represents a vacant coordination position, and P the polymer chain):



The catalytic polymerisation of alkenes has been most extensively studied for the determination of the kinetic parameters of the individual steps. The rate constants obtained for the individual reactions, however, are usually not the absolute rate constants of the elementary steps, and their physical significance depends on the way in which the individual reaction takes place. For example, for a growth reaction in which two activated complexes are formed (see above scheme), the growth rate constant k_g depends on the rate constants of these steps:

$$k_g = \frac{k_1 k_2}{k_2 + k_{-1} + k_1 \cdot [M]} \qquad (1)$$

where [M] is the concentration of the monomer, and k_1, k_{-1}, and k_2 the rate constants of the corresponding elementary steps.

In this connection, care must be taken when applying the theory of absolute reaction rates to the interpretation of the rate constants of the separate stages of catalytic polymerisation, and also when examining various correlations between these constants and the physical characteristics of the catalyst. Despite this, however, the determination of the rate constants of the separate reactions in polymerisation is of considerable importance in connection with the problem of predicting catalytic activity.

The activity A of a polymerisation catalyst is proportional to the number of growth centres n and the growth rate constant k_g:

$$A \sim k_g \cdot n$$

In catalytic polymerisation it is possible and necessary to distinguish clearly two factors influencing the catalytic activity: a) the number of growth centres, which is determined by the original state of the catalyst and the reactions taking place in the formation of the growth centres (separated from possible reactions involving subsequent deactivation of the growth centres by reaction with components of the reaction medium); and b) the growth rate constants, that is the reactivity of a single growth centre.

To develop methods for controlling catalyst activity, it is necessary to study the influence of these factors separately. The determination of the rate constants of reactions limiting the growth of a polymer chain is related to the problem of controlling the molecular weight of the polymer.

The determination of the kinetic characteristics of the growth centres also makes it possible to reach a number of important conclusions regarding the mechanism of catalytic polymerisation. The direct use of such quantities as the rate of polymerisation (V) and the degree of polymerisation ($\bar{P}$), cannot give unambiguous information regarding the nature of the individual elementary reactions, since V and $\bar{P}$ are complex quantities which depend on the ratio of the rates of initiation, growth, transfer, and termination of the chains.

The results of the determination of the number of growth centres in catalytic polymerisation have been reviewed briefly by Boor[4]. At the Budapest Symposium on Macromolecular Chemistry (August 1969), Kern[5] described the determination of the number of growth centres for Ziegler–Natta catalysts (chiefly by a method involving the termination of the polymerisation by a radioactive alcohol), but this paper similarly does not contain a sufficiently complete review of the results obtained in the important field of the determination of the kinetic characteristics of growth centres in catalytic polymerisation.

It is possible to distinguish three basic groups of methods used for the determination of the kinetic characteristics of growth in catalytic polymerisation.

1. Methods based on the determination of the dependence of V and $\bar{P}$ on the duration and conditions of the reaction. These will subsequently be referred to conditionally as kinetic methods.
2. The inhibition method, in which the number of growth centres is calculated from the quantity of added inhibitor which brings about complete termination of polymerisation.
3. Methods based on the labelling of the growing polymer molecule.

II. KINETIC METHODS

These methods are based on the study of the dependence of the rate of polymerisation and the molecular weight of the polymer on the conditions of polymerisation. For processes in which the number of growth centres is independent of time (steady-state polymerisation), methods based on the use of the dependence of V on the concentrations of the reagents and the dependence of $\bar{P}$ on time and the concentrations of the reagents have been proposed for the calculation of the rate constants. For processes in

which the number of growth centres changes with time (non-steady-state polymerisation), the time dependence of V is also used in the calculation of rate constants.

1. Steady-state Polymerisation Kinetics

The method of calculating the rate constants of the separate reactions from the dependence of V and $\bar{P}$ on the concentrations of the reagents has been described by Chirkov and coworkers [6] and Natta and coworkers [7]. These authors used a comparatively simple kinetic scheme, based on the following assumptions: a) the total number of active centres remains constant throughout the process; b) the initiation involves the attachment of the first monomer molecule to the active centre; c) transfer takes place with the participation of the monomer, impurities, components of the catalyst, and spontaneously; d) transfer is followed by regeneration of the active centre.

In accordance with the foregoing:

$$n_0 = n_g + n_i \qquad (2)$$

where n_0 is the total number of active centres in the catalyst, n_g the number of active centres joined to a growing polymer molecule, and n_i the number of centres in a state of temporary deactivation. The steady-state conditions for this scheme gave the dependence of V and $\bar{P}$ on the concentrations of the reagents:

$$\frac{[M]}{V} = \frac{1}{k_g \cdot n_0} + \frac{k_M}{k_g \cdot k_i \cdot n_0} + \frac{\sum_{j-1} k_j \cdot c_j^a}{k_g \cdot k_i \cdot n_0} \cdot \frac{1}{[M]} \qquad (3)$$

$$\frac{1}{\bar{P}_n} = \frac{V_0}{V_g} = \frac{k_M}{k_g} + \frac{\sum_{j-1} k_j \cdot c_j^a}{k_g} \cdot \frac{1}{[M]} \qquad (4)$$

where V_g is the rate of growth, V_0 the rate of transfer, k_j the rate constant for transfer involving the agent j, k_M the rate constant for transfer involving the monomer, k_i the initiation rate constant, c_j the concentration of transfer agent j; [M] the concentration of monomer, and n_0 the total number of active centres.

The experimental dependence of V and $\bar{P}$ on the concentrations of the reagents can be used to calculate products of the rate constants of the separate reactions and the concentrations of the active centres, but this method does not yield absolute values of the rate constants. This method has been used to study the polymerisation of propene on heterogeneous catalytic systems based on $TiCl_3$ and VCl_3 combined with various organometallic components [3-17] (see Table 1). It should be noted that the correct application of this method requires the use of the experimental values of the number-average degree of polymerisation ($\bar{P}_n$). In the calculations, however, the weight-average factor ($\bar{P}_w$) is usually employed, with the assumption that the polydispersion factor γ ($\gamma = \bar{P}_w/\bar{P}_n$) remains constant over the range of values of the parameters studied. The applicability of this assumption will be discussed below. Because of the assumptions made in the derivation of the kinetic equations and the calculation, the results of the calculation are approximate and suitable only for the comparative estimation of the efficiency of chain transfer agents for catalytic systems with similar compositions.

A method for calculating the rate constants of the separate reactions for steady-state polymerisation, based on an analysis of the dependence of the molecular weight

Table 1. Determination of the kinetic parameters of growth for the catalytic polymerisation of propene.

Catalytic system	Temp. of reaction, °C	$10^2 n$, mole per mole of M[a]	k_g, litre mole^{-1} s^{-1}	Method of calculation[b] and remarks	References
$TiCl_3+AlEt_2Cl$	50	1.35	4.7	II-2. Maximum values of n given;	18
	70	2.8	7.5		
	90	9	11.5	E_g = 5.0 kcal mole^{-1}[c]	
$TiCl_3+AlEt_3$	70	0.3	48	III-2. AMP = amide hexamethyltriphosphoric acid	19
$TiCl_3+AlEt_2Cl$	70	0.1	40		
$TiCl_3+AlEtCl_2+AMP$	70	0.02	50		
α-$TiCl_3+AlEt_2Cl$	50	—	1.2	I-4	20
α-$TiCl_3+AlEt_3$					
α-$TiCl_3+AlEt_2Cl$	50	2.3—7.0	3—0.48[c]	III-2. k_g changes with change in the duration of polymerisation	20
α-$TiCl_3+AlEt_3$	50	1.1—4.5	5.9—0.48[c]		
$TiCl_3+AlEt_2Cl$	70	0.19	5.5	I-4	21
$TiCl_3+AlEt_2Cl$		1.9	7.5	I-3. Parallel values of n and k_g obtained for different $TiCl_3$ specimens	22
	60	0.57	6.2		
$TiCl_3+AlEt_2Cl$	60	0.3*	26*	III-2.	
	60	0.45**	18**	*I_2 used as stopper	5
				**CH_3O^3H used as stopper	
$TiCl_3+AlEt_2Cl$	30	5.1	0.8[c]	III-2. Initial values of n and k_g given; n increases with increase in the duration of polymerisation, and k_g decreases;	23
	50	4.4	2.5[c]		
	70	3	7.0[c]		
				E_g = 8.0 ± 1 kcal mole^{-1}	24
$TiCl_3+AlEt_2Cl$	30	9.5	0.10	III-1.	
	50	7.6	0.42	E_g = 13.0 kcal mole^{-1}	
	70	5.5	1.25		
	90	3.3	3.50		
$Al_xTi_yCl_2+(C_5H_5)_3N$	50	0.0007—0.0012	1.1—0.28	III-2. n increases with increase in the duration of polymerisation, and k_g decreases	25
$TiCl_3+AlEt_3$	70	1.0	2.5[c]	III-1.	26
$TiCl_3+AlEt_2Cl$	70	0.4	5.6[c]		
$TiCl_3+AlEt_3$	70	1.16—1.40	4.3	I-3.	27
	35	4	1.0[c]	I-3.	28
$TiCl_3+AlEt_3$	60	25	0.3[c]		
$TiCl_3+AlEt_3$	70	0.54	—	II	29
$TiCl_3+AlEt_2Cl$	60	0.40	10[c]	II	30
	20	1.0	—	III-1. Parallel values of n obtained for $TiCl_3$ specimens with different activities	31
	46	1.1	—		
$TiCl_3+AlEt_3$	70	1.1—0.7	2.9[c]		
	100	0.3	—		
	70	1.7	2.8[c]		15
$VCl_3+Al(i\text{-}Bu)_3$	60	0.8	23	I-1 and I-2.	32
$VCl_3+Al(i\text{-}C_7H_9)_3$	70	0.8	46.5	I-2, E_g = 12.9 kcal mole^{-1}	32, 33
α-$TiCl_3+AlEt_3$	70	0.54	3.8		
α-$TiCl_3+Al(C_3H_7)_3$	70	0.54	5.2	I-2, II	
α-$TiCl_3+Al(i\text{-}Bu)_3$	70	0.54	2.9	E_g = 13.5 kcal mole^{-1}	34
α-$TiCl_3+Al(CH_3)_3$	25	—	$1\cdot10^3$—$1\cdot10^6$	IV.	

[a] M represents the transition metal compound.

[b] Arbitrary symbols for methods of determining n and k_g.
I—Kinetic methods:
I-1—calculation from the dependence of V and $\bar{P}_n$ on the concentrations of the reagents for steady-state kinetics;
I-2—calculation from the dependence of V on the conditions of polymerisation for non-steady-state kinetics;
I-3—calculation from the dependence of $\bar{P}_n$ on the duration of polymerisation for steady-state kinetics;
I-4—calculation from the dependence of V and $\bar{P}_n$ on the duration of polymerisation for non-steady-state kinetics;
II—Inhibition method
III—Methods based on the labelling of the polymer:
III-1—labelled catalysts;
III-2—stopper method
IV—Calculation from the results of an electron-microscope study of the morphology of the polyalkene formed in the initial stage of the polymerisation.

[c] Calculated by us from published data.

on the duration of polymerisation, was proposed by Natta and coworkers [8,9,31,35]. This method uses the following expression for the number-average degree of polymerisation:

$$\overline{P}_n = \frac{Q}{N} = \frac{\int_0^\tau k_g \cdot n \cdot [M] \cdot d\tau}{n + \int_0^\tau \sum_j k_j \cdot n \cdot c_j^a \, d\tau} \qquad (5)$$

where N is the number of polymer molecules formed in polymerisation for time τ, Q the yield of polymer, k_j the rate constant for transfer involving agent j, and [M] the concentration of monomer.

For steady-state systems (n = const), the rate constants can be calculated from the linear dependence of $1/\overline{P}_n$ on $1/\tau$, which follows from Eqn.(5). With values of the polymerisation factor $\overline{P}_V$, calculated from measurements of the characteristic viscosity, the authors cited [8,9] used the equation

$$\frac{1}{\overline{P}_V} = \frac{1}{k'_g[M]} \cdot \frac{1}{\tau} + \frac{\sum_j k_j \cdot c_j^a}{k'_g \cdot [M]} \qquad (6)$$

where k'_g is the viscosimetric-average rate constant for chain growth, taken as a measure of the activity of one growth centre, and $k'_g = k_g/\gamma$, where γ is the polydispersion factor. The method based on Eqn.(5) makes it possible in principle to determine the absolute values of the kinetic parameters of growth.

Table 2. Determination of the kinetic parameters of growth for the catalytic polymerisation of α-butene at 0° (method of calculation I-3, see Table 1).

Catalytic system	k'_g[M], s^{-1}	E^*_g, kcal $mole^{-1}$	Catalytic system	k'_g[M], s^{-1}	E^*_g, kcal $mole^{-1}$
VCl_3 + $AlEt_3$ / $BeEt_2$	3100	2.3	$TiCl_3$ + $AlEt_3$	280	—
α-$TiCl_3$ + $BeEt_2$ / $AlEt_3$ / $AlEt_2Cl$ / $AlEt_2I$ / Al(*i*-Bu)·Cl	275	4.5	β-$TiCl_3$ + $AlEt_2Cl$ / $AlEt_2Cl + AlCl_3 \cdot (C_5H_5)_3N$	54	—

*E_g is the activation energy of growth, calculated from the temperature dependence of k_g.

This method has been used [8,9] to determine k_g for the polymerisation of α-butene on catalytic systems based on VCl_3 and different crystalline modifications of $TiCl_3$ (see Table 2). The dependence of P_V on τ was determined for comparatively small polymerisation times (30–600 s). The value of k_g depended on the form of the compound of the metal with variable valency, but was almost independent of the organometallic co-catalyst, although the replacement of the co-catalyst influenced the overall rate of the process, the stereoregularity, and the molecular weight of the polymer.

The Italian authors [9] used the same method to study the polymerisation of propene into a syndiotactic polymer on the VCl_4 + $AlEt_2Cl$ catalytic system in the presence of anisole. The graphs giving the dependence of the stereospecificity of the catalysts and the rate of polymerisation on the concentration of anisole showed maxima; the value of k'_g decreased considerably when anisole was added and was independent of its concentration in the system. The Italian authors [9] introduced into the expression for the "viscosimetric-average" growth rate constant a coefficient making allowance for the change in the number of growth centres during the polymerisation, but the choice of value for this coefficient was somewhat arbitrary.

Table 3. Determination of the kinetic parameters of growth for the catalytic polymerisation of ethylene.

Catalytic system	Temp. of reaction, °C	$10^2 n$, mole per mole of M[a]	k_g, litre $mole^{-1} s^{-1}$	Method of calculation[b] and remarks	References
$TiCl_4$ + $AlEt_3$	39	4.8	52	III-2.	38
	54	1.1	127	E_g = 12 ± 2.5 kcal $mole^{-1}$	
	57	23	175		
α-$TiCl_3$ + $AlEt_2Cl$	40	1.5	76.5	I-1 and I-3	37
α-$TiCl_3$ + $AlEt_2Cl$ + H_2	40	0.6	80		
VCl_3 + Al-*i*-Bu_3	60	0.3	266	I-1 and I-2	39
VCl_4 + Al-*i*-Bu_3	0	4	1900	I-4	40
$VOCl_3$ + $AlEt_3$	0	0.82	1200	I-4. Maximal value of n given	41
$(C_5H_5)_2TiCl_2$ + $Al(CH_3)_2Cl$	0	40	1.50	III-2. Values of n given for one of several series of experiments; the values depend on the conditions of polymerisation. E_g = 12.2 kcal $mole^{-1}$	42
	15	5	5.13		
	30	78	13.6		
	45	98.0	39.0		
$(C_5H_5)_2TiCl_2$ + $Al(CH_3)_2Cl$	20	$1 \cdot 10^{-4}$	$1 \cdot 10^6$	n calculated from data on the dissociation of the original catalytic complex	43
$(C_5H_5)_2TiCl_2$ + $AlEt_2Cl$	15	10	1.5	I-4	44
CrO_3/aluminosilicate (3% Al_2O_3)	75	0.85	97	II	45
ditto	60	—	140	I-4. Values of $\gamma.k_g$ given, where γ is the polydispersion factor	46
	70	—	137		
	120	—	55		
	140—	—	39		
»	50	1.10	280	I-2	18
CrO_3/SiO_2, reduced with CO	75	—	2600	IV	47
α-$TiCl_3$ + $AlEt_3$	70	0.54	410	I-1,	32
α-$TiCl_3$ + Al(*i*-Bu)$_3$	70	0.54	380	II, E_g = 12 kcal $mole^{-1}$	
α-$TiCl_3$ + $AlEt_2Cl$	70	0.54	80		
$V(AcAc)_3$ + Al(*i*-Bu)$_2$Cl	—10°	—	30	I-4, E_g = 4.4 kcal $mole^{-1}$	32
$(C_5H_5)TiCl_2$ + $Al(Et)_2Cl$	20	—	4	I-4	32
$TiCl_2$	75°	0.003	$1.5 \cdot 10^4$	III-2	48, 49

[a] M represents the transition metal compound.
[b] Arbitrary symbols for methods of calculation; see footnote to Table 1.

A method for determining the kinetic parameters for steady-state catalytic systems, based on an analysis of the dependence of $\overline{P}_V$ on τ, was used [36,37] for the polymerisation of ethylene (the γ-$TiCl_3$ + $AlEt_2Cl$ system) in the presence and absence of hydrogen (see Table 3). After the initial non-steady-state period, the duration of which was not correlated with any of the parameters of the reaction, the rate of polymerisation remained stable for a prolonged period. Determination of the polydispersion of several polymers obtained under different conditions showed that the value of γ varies from 7 to 16. A constant value of γ equal to 10 was taken for the calculations. It was recognised [37] that the numerical values obtained for the rate constants are only approximate, because of the assumptions made and the limited accuracy of the measurement of the characteristic viscosity for polymers with high molecular weight. This method was also used [27,28] for the polymerisation of propene in the presence of the α-$TiCl_3$ + $AlEt_3$ system, although this system is not a steady-state system: the rate of polymerisation in the initial period increased until a constant value was established. The calculation based on the dependence of $\overline{P}_V$

and $\bar{P}_n$ on τ showed a decrease in the concentration of active centres during the polymerisation. The probable reason for this contradiction is that in this instance the condition for applicability of the method used to calculate the rate constants (n = const) was not satisfied.

2. Non-steady-state Kinetics

A number of authors have examined methods for calculating n and k_g for catalytic systems with variable activity from the dependence of the rate of polymerisation and the yield of polymer (Q) on time (τ). The dependence of V and Q on τ for one of the possible kinetic schemes for non-steady-state polymerisation has been derived [50]. For the interpretation of the time dependence of the number of growth centres in the kinetic scheme, the deactivation of the active centres in their reactions with monomers, with one another, and spontaneously were examined. The rate constants for the separate reactions involved in the polymerisation of propene were calculated [17] from the dependence of V on τ for the $VCl_3 + AlR_3$ system. In the interpretation of the non-steady-state behaviour of the system at elevated temperatures and high Al/V ratios, the kinetic scheme for steady-state polymerisation, examined earlier [14-16], was supplemented by deactivation of the catalyst, which, in the opinion of the authors cited, is associated with the extensive reduction of vanadium by the organoaluminium compound. By assuming that the period of accelerating rate of polymerisation is due to slow initiation with rate constant k_i, the product $k_i k_g n$ was calculated. Comparison of this quantity with the values of $k_i n$ and $k_g n$ found under conditions of steady-state behaviour of the system [16], made it possible to calculate n and the values of the rate constants for the separate reactions (Table 1) with an accuracy equal to that of γ.

A variant of the kinetic method of determining the constants of the elementary steps in non-steady-state catalytic polymerisation from the dependence of the rate of polymerisation on the conditions of the process was described by Ermakov and coworkers [51]. Its unique feature is that the description of the kinetics is not taken as far as the overall kinetic equation in integral form, which either includes a considerable number of variables, or requires for its simplification a large number of assumptions, but is represented in the form of a system of differential equations, derived from the kinetic scheme adopted for the process. This mathematical description is studied by means of an electronic computer. The mathematical description of the polymerisation of ethylene on a chromium oxide catalyst, compiled on the basis of a kinetic scheme involving initiation, growth, transfer, and deactivation of the catalyst was studied [51]. This kinetic scheme was proposed on the basis of data obtained in a study of the kinetics of the process [52]. The rate constants for the separate reactions were adjusted to obtain a dependence of V on time, the concentration of the catalyst, and the monomer which agreed with experiment. The chief limitations of this method are the indefinite nature of the choice of kinetic scheme and the ambiguous nature of the numerical solution of the system of equations. Considerable difficulties also arise in the selection of the initial conditions: the concentrations of the active component, the chain transfer agent, and the catalyst deactivator.

A method for determining the rate constants of the separate reactions from the dependence of $\bar{P}_V$ on τ for non-steady-state polymerisation was proposed by Matkovskii [41]. In order to apply this method it is necessary to establish, in a reaction vessel with ideal mixing, a constant concentration of active centres by selection of the rates of supply of catalyst and removal of polymer and catalyst. Under steady-state conditions, the rate constants can in principle be calculated by the methods proposed for steady-state catalytic systems [6,7,13]. For one of the probable kinetic schemes, equations relating V to the rate constants of the separate reactions, the concentrations of the reagents, and the amount of material exchange with the external medium, and also equations relating the mean time (τ_{mean}) for which the reaction mixture is in the reaction vessel to the concentration of the active centres and the rate constants of the deactivation processes, were derived. For a certain intensity of mass exchange, a linear relationship is observed between τ_{mean} and $\bar{P}_V$; this dependence was used to calculate n and k_g for the polymerisation of ethylene in the presence of the $VOCl_3 + Al(i\text{-}Bu)_3$ system (see Table 3).

An approach to the determination of the rate constants of the separate reactions on the basis of data on the dependence of V, Q, and $\bar{P}_n$ on the duration of polymerisation has been described [46,53,54]. For non-steady-state polymerisation, when chain transfer involving the monomer and spontaneous chain transfer take place, Eqn.(3) can be rewritten in the form [53]

$$\frac{1}{\bar{P}_n} = \frac{1}{k_g \cdot [M]} \cdot \frac{V}{Q} + \frac{k_M}{k_g} + \frac{k_S}{k_g \cdot [M]} \qquad (7)$$

(k_S is the rate constant for the spontaneous transfer).

Expression (7) has a relatively simple form, since it does not include the rate constants for initiation and deactivation of the growth centres. The change in the number of growth centres with time as a consequence of these reactions is included in implicit form in the ratio V/Q. Thus Eqn.(7) gives the dependence of the molecular weight on the duration of polymerisation, resulting from the change in the number of growth centres. This method can be used to determine the values of k_g (with an accuracy equal to that of the coefficient γ), k_M, and k_S. When this method was used to study the polymerisation of ethylene on a chromium oxide catalyst [46,53], a decrease in the quantity $\gamma . k_g$ with decrease in the temperature of polymerisation was observed, and this was attributed to a decrease in the polydispersion of the polymer (data on the possibility of narrowing the molecular weight distributation of a polymer by decreasing the temperature of polymerisation on oxide catalysts have been published [55]). This method is also used for the polymerisation of ethylene in the presence of a soluble catalytic system [44].

3. Applicability of Kinetic Methods

The following possible sources of error in the determination of the absolute values of n and k_g by kinetic methods may be noted.

1. Lack of correspondence between the kinetic scheme adopted and the actual mechanism of the process. For non-steady-state polymerisation, when a method based on the analysis of the dependence of V and $\bar{P}$ on τ is used, the choice between different mechanisms of chain transfer and termination is somewhat arbitrary; different authors have

proposed different transfer and termination reactions for catalytic systems with similar compositions [13,18,24,30,42,56-60]. For steady-state polymerisation, k_g can be calculated on the basis of the linear dependence of $1/\bar{P}_V$ on $1/\tau$ if the catalytic system is suitable from the start of polymerisation. Most authors who have used this method, however, do not give kinetic curves justifying the assumption that the number of active centres is constant in the initial period of polymerisation for which the dependence of $\bar{P}_V$ on τ is determined. When methods based on the analysis of the dependence of $\bar{P}_V$ on τ are used, errors may arise because processes involving the temporary deactivation of active centres, not associated with rupture of the active chain, are not taken into account in the derivation of the equations (6) and (7) used in the calculations. When these processes take place, the growth of an individual molecule is interrupted periodically; the temporary interruption of growth ("falling asleep") leads to a decrease in the overall rate of polymerisation, but does not increase the number of polymeric molecules.

2. Use of $\bar{P}_V$ instead of $\bar{P}_n$. Most authors who have used kinetic methods have calculated the number-average polymerisation factor ($\bar{P}_n$) from the results of the measurement of the characteristic viscosity (η). In this instance, errors may arise as a consequence of errors in the determination of η for polymers with high molecular weight, and also because of the arbitrary nature of the selection of the method for calculating $\bar{P}_V$ from η. It is known that even for narrow fractions of linear polyethylene [61], the equations proposed by different authors, for the same values of the viscosity, give molecular weight values which differ considerably. Moreover, it appears that one of the fundamental assumptions which is usually made when kinetic methods are used—the assumption that the polydispersion of the polymer (the factor $\gamma = \bar{P}_V/\bar{P}_n$) is independent of the conditions of the process—is not always satisfied. It should be noted that the experimental determination of the quantity γ for polyalkenes with high molecular weight involves considerable difficulty, and published data on this topic are somewhat contradictory. For soluble catalytic systems, a narrower molecular weight distribution is observed, but even for these systems, the values of γ given by different authors [20,62-64] vary from 1.5 to 6, and Chien [62] points out that the quantity γ shows a complex dependence on τ, increases with decrease in temperature, and changes with change in the catalyst concentration and the Ti/Al ratio. It has been noted [63,64] that γ depends on the concentration of the catalyst and monomer, and the nature of the solvent. For heterogeneous catalysts, the polymers obtained have a wider molecular weight distribution; according to the data of various authors [20,27,37,62,65,66], the value of γ may vary for a given catalytic system with change in the duration and conditions of polymerisation. A change in the width of the molecular weight distribution is even more probable with change in the chemical composition of the catalyst (either the metal with variable valency [66,67] or the organometallic component [68]). According to some authors [69], the polydispersion decreases considerably when hydrogen is used to control the molecular weight of polyethylene obtained on Ziegler–Natta catalysts.

Thus the absolute values of the rate constants of the separate reactions and the number of active centres determined by kinetic methods cannot be taken as sufficiently reliable. Particularly large errors may arise when catalysts with different chemical compositions are compared.

III. INHIBITION METHOD

A number of authors [29,30,45,70], for the estimation of a number of active centres on heterogeneous catalytic systems in the polymerisation of α-alkenes, have used the inhibition method, which is often used for radical polymerisation. In this method, the concentration of growth centres is estimated from the quantity of inhibitor required for the complete or partial termination of polymerisation.

Carbon tetrachloride [45] and allyl alcohol [70] have been used to inhibit polymerisation on chromium oxide catalysts; the inhibiting action of CCl_4 was found to be much stronger. The inhibition method has also been used [29] to determine the concentration of active centres in the polymerisation of propene on an α-$TiCl_3$ + $AlEt_3$ catalyst. Before the polymerisation, the titanium trichloride was treated with ethanol, and this led to the production of an induction period during polymerisation. Comparison of the initial rates of polymerisation in the "pure" experiments and the experiments in the presence of different quantities of alcohol and catalyst makes it possible, in the opinion of the authors cited, to calculate the concentration of growth centres (Table 1). As in the work with CCl_4, [45] it is assumed that the inhibition of one active centre requires one molecule of alcohol, and allowance is not made for the consumption of alcohol in possible side reactions or as a result of adsorption on the surface of the catalyst, not associated with the catalytic activity. This may lead to high values for the measured number of active centres.

In general it may be noted that the inhibition method in catalytic polymerisation provides only limited possibilities, since it is difficult to select an inhibitor which is used up only in deactivation of the growth centres and which is not used up in reaction with the surface of the catalyst or with components of the reaction system.

IV. METHODS BASED ON LABELLING OF THE POLYMERIC MOLECULE

A tracer can be introduced into a polymeric molecule either at the initiation stage (the use of labelled catalyst components) or during the termination of growth (the stopper method). In the formation of a polymer with high molecular weight, in order to attain the necessary sensitivity in the determination of the number of labelled polymer molecules, it is best to use radioactive isotopes as tracers. Iodine has been used as a non-radioactive tracer for the termination of catalytic polymerisation [6,30,71]. Compounds labelled with carbon-14 and tritium are most frequently used in the study of catalytic polymerisation. Chlorine-36, iodine-131, and zinc-65 have also been used.

1. Use of Labelled Catalyst Components as Tracers

Natta's school [26,31,78] and Chien [24,42] determined the kinetic parameters of growth and initiation from the radioactivity of a polymer obtained in the presence of a labelled catalyst. For heterogeneous systems based on $TiCl_3$, the number of active centres [26,31,72] was determined by two methods: a) by adsorption of labelled alkylaluminium on $TiCl_3$ with subsequent analysis of the reaction products for radioactivity; and b) by carrying out the polymerisation in the presence of labelled trialkylaluminium.

The use of the adsorption method made it possible to establish that the number of labelled alkyl groups on the

surface of titanium trichloride depends on the temperature of adsorption, the conditions of the subsequent washing of the catalyst with a hydrocarbon solvent, and the nature of the organometallic compound. The radioactivity of polypropene obtained on a catalyst treated with labelled alkylaluminium was used to calculate the number of alkyl groups transferred to the polymer; this was taken to be equal to the number of active centres. The value found in this way for the number of active centres was less than or equal to the number of alkyl groups initially combined with the $TiCl_3$ surface. The adsorption method gives the number of active centres initially present on the catalyst surface (n_0). It may not correspond to the steady-state value of the concentration of active centres; this may change after the start of polymerisation and reach a certain constant steady-state value. To estimate the steady-state number of growth centres, use has been made of a method [31] based on the determination of the number of labelled ethyl groups in a polymer, obtained after polymerisation for different periods of time in the presence of free triethylaluminium labelled with ^{14}C. The calculation of the number of active centres from the concentration of labelled ethyl groups in the polymer was based on the assumption that the rate of chain transfer by triethylaluminium and the rate of growth are independent of the duration of polymerisation. Table 1 gives data on the determination of the kinetic parameters of growth [26,31] obtained by both methods.

In an evaluation of the results obtained by the two methods for determining n with a labelled catalyst, it was assumed [31] that the results obtained by the introduction of a labelled co-catalyst into the polymerisation system are more accurate, since when this method is used the influence of foreign radiochemical contamination is smaller and more effective allowance is made for the effect of transfer processes.

A labelled catalyst was also used by Chien [24] to study the kinetics of the polymerisation of propene. Before the reaction, titanium trichloride was treated with diethylaluminium chloride labelled with ^{14}C. An increase in the number of active centres with increase in the $TiCl_3$ concentration at a constant ratio of the titanium and aluminium components was observed; the number of active centres increased with increase in the concentration of $AlEt_2Cl$ at constant concentration of $TiCl_3$, and decreased with increase in temperature in the range 30–90°. Change in the pressure of the monomer had no influence on the concentration of the active centres. The calculated values of k_g were constant in experiments with different concentrations of the monomer, titanium trichloride, and diethylaluminium chloride, and for different yields of polymer (see Table 1).

2. Introduction of Tracers on Termination of Polymerisation

This method is based on the introduction, into the reaction system, of substances (stoppers) which terminate the polymerisation in such a way that a molecule of the substance, or part of it, is attached to the growing polymer chain. If the stopper reacts quantitatively with the growing polymer chains, the number of growth centres can be calculated from the concentration of tracer in the polymer. If however the polymerisation takes place in the kinetic range, the growth rate constants can be calculated from data on the number of growth centres, the rate of polymerisation, and the concentration of monomer.

The stoppers which have been used in anionic and anionic-coordination polymerisation include carbon dioxide labelled with ^{14}C, [73–76] acetic acid in which the active hydrogen was replaced by tritium [77,78], alcohols labelled with tritium in the hydroxyl group [18,19,23,25,38,73,74,79,80], and radioactive iodine [42]. Alcohols labelled with ^{14}C in the alkoxy group [73,81] have been used for cationic polymerisation.

The stopper method has been widely used to determine the number of growth centres in the polymerisation of α-alkenes on complex organometallic catalysts. In most instances, alcohols in which the hydroxyl hydrogen was replaced by tritium were used. This was first done by Feldman and Perry [38] in a study of the polymerisation of ethylene in the presence of the $TiCl_4 + AlEt_3$ system. This work was based on the assumption that if the active catalyst–carbon bond is polarised in such a way that the carbon atom carries a negative charge, as should be the case for a metal–carbon bond, the hydroxyl group should combine with the negatively charged carbon on rupture of the active bond, and the polymer should become radioactive:

$$\text{Cat.}^{+\delta}\!-\!-\!-\overset{-\delta}{\underset{|}{\text{C}}}\!-\!\text{P} + \text{ROT} \rightarrow \text{Cat.}\!-\!\text{OR} + \text{T}\!-\!\underset{|}{\text{C}}\!-\!\text{P}$$

where P represents the polymer chain.

Quantitative reactions of this kind are known for organotitanium compounds of low molecular weight [82]. When CH_3OT is introduced in the polymerisation of alkenes on Ziegler–Natta catalysts, a radioactive polymer is obtained, whereas when methanol $^{14}CH_3OH$ is used as inhibitor, radioactivity is not detected in the polymer [38]. These results indicate that growth takes place at a catalyst–carbon bond, polarised as follows:

$$(\text{catalyst})^{+} \cdots {}^{-}\text{CH}_2\!-\!\text{P}$$

This result corresponds to the anionic-coordination mechanism of the polymerisation of α-alkenes, accepted for Ziegler–Natta catalysts.

The method involving the introduction of a tracer into a polymer on termination of the polymerisation by stoppers (chiefly by alcohols labelled with tritium in the hydroxyl group [19,23,25,38,42,79,80] and less frequently by radioactive or non-radioactive iodine [30,42,71]) has been used to obtain the kinetic characteristics of growth in the polymerisation of α-alkenes on many Ziegler–Natta catalytic systems; the results are given in Tables 1 and 3.

The method involving termination by radioactive alcohol has been used to study the polymerisation of ethylene on oxide catalysts [83–89]. In the termination of polymerisation by alcohol in which the hydroxyl hydrogen was replaced by tritium, radioactivity was not detected in the polymer. A radioactive polymer was obtained when methanol labelled with ^{14}C was used for the termination. From these results it was concluded [83,84] that in oxide catalysts the terminal atom of the growing polymer chain carries a positive charge:

$$(\text{catalyst})^{-} \cdots {}^{+}\text{CH}_2\!=\!\text{P}$$

Thus polymerisation on oxide catalysts can be classified as belonging to the "cationic-coordination" type of catalytic polymerisation. To explain the nature of the polarisation of the active bond, it was suggested that in this bond the carbon is joined to a more electronegative element; for oxide catalysts, this element may be oxygen [83,86]. The possibility that an active M–C bond with an unusual type of polarisation is formed cannot however be excluded.

Data on the number of growth centres and the growth rate constants for the polymerisation of ethylene on oxide catalysts with different compositions, obtained by terminating the polymerisation by the introduction of $^{14}CH_3OH$, are given in Table 4.

Table 4. Determination of the kinetic parameters of growth for the polymerisation of ethylene on deposited oxide catalysts, by the radioactive stopper method [81-89].

Composition of catalyst	Conditions of activation	Temp. of polymerisation, °C	$10^2 n$, mole per mole of M	k_g, litre mole^{-1} s^{-1}	E_g, kcal mole^{-1}
Cr/SiO_2	Vacuum activation at 400°	75	0.45	695	—
Cr/aluminosilicate (3% Al_2O_3)	To же	75	0.39	350	—
Cr/TiO_2	»	75	0.11	195	—
Cr/ZrO_2	»	75	0.023	133	—
Cr/Al_2O_3	»	75	1.50	47	—
Cr/aluminosilicate (3% Al_2O_3)	»	75	0.255	262	—
ditto	Vacuum activation at 710°	75	0.260	680	—
»	Vacuum activation at 400°	75	0.39	350	—
»	Activated by reduction with SO_2	75	0.47	208	—
»	Ditto CO	75	0.50	1390	—
»	» H_2	75	0.056	695	—
»	» NH_3	75	0.046	2640	—
»	» HCN	75	0.065	2910	—
Cr/Al_2O_3	Activated by reduction with H_2	75	0.043	103	—
Mo/Al_2O_3	ditto	75	0.04	15.3	—
W/Al_2O_3	»	75	0.11	4.7	—
Cr/aluminosilicate	Activated by reduction with CO	75	0.50	1390	—
V/aluminosilicate	ditto	75	0.0057	28	—
Cr/SiO_2	Vacuum activation at 400°	90	0.27	—	—
ditto	ditto	75	0.24	670	—
»	»	60	0.16	468	4.2±0.5
»	»	50	0.130	412	—
»	»	40	0.060	334	—
Cr/Al_2O_3	Vacuum activation at 400°	90	0.86	—	—
ditto		75	0.65	61	5.4±1.0
»		50	0.216	33	—
Cr/Al_2O_3	Activated by reduction with CO	90	0.58	—	—
ditto	ditto	75	0.59	139	—
»	»	60	0.62	103	4.7±1.0
»	»	50	0.45	83	—
»	»	40	0.44	56	—

Evaluation of methods based on the introduction of a tracer. One of the chief difficulties in the quantitative determination of the number of growth centres by the introduction of a tracer into a polymer when complex organometallic catalysts are used is associated with the formation of inactive metal-polymer bonds (MPB) during polymerisation. These bonds arise as a result of chain transfer involving the organometallic co-catalysts. The reaction of inactive MPB with a stopper (alcohol or iodine) also leads to the introduction of a tracer into the polymer, as with active catalyst–carbon bonds. A direct indication of the formation of inactive MPB in a polymerisation system was obtained, for example, by Kohn and coworkers [18], who found that with increase in the duration of polymerisation the number of labelled polymer chains gradually increased, whereas the rate of polymerisation decreased (polymerisation of propene in the presence of $TiCl_3 + AlEt_2Cl$). A sharp increase in the number of labelled chains at constant rate of polymerisation was observed by Coover and coworkers [19].

Different authors have used different methods to introduce corrections for the formation of inactive MPB. The assumptions regarding the mechanism of polymerisation on which these calculations have been based have not always been sufficiently well-founded. According to the results obtained by Coover and coworkers [19], the rate of formation of MPB does not remain constant during the polymerisation—it is much greater in the initial stage than in later stages. In the opinion of the authors cited [19], this result casts doubt on data on the number of growth centres obtained by Natta and coworkers [31], Kohn and coworkers [18], and Chien [42], where the rate of transfer involving the organometallic compound was assumed to be constant, and the analysis for the concentration of tracer was carried out with a polymer obtained after polymerisation for a considerable period of time, as a result of which high values were obtained for the calculated number of active centres. In the calculation of the number of inactive MPB, [18,19] it was assumed that tracers enter all the polymeric molecules; the possibility that polymeric molecules are formed as a result of transfer involving the monomer or spontaneous termination was not taken into account. Coover and coworkers [19] recognise that, because of the difficulty of making allowance for inactive MPB, the accuracy of the determination of n and k_g is insufficient to permit the comparison of catalytic systems with different compositions.

The results obtained by Bier and coworkers [20,80] in a study of the polymerisation of propene on the catalytic system α-$TiCl_3 + AlEt_2Cl$ (or $AlEt_3$) with termination of the reaction by labelled alcohol, differ in many respects from the results of the study of analogous catalytic systems published by other workers [18,19,24,26,31]. In the opinion of Bier and coworkers, reactions involving transfer and termination of the chain with the formation of inactive MPB play a very small role for these catalytic systems, since they found that the molecular weight of the polymer was not influenced by the concentration of organoaluminium compound. The number of growth centres was therefore calculated directly from the concentration of tritium in a polymer obtained after termination of the polymerisation by butanol-^{3}H. These results were criticised by Kohn [30] and Medvedev and coworkers [90], who found for the same catalytic systems that the molecular weight of the polymer depends on the concentration of organometallic co-catalyst, indicating chain transfer, in which the formation of inactive MPB is possible.

The difficulties associated with the formation of inactive MPB can apparently be avoided by using catalytic systems which do not contain free metal alkyls. Youngman and Boor [25] tried to use this system as a model for the determination of the kinetic characteristics of the growth centres (see Table 1), but the results of the determination of k_g obtained by these workers cannot be regarded as unambiguous, since an increase in the number of metal–polymer bonds with time was observed, together with a decrease in the rate of polymerisation.

Oxide catalysts have been found to be more convenient when the method of radioactive stoppers is used, since these catalysts are one-component catalytic systems, which exhibit activity without the addition of organometallic compounds. All the catalyst–polymer bonds present in the system are active, and this makes it possible to calculate the number of growth centres directly from the radioactivity of the polymer [86,88]. For catalysts with the same chemical composition, within the limits of possible experimental error, the value of k_g was not affected by the quantity of inhibitor introduced, the concentration of catalyst in the solvent, the duration of polymerisation up to the moment of termination, the rate of polymerisation, and the porosity and original particle size of the catalyst. The value of k_g was also found to be independent of whether the polymerisation was carried out with or without

a solvent. The fact that the values of k_g were found to be constant provides evidence that the number of growth centres for this catalytic system is determined quantitatively, and that there is no diffusion retardation under these conditions.

The unsatisfactory features of methods in which tritium is used as a tracer include the difficulty of making allowance for the kinetic isotope effect. The magnitude of the isotopic effect in work in which alcohols labelled with tritium were used as stoppers has been estimated from the change in the radioactivity of the polymer on termination of the polymerisation by different quantities of stopper [18,80] or by altering the time interval within which the stopper is introduced into the reaction medium [38]. Considerable differences were observed in the values found for the kinetic isotope effect, the values obtained by different authors [18,19,38,79,80,91] varying from 1 to 4.5.

When iodine is used as stopper, the results of the determination of the number of active centres may be distorted by side reactions leading to a change in the concentration of the tracer in the polymer. One such reaction may be, for example, the formation of terminal vinylidene groups in polypropene with the liberation of hydrogen iodide [15].

In a number of instances, the possibility that the results of the determination of the number of active centres and the calculation of k_g may be distorted because of the influence of the rate of diffusion of the stopper and monomer to the growth centres cannot be excluded. The possibility that the formation of solid polymer during the reaction affects the kinetic relationships has been examined by many authors [23,80,92,93] in studies of the kinetics of the polymerisation of alkenes on Ziegler–Natta catalysts. Coover and coworkers [19] regarded the decrease in the concentration of aluminium alkyl on the catalyst surface due to slow diffusion through the layer of polymer formed as the reason for the decrease in the rate of formation of metal–polymer bonds during polymerisation. Youngman and Boor [25] attributed the decrease in the calculated value of k_g during polymerisation to an increase in the diffusion retardation of the transport of monomer as result of the formation of polymer on the surface of the catalyst. The possibility that the values of k_g found from the results of analysing a radioactive polymer may be distorted by diffusion retardation was also noted by Feldman and Perry [38]. Diffusion retardation was not observed in the polymerisation of ethylene on oxide catalysts when a loose porous polymer powder was formed [94]. When the polymerisation is carried out above 90° in a solvent, a decrease in the concentration of monomer at the surface of the catalyst particles is possible as a consequence of the resistance to diffusion through the layer of partly soluble polyethylene fraction with low molecular weight. This leads to a decrease in the rate of polymerisation on going from 75° to 90° with a constant number of growth centres [88], so that the calculated value of k_g decreases.

V. MECHANISM OF CATALYTIC POLYMERISATION BASED ON MEASUREMENT OF n AND k_g

The value of k_g provides a measure of the reactivity of the active centres with respect to growth. The conclusions which may be drawn from data on the change in n and k_g are more reliable than those obtained by comparing catalysts with respect to the rates of polymerisation relative to unit weight or surface area of the catalyst. We can consider some examples of the use of data on the kinetic parameters of growth to reach conclusions regarding the mechanism of the catalytic polymerisation of alkenes.

1. Number of Growth Centres and Degree of Utilisation of the Metal with Variable Valency

By determining the relative fraction of the metal with variable valency taking part in the formation of the growth centres it is possible to reach certain conclusions regarding the state of the transition element necessary for the manifestation of catalytic activity. In the examination of the mechanism of action of catalysts based on $TiCl_3$, two contradictory viewpoints have been put forward on the question as to which of the surface titanium atoms are potential active centres. Cossee and Arlman [10–12,95–97] formulated a theory, according to which catalytic activity is exhibited by coordinatively unsaturated titanium atoms, with chlorine vacancies, situated on the lateral faces of the $TiCl_3$ crystal; according to this theory, the titanium atoms adjoining the (001) basal plane do not take part in the formation of growth centres. Rodriguez and Van Looy [91] observed the formation of patches of polymer on the surface of a $TiCl_3$ crystal, the positions of which coincided with the points of emergence of spiral dislocations. In their opinion, these results confirm the view that the active centres arise only on the lateral faces of the $TiCl_3$ crystals; active centres are not formed on the basal plane, which makes up 95% of the total surface area of the $TiCl_3$ crystal.

Chirkov and coworkers [17,39] determined the number of growth centres by a kinetic method for a system based on VCl_3 (specific surface $\sim 5\ m^2\ g^{-1}$) and found that the maximum number of active centres amounts to $\sim 5 \times 10^{14}$ centres per cm^2, the order of magnitude of which corresponds to that of the total number of surface vanadium atoms. Thus according to these results, active centres should form on the basal plane of the crystals of the halides of the metals with variable valency.

It should be noted that when the fraction of the metal with variable valency taking part in the formation of growth centres is compared with the total number of surface atoms of the transition metal halides, it is necessary to consider the possibility that reversible deactivation (transfer processes) and irreversible poisoning of the growth centres take place. In general, the following relationship applies for catalytic polymerisation:

$$N = n_g + n_x + n_y \qquad (8)$$

where N is the total number of transition metal atoms capable of taking part in the formation of growth centres ("potentially active centres" or "active component" of the catalyst), n_g the centres joined by an active bond to the growing polymer molecule (actual growth centres), n_x the centres in a state of reversible deactivation as a result of transfer processes ("initiation centres"), and n_y the irreversibly deactivated centres.

Data on the value of n_g, which usually depends markedly on the purity of the polymerisation system and the conditions of preparation of the catalyst, cannot provide an unambiguous basis for obtaining information as to the number of potentially active transition metal ions (the value of N). Analysis of data on the fraction n_g relative to the total number of transition metal atoms in Ziegler–Natta catalysts is made difficult by the fact that most authors do not give data on the surface area of the heterogeneous component of the catalytic system. It may be noted that most papers on catalysts based on $TiCl_3$

($AlEt_2Cl$ and $AlEt_3$ co-catalysts) give similar values for n_g ($0.5\times10^{-2}-5\times10^{-2}$ mole per mole $TiCl_3$ for temperatures in the range 50–70°, which for $TiCl_3$ specimens with a surface area of 5–25 $m^2\,g^{-1}$ corresponds to 10–100% of the surface atoms). Some authors [28] have obtained values of n_g which are clearly greater than the number of titanium atoms adjoining the surface. For systems based on $TiCl_4$ and VCl_4, used for the polymerisation of ethylene (see Table 3), a higher fraction n_g is observed, probably due to the high degree of dispersion of the heterogeneous component.

For oxide catalysts, the fraction of growth centres relative to the total concentration of deposited metal with variable valency depends on the composition of the catalyst (see Table 4). The maximum degree of utilisation of the metal with variable valency, observed for a chromium oxide catalyst on an Al_2O_3 base, amounted to 1.5%. It should however be noted that these results were obtained for comparatively low rates of polymerisation. By decreasing the concentration of impurities in the reaction medium, in particular by carrying out the polymerisation in the gaseous phase, when there is no deactivation of the growth centres by impurities in the solvent, a high rate of polymerisation is achieved on chromium oxide catalysts (up to 1.5×10^5 g polyethylene per g of chromium per hour). Under these conditions, up to 25% of the deposited chromium is present in growth centres. From these results it was concluded [98] that all the chromium with oxidation state +6, present in the deposited oxide catalysts in the form of surface compounds of the chromate type [99], can act as active centres. The formation of growth centres is accompanied by the reduction of Cr^{6+} to compounds of chromium in one of its lower oxidation states (Cr^{2+} and Cr^{3+}). The decrease in the number n_g relative to N is due both to reversible deactivation [100] as a result of transfer involving impurities such as CO, CO_2, and C_2H_2, and to irreversible poisoning (for example as a result of the action of water [51,52]).

The dependence of the number of growth centres on the conditions of polymerisation can give information on the mechanism of their formation. The most detailed results have been obtained by studying the dependence of the number of growth centres on the temperature of polymerisation. If the number of growth centres changes with change in temperature, the total activation energy (E_{form}), determined from the temperature dependence of the rate of polymerisation, differs from the activation energy of growth (E_g), which can be determined from the temperature of k_g. A large amount of published information indicates that the number of growth centres depends on the temperature of the catalytic polymerisation [18,23,24,31,38,42,80,101]. It has been shown [81,101,102] that for systems based on $TiCl_3$ the number of growth centres is inversely proportional to the temperature of the process. The explanation is that the reaction involved in their formation, which takes place when $TiCl_3$ reacts with the metal alkyl, is reversible and reaches equilibrium under the conditions of polymerisation. A characteristic feature is the marked scatter in the values of E_{form} obtained by different authors for catalytic systems with similar compositions [36,38,103–105]. Data on the dependence of E_{form} on the composition of the catalyst are equally contradictory [65,103,105–109].

There is comparatively little published information on the direct determination of E_g from the change in k_g with temperature for complex organometallic catalysts (see Tables 1–3). The values of E_g differ considerably from the values of E_{form} [5,8,18,53,38].

For oxide catalysts it has been shown by the radioactive stopper method that the number of growth centres changes with change in the temperature of polymerisation [88,101]. The nature of this dependence (and hence the value of E_{form}) varies with the composition of the catalyst. From data on the influence of preliminary reduction of the catalyst on the temperature dependence of the number of growth centres, it was concluded that the formation of growth centres in chromium oxide catalysts involves the reduction of sexavalent chromium and is irreversible.

2. Composition of Growth Centres

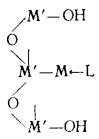
Data on the influence of the composition of a catalyst and the conditions of its preparation on the value of k_g can be used to reach a number of conclusions regarding the composition of the active centres. Unfortunately, for Ziegler–Natta catalysts, different methods for determining k_g for a given catalytic system give values which differ considerably (for example, by a factor of 30 at 70° for the simplest system studied—the polymerisation of propene in the presence of $TiCl_3 + AlEt_2Cl$) (see Table 1). There is little published information on the comparison of catalysts with different compositions using values of k_g obtained by the same method. Natta and coworkers [8,35] compared the "viscosity-average" growth rate constants (k_g) for the polymerisation of but-1-ene in the presence of different catalytic systems. They found (Table 2) that k_g is independent of the form of organometallic compound used, but depends on the compound of the metal with variable valency. On the basis of these results, it was concluded [8,35] that for systems based on the same transition metal halide, the growth centres are kinetically equivalent, and their reactivity is independent of the alkylating compound. The difference in the rate of polymerisation for different organometallic components, which in some instances amounts to more than two orders of magnitude, is due entirely to the difference in the number of active centres. Change in the metal with variable valency leads to a change in both the growth rate constant and the number of active centres. The stereoregularity of the polymer was found to depend on the type of metal alkyl, from which it was concluded [8,35] that the active centres are "bimetallic" (include both the metal with variable valency and the metal of the alkylating compound). Cossee and Arlman [10,95–97] formulated the theory that the active centres of the Ziegler–Natta catalysts are "monometallic". Unfortunately, the change in k_g for catalysts not containing alkyls [25], prevents unambiguous results on the influence of the organometallic compound on the kinetic properties of the growth centre being obtained.

Data have been published on the change in the kinetic properties of the growth centres when electron-donor additives are introduced into a catalytic system [9], when hydrogen is introduced into the system [110], and with change in the ratio of the organometallic co-catalyst to the compound of the metal with variable valency [9,38,42,111].

Interesting results were obtained [31] by comparing the radioactivity of the atactic and isotactic fractions of polypropene with their concentration in the polymer; from these results it was concluded that the rate constant for the centres on which the atactic polymer is formed is smaller by a factor of 6 than that for the centres on which the stereoregular polymer is formed.

In a study of the effect of the composition and conditions of preparation of oxide catalysts on the value of k_g, it was

established that k_g is influenced by change in the metal with variable valency (M), the cation of the oxide carrier (M'), the agent used for the preliminary reduction of the catalyst, and the temperature of activation of the catalyst. On the basis of these results, the following scheme [89], giving the composition of the immediate environment of the metal with variable valency in the growth centre of oxide catalysts was proposed:



Here, L represents the ligand which forms part of the growth centre after treatment of the catalyst with an agent capable of forming coordination compounds. The rate constants for transfer (involving the monomer and the spontaneous process), determined from the dependence of the molecular weight on the conditions of polymerisation, depend on the same factors as the value of k_g. [112]

3. Mechanism of Growth

The number of growth centres for different concentrations of monomer has been measured, and it has been shown that the reaction involved in growth is first order with respect to the monomer for catalysts based on transition metal halides [8,18,24,35] and for chromium oxide catalysts [88].

In most schemes proposed to explain the mechanism of the catalytic transformation of alkenes in the presence of transition metal compounds, it is considered that a necessary stage is preliminary complex formation by the alkene (the so-called coordination mechanisms [109,113]), as a result of which the double bond is weakened and its reactivity increases. For a two-stage mechanism of polymerisation, including as first stage the formation of a π-complex [9-12], the first order kinetics of the reaction with respect to monomer may correspond to case 2 [see Eqn. (1)]:

1. $k_g = k_1$; in this instance, E_g corresponds to the activation energy of the formation of the π-complex;
2. $k_g = K_a.k_2$; in this instance, $E_g = E_2 - Q$, where E_2 is the activation energy of the introduction of ethylene at the active bond; Q the heat of formation of the π-complex, and $K_a = k_1/k_{-1}$ the equilibrium constant for the formation of the π-complex.

In the opinion of Natta and coworkers [8], the limiting stage in the polymerisation of alkenes on catalysts based on transition metal halides is the first stage (the formation of the π-complex). In a number of instances, low values were found for E_g (2.5 kcal mole^{-1} for a catalyst based on VCl_3; 4.5 kcal mole^{-1} for a catalyst based on $TiCl_3$; and 4–5 kcal mole^{-1} for chromium oxide catalysts). In these instances the pre-exponential factors have anomalously low values (10^5–10^6 litre mole^{-1} s^{-1}). A possible reason is that the formation of the surface π-complexes is accompanied by a marked decrease in entropy. At the present time, however, there are no unambiguous data which exclude the possibility that for the catalytic polymerisation of alkenes the second situation is realised ($k_g = K_a.k_2$), and the value found for E_g is not the activation energy of the elementary stage.

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After the present review had been written, a number of new papers were published [32-34,47-49], giving results of the determination of the number of growth centres and the growth rate constants for the catalytic polymerisation of alkenes. These results are included in Tables 1 and 3.

Papers [32,33] based on previously developed kinetic methods and the inhibition method give new data on the values of n and k_g for the polymerisation of alkenes in the presence of complex catalysts based on $TiCl_3$ and VCl_3. The values obtained for n correspond to almost complete coverage of the catalyst surface, from which it follows that the active centres are situated chiefly on the basal planes of the $TiCl_3$ and VCl_3 crystals. These results were used to provide a basis for a model of a stereospecific active centre, which is localised on the basal plane and which has two vacancies per transition metal ion in the growth centre.

Radioactive inhibitors have been used [48,49] to determine the kinetic parameters of growth in the polymerisation of ethylene on titanium dichloride, which is active in the polymerisation of alkenes without the addition of organometallic compounds. In addition to the labelled alcohol which is usually employed for this purpose, $^{14}CO_2$, ^{14}CO, and $^{14}CH_3CH_2CH_2I$ were used. For this one-component heterogeneous catalytic system, since there are no inactive aluminium–polymer bonds, the method of radioactive inhibitors makes it possible to determine reliably the number of growth centres. The results obtained show that the value of n amounts to not more than ~0.1% of the number of surface titanium atoms in the $TiCl_2$ specimens used. The probable explanation is that the alkylation of titanium by ethylene under mild conditions takes place on surface defects of the $TiCl_2$ crystals. The value of k_g found in these experiments is greater by about two orders of magnitude than the values of k_g obtained for the polymerisation of ethylene on catalysts based on $TiCl_3$. [32,37,38]

The use of radioactive inhibitors of different types to study one-component heterogeneous catalysts (chromium oxide and titanium dichloride) also gave results [49] confirming the coordination mechanism of growth in the catalytic polymerisation of alkenes.

A number of papers published in recent years have been devoted to the study of the morphology of polyalkene crystals formed directly during polymerisation ("primordial morphology"). These results can be used to reach an understanding of the mechanism of formation of a solid polymer on the surface of a solid catalyst. In particular, values of the growth rate constants have been calculated [34,47] from the results of an electron-microscope study of polyalkene crystals produced in the initial stage of polymerisation. The value of k_g found [47] for the polymerisation of ethylene on a chromium oxide catalyst is close to the value of k_g obtained for catalysts with the same composition by the radioactive inhibitor method. The value of k_g obtained [34] for the polymerisation of propene on the $TiCl_3 + Al(CH_3)_3$ catalytic system is smaller by two orders of magnitude than the values given above for analogous systems (see Table 1).

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Conformational and Thermodynamic Properties of Macromolecules in Ternary Polymeric Systems

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An account is given of the present state of knowledge on the properties of solutions of homopolymers and copolymers (having different distributions of monomer units in the chain) in binary mixtures of solvents. Several specific features of the hydrodynamic behaviour of macromolecules in such systems are discussed. Selective adsorption, which develops in mixed solvents, cannot be responsible for the lack of agreement between theory and experiment. Results reported here indicate that macromolecules retain a Gaussian structure ($[\eta]_\theta \propto M^{1/2}$) in several polymer-binary mixture systems. Conformational properties and transitions of macromolecules from a "segregated" to a random form are examined as functions of the composition of the mixed solvents. A list of 61 references is included.

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1. Introduction

Considerable attention has been paid during recent years [1-8] to investigating the properties of solutions of polymers involving ternary systems†. However, experimental information on this question is still inadequate and contradictory, perhaps owing to specific features of the hydrodynamic behaviour of copolymers in solution [9,10] or to the development of selective interactions (selective adsorption) in ternary systems comprising a polymer plus a binary mixture [11]. A final solution to the problem may be obtained from further special investigations, for the correlation of theory with experiment in ternary systems is still mainly qualitative.

The present paper gives a brief account of modern views on the thermodynamics of solutions of polymers in ternary systems. It considers also certain results obtained by the Reviewer when investigating the structure and the hydrodynamic behaviour of molecules of random chloroprene–isoprene and chloroprene–dichlorobutadiene copolymers and of the corresponding homopolymers in ideal mixed solvents [12-18]. In contrast to homopolymers, copolymers are inhomogeneous with respect not only to conformation but also to composition, but we shall not deal with the latter type of variability, and refer merely to the survey by Litmanovich and Izyumnikov [19].

2. θ-Conditions and Unperturbed Dimensions of Macromolecules in Ternary Polymeric Systems

According to modern views, "equilibrium dimensions" of macromolecules, whose structure is unperturbed by the solvent, are established under θ-conditions, when the osmotic forces of repulsion between the dissolved polymer macromolecules and the solvent molecules are balanced by coiling of the molecular chains because of the energetic unfavourability of the contacts between polymer and solvent [20]. In other words, the condition of zero second virial coefficient A_2 in the expansion of the osmotic pressure should correspond unambiguously to the absence of swelling of the molecular coil ($\alpha = 1$) and maintenance of the conditions $[\eta]_\theta \propto M^{\frac{1}{2}}$. However, recent results indicate that the Gaussian distribution may break down in ternary systems ($[\eta]_\theta \neq K_\theta M^{\frac{1}{2}}$).[9] Furthermore, the very concept of θ-point (and also α-point) now requires some elaboration, as indicated by results on the conformational transitions of macromolecules in the critical region of polymer–solvent mixing [21-23]. Attention must be paid also to the existence of both upper and lower critical temperatures for several rigid and semi-rigid macromolecules [24,25]. The Reviewer [26] has also observed phase separation with rise in temperature for aqueous solutions of poly(methyl vinyl ether)—"thermal denaturation" of the macromolecules—caused by rupture of polymer–solvent intermolecular hydrogen bonds [27].

It is noteworthy that Benoit and Dondos have recently suggested [28] that solutions of polymers in binary mixtures may have two θ-points, owing to the development of selective interactions (selective adsorption), which distort the Gaussian structure of the macromolecules even when $A_2 = 0$. From investigations of the temperature dependence of the unperturbed coil dimensions of several polymers in binary mixtures these workers concluded further that the present classical theory of solutions is unsuitable for strongly associated solvents [29]. It was found that K_θ in such solvents was smaller than $K_{\theta,\text{ideal}}$ and increased with rise in temperature (Fig. 1). Extrapolation of K_θ to the boiling point of the solvent, when association of solvent molecules disappears, yields the ideal value of K_θ. The decrease in the unperturbed dimensions of the macromolecules in associated solvents is explained [29] by intermolecular polymer–solvent interaction, leading to the formation of cyclic structures bound by hydrogen bonds of the solvent, which in turn produces a decrease in $(\overline{h^2})_\theta^{\frac{1}{2}}$ of the macromolecules.

However, the conclusions reached in the above papers are open to question, since they are based not on direct experiment but on extrapolation by the Stockmayer–Fixman method [30] far from the θ-point:

$$[\eta] \cdot M^{-1/2} = K_\theta + 0.51 \cdot \Phi_0 \cdot BM^{1/2}; \quad B = \bar{V}^2(1-2\chi_1)/V_1 N_A \qquad (1)$$

† We shall hencefore take a ternary polymeric system to imply solutions of copolymers (with different types of distribution of monomer units in the chain–random, block, and graft copolymers) and of homopolymers in binary mixtures of solvents.

where $\bar{V}$ is the partial specific volume of the polymer, V_1 the molar volume of the solvent, and χ_1 a thermodynamic parameter of intermolecular polymer–solvent interaction. Although Eqn. (1) is regarded as soundly enough based for estimating the unperturbed dimensions of macromolecules in solution [31], it is premature to consider that calculations using this equation establish a specific effect of the solvent.

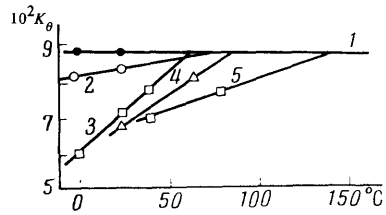

Figure 1. Temperature dependence [29] of K_θ for poly-2-vinylpyridine in dilute solution in: 1) chloroform; 2) ethanol; 3) methanol; 4) propan-2-ol; 5) cyclohexane.

On the other hand, Cowie [32], who investigated the unperturbed dimensions of a polystyrene fraction ($\bar{M}_w = 2.2 \times 10^6$) in binary solvent mixtures, demonstrated that selective adsorption cannot be responsible for the dependence of $(\overline{h^2})_\theta^{\frac{1}{2}}$ on the composition of the θ-solvent, since a unique relation between $(\overline{h^2})_\theta^{\frac{1}{2}}$ and the selective adsorption parameter λ' was not observed.

Several new results have been obtained [33,34] on selective adsorption in ternary polymeric systems, its thermodynamic interpretation, and also the effect on the conformation of the macromolecules. These workers state that a definite correlation exists between the swelling α of a macromolecule and selective adsorption in ternary systems, the change in the radius of inertia of the macromolecules $(R^2)^{\frac{1}{2}}$ being $\leq 10\%$ for solutions of non-polar polymers. Nevertheless, a quantitative relation is observed in the well known dependence on composition of the dimensions: $[\eta]_\theta$ and $(\overline{h^2})_\theta^{\frac{1}{2}}$ pass through a sharp maximum (this change in these parameters amounts to ~30% and 10% respectively).

Conformational transitions of cooperative character have been observed also for molecules of unionised polymethacrylic acid with change in composition of the θ-solvent [35,36].

The specific effect of θ-solvents on the structure of macromolecules observed by Poddubnyi et al. [37] in ternary systems was explained mainly by the considerable polarity of the copolymer examined. Other workers [11,38] attribute this effect to the thermodynamic interaction parameter χ_{AB} of the copolymer components in the given solvent. A linear relation is reported [38] between the values found for K_θ (extrapolated as in Ref. 30) and χ_{AB}, so that extrapolato $\chi_{AB} = 0$ (Fig. 2) will give the additive value of K_θ. The temperature variation in the parameter χ_{AB} is due also to the strong temperature dependence of the unperturbed dimensions.

Incidentally, analysis of the unperturbed coil dimensions of styrene–acrylonitrile and styrene–methyl methacrylate copolymers and of the corresponding homopolymers in solution shows that freedom of rotation about a single bond between unlike monomers is more strongly temperature-dependent than is that about similar bonds between units of the same type [39]. Considerable sensitivity of short-range action to variation in the θ-temperature has been established also by the Reviewer [15,16] for molecules of a random chloroprene–dichlorobutadiene copolymer, although additional short-range interactions between unlike monomer units in copolymer chains have a quite insignificant effect of $(\overline{h^2})_\theta^{\frac{1}{2}}$. [12,13] Fig. 3 shows that increase in the θ-temperature (by ~50 deg) leads to an average decrease of 15% in the unperturbed dimensions.

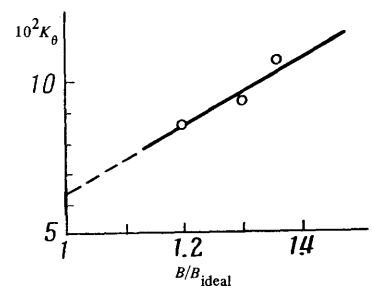

Figure 2. Variation in K_θ with the ratio of B to its "ideal" value: this relation represents the incompatibility of the components of the copolymer chain in solution [38].

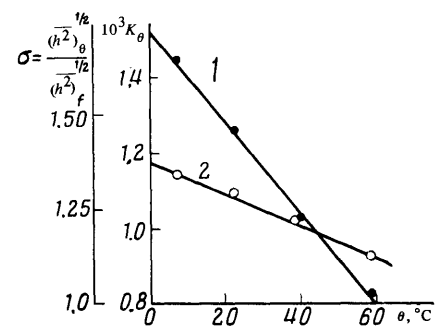

Figure 3. Variation with the θ-temperature, for a random chloroprene–dichlorobutadiene copolymer in solution, of the conformational parameters: 1) $K_\theta = \Phi_0(\overline{h_\theta^2}/M)^{\frac{3}{2}}$; 2) $\sigma = (\overline{h^2})_\theta^{\frac{1}{2}}/(\overline{h^2})_f^{\frac{1}{2}}$.

The above considerations do not exclude the possible preservation of the Gaussian structure of molecular coils in binary mixtures. In fact, the Reviewer has shown [18] (Fig. 4) that the nature of the θ-solvents (in this case their polarity) neither changes the Gaussian distribution in the chloroprene–dichlorobutadiene copolymer nor affects the values of $[\eta]_\theta$, although the influence of electrostatic

polymer–binary mixture interaction of $[\eta] \propto (\overline{h^2})_\theta^{\frac{3}{2}}$ is quite appreciable for molecular chains comprising monomer units of the same type[14]. The fact that it is not apparent in the above copolymer chains can probable be explained by the lower polarity of the dissolved copolymer molecules, caused by the predominance of *trans*-1,4-dichlorobutadiene units. An analogous dependence of unperturbed macromolecular dimensions on molecular weight (i.e. $[\eta]_\theta \propto M^{\frac{1}{2}}$) was obtained[40] for butadiene–nitrile copolymers, and was attributed to the impossibility of forming sufficiently long microblocks of units of the same type in the copolymer chains.

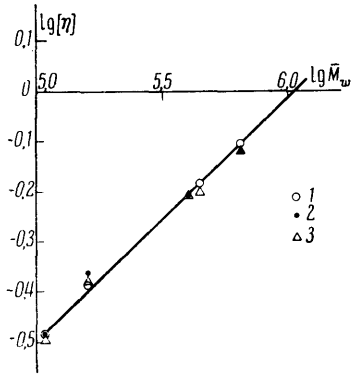

Figure 4. Dependence of $\lg[\eta]$ on $\lg\bar{M}_W$ for chloroprene–dichlorobutadiene copolymer fractions at $\theta = 25.4°C$ in binary solvent mixtures (by volume): 1) 1.33 : 1 chloroform + acetone; 2) 5.18 : 1 benzene + methanol; 3) 1 : 1 carbon tetrachloride + n-octane.

Nor is the Gaussian structure of the copolymer macromolecules distorted in the θ-state if the polymer–solvent interaction is almost the same for the chain components[10,41]. Results obtained by Inagaki et al. in a detailed study of the properties of solutions of block and random copolymers of styrene with methyl methacrylate show[41] that in cyclohexanol the θ-temperatures differ very little for block copolymers (with different styrene contents) and for the corresponding homopolymers, whereas for random copolymers the θ-temperature varies appreciably with different styrene contents, passing through a minimum in the vicinity of the equimolecular copolymer (Fig. 5). In 2-ethoxyethanol block copolymers have higher θ-temperatures than random copolymers of similar composition, probably as a consequence of intramolecular interaction between styrene and methyl methacrylate units. Nevertheless, the closeness of the conformational and thermodynamic properties of block copolymers to the average properties of homopolymers somewhat contradicts existing views[3].

Conformational analysis of macromolecules for a large number of copolymers differing in structure shows[42–46] that the unperturbed coil dimensions follow (with insignificant deviations) a simple additivity rule (i.e. short-range interactions in the copolymer chains are the same as in the corresponding homopolymers). A clear exception to this rule is provided by graft (particulate and block) copolymers, in which interactions between unlike units have a substantial effect of $(\overline{h^2})_\theta^{\frac{1}{2}}$ (or the thermodynamic flexibility). For example, the optical and hydrodynamic properties of solutions of graft poly(methyl methacrylate)–polystyrene copolymers show[47] that the rigidity of such a macromolecule, regarded by Tsvetkov and his coworkers as a persistent chain, exceeds the value usually obtained for carbon-chain macromolecules[20] by an order of magnitude. The greater rigidity of the graft copolymer chains is assumed[47] to be due to the interaction of side-groups, which form intramolecular structures, having a high degree of orientational order, this being responsible for the great optical anisotropy of the macromolecule.

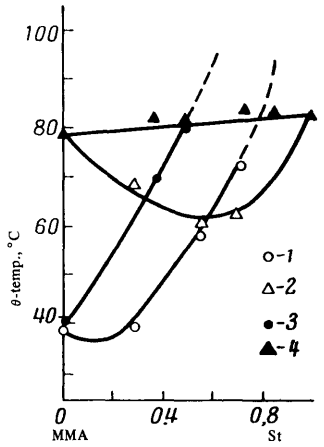

Figure 5. Dependence of θ-conditions on styrene (St) content for copolymers with methyl methacrylate (MMA):[41]
1) random copolymers in 2-ethoxyethanol;
2) random copolymers in cyclohexanol;
3) block copolymers in 2-ethoxyethanol;
4) block copolymers in cyclohexanol.

3. Ternary Polymeric Systems in Good Solvents

Several studies of ternary polymeric systems have demonstrated[50–53] that an intrachain phase separation of the copolymer (a "segregated conformation" of the coil) occurs in selective solvents, when the insoluble portion "settles out", being twisted "on itself", which diminishes to a minimum the interaction between unlike chain units (or the number of "heterocontacts"). In such a solution, therefore, intrachain and interchain interactions between segments differ markedly.

It has been reported[54] that the transition from the "segregated" to the random form corresponds to a definite composition of the binary solvent mixture: the "segregated conformation" exists above this transition composition (or temperature), and a random conformation below it, the former excluding and the latter permitting contact between unlike monomer units of the copolymer. These transitions are, of course, accompanied by great conformational changes (the dimensions of the copolymer chain and hence the viscosity of the solution either decrease or increase sharply). The presence of selective interactions in solutions of copolymers is responsible for their specific

thermodynamic and hydrodynamic behaviour. Fig. 6 [40] illustrates a peculiar effect associated with the development of such interactions for solutions of fractions of a random butadiene–acrylonitrile copolymer.

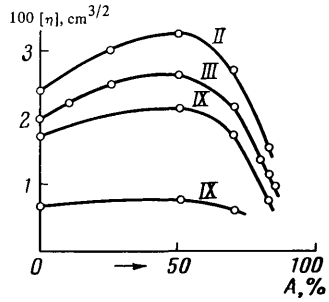

Figure 6. Dependence of intrinsic viscosity of butadiene–acrylonitrile copolymer fractions on composition of butan-2-one–cyclohexane mixtures (numbering of curves indicates that of the fractions [40]).

If we extend to solutions of copolymers the usual concepts applicable to homopolymers, and characterise the hydrodynamic behaviour of a molecular coil by the excluded segment volume

$$Z = \int_0^\infty \{1 - \exp[-U(r)/kT]\}\, 4\pi r^2\, dr \qquad (2)$$

where $U(r)$ is the potential interaction energy of two segments distant r apart, we obtain for a random copolymer [55]

$$\langle Z\rangle_{rand} = X^2 Z_{AA} + (1-X)^2 Z_{BB} + 2X(1-X) Z_{AB}, \qquad (3)$$

in which X is the proportion by weight of component A in the chain. The parameters representing interaction between A, B, and AB units are respectively

$$Z_{AA} = 2V_1\left(\frac{1}{2} - \chi_{A_1}\right);\ Z_{BB} = 2V_1\left(\frac{1}{2} - \chi_{B_1}\right);$$
$$Z_{AB} = \frac{Z_{AA} + Z_{BB}}{2} + V_1\chi_{AB}. \qquad (4)$$

(The subscript "1" denotes the solvent). Analogous deductions were made [55] for graft and block copolymers, but the formulae are too cumbersome to be considered here.

The above relations show that, when the θ-conditions are satisfied for a random copolymer and one of the corresponding homopolymers A (i.e. $\langle Z\rangle_{rand} = 0$ and $Z_{AA} = 0$), and χ_{AB} is positive, the other component may be somewhat below its θ-temperature ($Z_{BB} < 0$). This represents the so called "negative volume effect", which has actually been observed by several workers [9,53]. However, experimental results [9] show that Z_{BB} for the copolymers investigated is still so small that there is no appreciable "settling out" of monomer units of B, and hence no distortion of the Gaussian structure. In selective solvents, however, when the coefficients of Z_{AA}, Z_{BB}, and Z_{AB} become functions of the selectivity, the probability of contacts between units of the insoluble component is increased, which obviously leads to distortion of the conformation of the coil and ultimately its "stratification" [48–52,54]. With solvents and mixtures of cross selectivity (for a random copolymer of methacrylic acid with methyl methacrylate [53]) it becomes possible to trace a continuous transition from a secondary structure of one type to a structure of another type, through a stage involving the most uncoiled conformation, as a consequence of non-selective solvation of both types of monomer unit in the binary mixtures (Fig. 7).

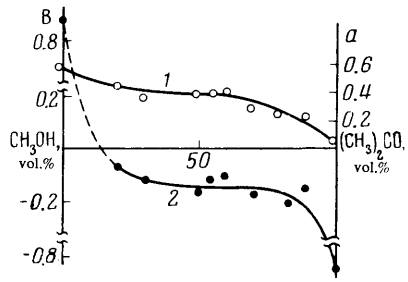

Figure 7. Effect of composition of mixed solvent (methanol + acetone) [49] on: 1) power of a in the Mark–Houwink equation; 2) the parameter B.

Since the literature frequently reports attempts to link the swelling coefficient α of copolymer molecules in solution with the thermodynamic parameter χ_{AB} of interaction between unlike monomer units of the copolymer one with the other and with the solvent [38,56], we must note a specific aspect of the thermodynamic properties of solutions of graft copolymers which was observed by Eskin and Baranovskaya [57,58]. These workers established that the second virial coefficient $A_2 \simeq 0$ for graft copolymers of polystyrene with poly(methyl methacrylate) ($X_A = 0.9$) having sufficiently high molecular weights ($\bar{M}_w > 10^6$). In fact calculation based on Flory's theory of polymer solutions [59]

$$A_2 = \frac{N_A Z}{2M^2} F(Z), \qquad (5)$$

(where $F(Z)$ is a function of the thermodynamic parameters of intermolecular polymer–solvent interaction), allowing for the hydrodynamic "non-flowability" of the coils [47], shows that the second virial coefficient A_2 for solutions of such graft copolymers [57] is of the order of 10% of that for solutions of the homopolymers, and decreases considerably more rapidly with molecular weight. This property of solutions of graft copolymers must, of course, be taken into account in determining the θ-conditions (e.g. by interpolating the temperature dependence of A_2 found by light scattering).

Experimental facts reported by Inagaki et al. [42] indicate, however, that long-range interactions between unlike monomer units do not disappear under any conditions, even when such interactions between units of the same type have absolutely no effect on the conformation of the macromolecules.

In conclusion we note that Dondos and Patterson [60] have examined the intrinsic viscosity of polymers in mixed solvents using theoretical results [61] on the effect of selective adsorption on the thermodynamic properties of polymer solutions. They find that the difference in the intrinsic viscosity of solutions of polymers in binary mixtures produced by taking selective adsorption into account is

$$\Delta[\eta] = \frac{1.02\bar{V}^2\Phi_0 M G^E(\varphi_2^0)}{N_A V R T}, \qquad (6)$$

where V is the molar volume of the mixed solvent, φ_2^0 the fraction by volume of the second component in the solvent, and G^E the excess free energy of mixing of the component with the solvent. Only qualitative agreement was obtained when this equation was tested on various ternary polymeric systems: the quantitative results differed by factors of $10-10^2$, a discrepancy between theory and experiment which could hardly be explained by selective adsorption, as the authors pointed out. Nevertheless, the theoretical slight temperature dependence of intrinsic viscosity in binary mixtures

$$-T\frac{\partial(\Delta[\eta])}{\partial T}=\frac{1{,}02\bar{V}^2\Phi_0 M H^E(\varphi_2^0)}{N_A V R T}, \qquad (7)$$

where H^E is the heat of mixing of the binary solvent mixtures, agrees quite satisfactorily with experiment.

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Separation of Isotopes by Electrical Migration and Determination of Ionic Mobilities in Molten Salts

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Problems of the use of ionic migration for the separation of stable isotopes under laboratory conditions and in large-scale plant are considered. The phenomenological theory of the process, the apparatus, the mode of operation, experimental conditions, and results obtained for twenty elements are discussed in detail. Results obtained by countercurrent and zone electrical migration for the structure of molten salts and the mechanism of the migration of ions in an electric field are examined. A list of 341 references is included.

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I. INTRODUCTION

Electrical migration is the directed movement of ions in an electric field, which is superimposed on the random thermal motion of the particles. Study of the motion of ions in an electric field is important both for elucidating the internal structure of a substance and the actual mechanism of such motion and, in application, for separating mixtures of substances in an ionised state, in particular for the separation of isotopes.

Electrical migration has been the subject of several reviews [1-25], some of which have become out of date. Yet many experimental and theoretical papers are continually being published on this method, which indicates the unflagging interest of research workers. It therefore appears useful to review the present-day state of the problem.

Electrical migration can be accomplished in solids, liquids, and gases possessing ionic conduction. The present review considers aspects of the migration of ions in molten salts. Information on analogous processes in other media—solid salts, solutions, liquid metals—is given only in the historical survey or for comparison with corresponding data for molten salts. Reviews have been published fairly recently on the movement of ions in aqueous solutions [26,27] and in liquid metals [28,29].

II. HISTORICAL SURVEY

The separation of isotopes by the migration of ions in an electric field is based on the fact that the mobility of isotopic ions is greater the smaller their mass. This idea was first put forward in 1921 by Lindemann [30]. Milliken and Harkins [31], however, then expressed doubt concerning the feasibility of the process owing to possible masking of the isotopic effect by diffusion and convection. These misgivings appeared to be confirmed by a series of experimental papers [32-37], for no change could be observed in the isotopic composition of lithium, magnesium, or chlorine in attempts to effect the electrical migration of their salts in aqueous solution, and Eilert's experiment [38] evidently passed unnoticed. And although rare-earth metal ions were successfully separated by this method [37,39-42], Jette [43] concluded, from a comparison of deductions from hydrodynamic and kinetic theories, that "differences in the mobilities of isotopic ions are extremely small, and cannot be detected by existing methods". Attention was therefore switched to other processes, and even in 1942 Kendall [44] still asserted that the method was powerless to effect the separation of isotopes.

These failures are explained by the low sensitivity of the method of isotopic analysis—determination of the atomic weight of the element undergoing separation—employed at that time. An isotope effect was, of course, present, but it was too small. This was proved later, when mass-spectrometric and activation methods of analysis became generally available, and radioactive isotopes began to be used as tracer atoms: when the experiments were repeated under identical conditions, a change in isotopic composition was not only observed qualitatively but also measured quantitatively [45-49].

In the initial attack on problems of producing an atomic bomb a detailed study was made of many methods—including electrical migration—suggested earlier for separating isotopes. As early as 1942 several groups of investigators in the U.S.A. were developing this method [50-58], but the first publication appeared only in 1946. [59] Accounts appeared later of the method of operation based on the countercurrent principle, and experimental results on the separation of the isotopes of potassium [60,61], chlorine [62], copper [63], and uranium [64,65], as well as the theory of the process [66,67]. During the War interest in this method was taken also in Germany [68-72].

In the postwar period the method of electrical migration was developed in several directions. Countercurrent electrical migration in aqueous solution applied to the separation of isotopes was studied in the Soviet Union [73-84], the Federal Republic of Germany [4,85-90], Switzerland [91-100], West Berlin [27,101-114], and Israel [115,116]. Electrical migration combined with ion exchange in resin-filled columns or with the use of ion-exchange membranes has been studied in Japan [117-130] and in the Soviet Union [131-137]. The electrical migration of ions on a paper strip impregnated with an aqueous salt solution has been studied in France by the use of radioactive and stable isotopes [13,14,138-144].

Study of the diffusion of ions in salt crystals by means of a radioactive tracer [145-148] suggested conducting this

process with a superimposed constant electric field: in this way electrical migration was effected in single crystals or compressed powders of salts[148-155]. The production of high-temperature fuel cells with solid electrolytes enabled them to be used to enrich oxygen isotopes by the electrical migration method[156-158].

Molten salts, which, like aqueous solutions, permit the countercurrent principle to be applied and thereby the effect of the difference in mobility between isotopic ions to be magnified many times, have attracted great attention from research workers. Following the successful enrichment in 1947 of lithium and potassium isotopes in a mixture of their molten chlorides[159], more than a hundred theoretical and experimental papers have appeared on countercurrent electrical migration in molten salts: studies have been made of the separation of the isotopes of lithium[20,21,159-197], sodium[192,198], potassium[20,21,159,191,192,199-201], rubidium[178,192,200,202,203], caesium[192], copper[204], silver[205], magnesium[191,206,207], calcium[21,206-214], strontium[206,207], barium[206,207], zinc[215,216], cadmium[214,217,218], thallium[219-222], tin[223-225], lead[214,225-227], uranium[228], chlorine[166,167,200,229-233], and bromine[200,234,235]. The technique developed for molten salts has been used to investigate electrical migration in solid salts of lithium[236-239]. The electrical migration of isotopic alkali-metal ions has been examined also in their molten nitrates impregnating a strip of asbestos[10-14,240-243].

In 1953 Haeffner[244] detected a slight change in isotopic composition when a current was passed through a capillary filled with mercury. This phenomenon, named after him the Haeffner effect, was investigated not only in mercury[245-247] but also in molten lithium[248,249], potassium[250-252], rubidium[251-254], zinc[255], cadmium[255], gallium[256-259], indium[252,258,260], tin[255,258], and lead[258] and in solid uranium[245]. Sharp differences were observed in the behaviour of isotopic ions in metals and in salts. The fact alone that in metals light isotopes accumulate at the anode—not at the cathode as in all other media—suggests that the migration of ions takes place by different mechanisms in metals and in salts. Many theoretical papers have been published[263-277] on isotope effects in the electrical migration of ions in liquid metals.

III. SEPARATION OF ISOTOPES BY COUNTERCURRENT ELECTRICAL MIGRATION

1. Principles and Phenomenological Theory of the Method

The underlying principle of countercurrent electrical migration consists in producing a flow of electrolyte in the opposite direction to the movement of the isotopic ions in the separating apparatus. The velocity of the electrolyte is adjusted so that the faster light isotopes overcome the countercurrent and accumulate in the "head" electrode compartment and in the adjacent portion of the separating tube joining the two electrode compartments, while the slower heavy isotopes are washed back by the counterflow of liquid. If isotopic cations are being separated, the cathodic compartment is the head electrode compartment in this sense.

The mathematical description of countercurrent electrical migration is based on the assumptions[67,96,278] that the velocities v of the ions, their diffusion coefficients D, and the electric field strength E are in general constant at any point in the system at any instant t. A one-dimensional process is considered: i.e. the variables change only along the x-coordinate in the direction of the axis of the separating tube, whereas all parameters are invariable in a radial direction, perpendicular to x. All non-kinetic factors which may affect the separation (degree of dissociation of the electrolyte, association and complex formation by the ions, reactions involving precipitation of a solid phase or the evolution of gases, etc.) are disregarded by the general theory; if one or more such processes are superimposed on electrical migration, this is regarded as a more complex particular case and is considered specially. Electrode reactions are assumed not to affect the separation of isotopes, and the electrolyte in the electrode compartments is perfectly mixed.

Such idealisation of the conditions of the process makes the problem much simpler to solve, while introducing only minor errors into the final results. Furthermore, if particular details of this method are disregarded, other methods of separation—gaseous diffusion, thermal diffusion, chromatography, etc.—can be described by the same mathematics. The phenomenology of the countercurrent electrical migration of ions is the same, of course, in molten salts, aqueous solutions, and liquid metals.

Let the mixture of isotopes to be separated consist of mole fractions ${}^i\gamma$ of n components:

$$\sum_i^n {}^i\gamma = 1.$$

When the current is switched on, the components acquire velocities ${}^iv$ in the direction of the x-coordinate, the speed of each component being inversely proportional to the square root of its mass[279]. Thus directed movement in the electric field—electrical migration—is superimposed on the random thermal motion of the molecules of the liquid. The transport of components along the separating tube results in a concentration gradient $\partial {}^i\gamma/\partial x$, which leads to diffusion in the opposite direction to the movement of the ions. The relation between these two factors—migration in the electric field and diffusion and in the opposite direction—determines the total flux ${}^i\varphi$ of the component along the separating tube:

$${}^i\varphi = {}^i\gamma {}^iv - {}^iD\frac{\partial {}^i\gamma}{\partial x}. \quad (1)$$

The more mobile components, overcoming the countercurrent of liquid, accumulate at the head of the tube, while the less mobile components are washed towards the other end. Since the rate of the countercurrent is equal to the mean speed of the ions, the mixture as a whole remains stationary with respect to the walls of the tube:

$$\sum_k^n {}^k\gamma {}^kv = 0. \quad (2)$$

The concentration of the components undergo redistribution along the separating tube at the rates

$${}^iv = \sum_k^n {}^k\gamma ({}^iv - {}^kv). \quad (3)$$

From the condition of continuity we can set up the differential equation

$$\frac{\partial {}^i\gamma}{\partial t} = -\frac{\partial {}^i\varphi}{\partial x} = -\sum_k^n ({}^iv - {}^kv)\frac{\partial {}^i\gamma {}^k\gamma}{\partial x} - \sum_k^n {}^i\gamma {}^k\gamma \frac{\partial ({}^iv - {}^kv)}{\partial x} + {}^iD\frac{\partial^2 {}^i\gamma}{\partial x^2}. \quad (4)$$

for the process of countercurrent electrical migration.

Since the strength of the electric field and the speeds of the components are everywhere constant, the second term on the right-hand side of Eqn. (4) vanishes. The inevitable

mixing of the liquid in the cell as a result of convection and electro-osmosis can usefully be allowed for by introducing, instead of the molecular diffusion coefficients ${}^{i}D$, an effective diffusion coefficient or coefficient of intermixing $D' > {}^{i}D$. There is then no need to distinguish between the diffusion coefficients of the components, and Eqn. (4) simplifies to

$$\frac{\partial {}^{i}\gamma}{\partial t} = -\sum_{k}^{n} ({}^{i}v - {}^{k}v)\frac{\partial {}^{i}\gamma {}^{k}\gamma}{\partial x} + D'\frac{\partial^2 {}^{i}\gamma}{\partial x^2}. \quad (5)$$

For a system of n components we have thus established a set of n differential equations of type (5), which are mutually dependent.

No general method has been found for solving this set of equations, and therefore simplifying artifices are used. A particular case of an actual n-component system—a binary mixture of isotopes—is usually considered. Since a two-component model can be used to describe the separation of isotopes of polyisotopic elements [280], the method of solution is evidently applicable also in the general case. Denoting light and heavy components by the affixes "l" and "h", we obtain ${}^{h}\gamma = 1 - {}^{l}\gamma$, ${}^{l}\gamma = \gamma$, and ${}^{l}v - {}^{h}v = \Delta v$; and Eqn. (5) becomes [74,281]

$$\frac{\partial \gamma}{\partial t} = -\Delta v(1-2\gamma)\frac{\partial \gamma}{\partial x} + D'\frac{\partial^2 \gamma}{\partial x^2} \quad (6)$$

It can also be assumed [8,282] that all the isotopes in the mixture, with one exception, are so rare that their mole fractions remain very small at any instant, and we then have a set of n independent equations. When in particular $\gamma \ll 1$, we have instead of (6) the linear differential equation

$$\frac{\partial \gamma}{\partial t} = -\Delta v\frac{\partial \gamma}{\partial x} + D'\frac{\partial^2 \gamma}{\partial x^2} \quad (7)$$

Mason and Weaver [283] discovered a method for solving an equation of the type (7) in a study of the distribution of fine particles, suspended in a liquid, in a gravitational field. Konstantinov and Fiks [74] suggested a direct solution for countercurrent electromigration. A general solution of Eqn. (6) was first given by Majumdar [284] when developing a theory of the thermal diffusion column. The general principle of the solution of such equations, which has since been used by all authors, consists in introducing the dimensionless variables

$$\xi = \frac{\Delta v}{D'}x, \quad \tau = \frac{(\Delta v)^2}{D'}t \quad (8)$$

whose physical meanings correspond to a coordinate along the separating tube and the time, both expressed in terms of the process parameters Δv and D'. For example, substituting (8) in (6) and replacing variables

$$\gamma = \frac{1}{2} + \frac{1}{q}\frac{\partial q}{\partial \xi}, \quad (9)$$

where q is some function [281,284], will give an equation of the type

$$\frac{\partial q}{\partial \tau} = \frac{\partial^2 q}{\partial \xi^2}, \quad (10)$$

the method of whose solution is well known.

Solutions of equations of the type (6), (7), and (10) have been published for several actual cases of countercurrent electromigration. If the salt containing the separable isotopes is located entirely inside the separating tube and is bounded by other salts at both ends, the system is simulated by the problem of a tube of finite length L closed at both ends [67,74,265,266,283,284]. The initial condition represents uniform distribution of the components throughout the length of the separation zone $0 \leqslant x \leqslant L$ at $t = 0$. The boundary conditions correspond to the fact that the components remain within the separation zone throughout the experiment, i.e. that their fluxes are zero at both boundaries of the zone, which can be written e.g.

$$\gamma(x, 0) = \gamma_0, \ \varphi(0, t) = 0, \ \varphi(L, t) = 0, \quad (11)$$

where γ_0 is the mole fraction of the component in the initial isotopic mixture.

If one end of the separation zone is bounded by another salt inside the separating tube, while the other end expands into a sufficiently large electrode compartment, the zone can be simulated by the problem of a tube of finite length with one end closed and a reservoir of infinite capacity at the other end [246,284] or by the problem of a tube of semi-infinite length with one end closed [67,74,265,266,281,282]. In such a system the second boundary condition is that the isotopic composition of the salt at the point $x = L$ or ∞ respectively should at any time t be equal to the initial composition.

If the separation zone occupies the whole separating tube, terminating at one end in an electrode compartment of small capacity (from which an enriched product can be withdrawn), while the other end is joined to a large electrode compartment, as in the preceding case, the model problem involves a tube of semi-infinite length with a reservoir of finite volume at one end [67,285]. Initial and boundary conditions are the same as in the preceding system, but with the refinement that zero flux of the component occurs at the point $x = -L'$:

$$\gamma(x, 0) = \gamma_0, \ \varphi(-L', t) = 0, \ \gamma(L, t) = \gamma_0 \quad (12)$$

where $L' = V/A$ is the reduced length of the reservoir (electrode compartment) of finite volume V, and A is the cross-sectional area of the separating tube (if the tube is filled with a packing, A is the free cross-section). These problems in effect cover all concrete cases of the separation of isotopes in an electromigration cell.

A solution to the differential equation is in general found as a more or less rapidly converging series suitable for practical calculations:

$$\gamma = \gamma_0 f(\xi, \lambda, \eta, \tau), \quad (13)$$

where ξ and τ are defined by formulae (8), while λ and η are also dimensionless variables. Their physical meanings correspond to the length of the separating tube and the reduced length of the reservoir:

$$\lambda = \frac{\Delta v}{D'}L, \quad \eta = \frac{\Delta v}{D'}L' \quad (14)$$

For a tube of finite length terminating in a reservoir, for example, the solution is [67]

$$\gamma = \gamma_0 \exp\xi - \frac{8}{\lambda}\gamma_0\left(\exp\frac{\xi-\lambda}{2}\right)\sum_{s=0}^{\infty}\frac{\sinh\frac{r_s\lambda}{2}\sinh\frac{r_s\xi}{2}\exp\left[-\frac{1}{4}(1-r_s)^2\tau\right]}{\frac{2}{\lambda}-1+r_s+\frac{2}{\lambda}\frac{\frac{\eta}{2}\left(1+\frac{\eta}{2}\right)(r_s^2-1)}{\left(1+\frac{\eta}{2}\right)^2-\eta^2\frac{r_s^2}{4}}}, \quad (15)$$

where the rs are the roots of the equation

$$\tanh\frac{r\lambda}{2} = \frac{r}{1+\frac{\eta}{2}(1-r^2)} \quad (16)$$

Equation (15) enables the distribution of the isotopic components along the tube to be calculated for any instant. A similar type of solution is obtained for the other problems enumerated above.

It is sometimes convenient to choose the separation factor of two isotopes

$$S = \frac{\gamma(1-\gamma_0)}{\gamma_0(1-\gamma)} \qquad (17)$$

instead of the mole fraction γ of a component of the isotopic mixture, as the variable for which a solution to the differential equation is sought [281]. Equation (17) has been written for a binary mixture. If an element consists of more than two isotopes, the separation factor for any pair is a linear function of the difference between their masses [215-217,226,246]. A method has been given [280] for calculating the separation factors of all pairs of isotopes provided that the value of S for any one pair of the mixture is known. Solutions analogous to (15) are found for S.

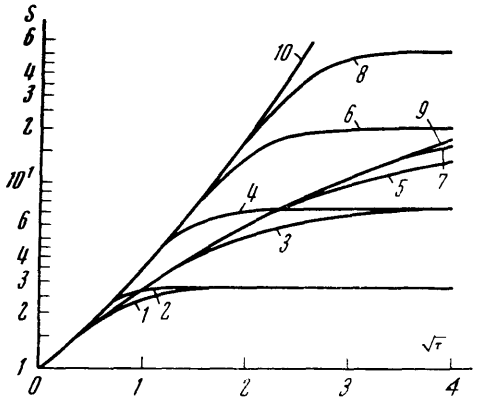

Figure 1. Dependence of separation factor S on time τ for separating tubes of different lengths λ with different initial mole fractions γ_0 of enrichable isotope [281]: 1) $\lambda = 1$, $\gamma_0 = 0$; 2) 1, 1; 3) 2, 0; 4) 2, 1; 5) 3, 0; 6) 3, 1; 7) 4, 0; 8) 4, 1; 9) ∞, 0; 10) ∞, 1.

Examination of expressions of the type (15) will give a theoretical description of the behaviour of an isotopic mixture during separation. Fig. 1 shows an example of such behaviour in separating tubes of various lengths, with one end closed and the other connected to an infinite reservoir [281]: it illustrates the dependence of S on $\tau^{1/2}$ for various reduced tube lengths λ. Initially enrichment follows an almost parabolic curve (Breit and Friedman [67] confirmed this by numerical calculations), and then it approaches a horizontal straight line asymptotically: it reaches a steady state.

For low values of τ the curve is described by the simple formula [281]

$$S = e^{2\sqrt{\tau/\pi}} \qquad (18)$$

i.e. initially the separation of an isotopic mixture is independent of the length of the separating tube. This holds provided that $L \geqslant 1.8(D'/|\Delta v|)\ln S$. Thus when τ is small we can put $\lambda = \infty$ in formulae of type (15), which greatly simplifies the calculations.

Fig. 1 shows that the rate of separation of the isotopes begins to diminish sooner the smaller is λ, i.e. the shorter the separating tube. If the closed end of the tube is replaced by a reservoir of limited volume, the overall rate of separation decreases: i.e. the corresponding $S-\tau^{1/2}$ curve is inclined at a larger angle to the horizontal axis than is the curve in Fig. 1. At $\tau = 0.002$, for example [67], the rates of accumulation of enriched isotope in the reservoir with $\eta = 0.1$ and 1 respectively are only one-third and one-tenth of the rate for $\eta = 0$.

An interesting feature is the dependence of the separation factor on the content of the enrichable isotope in the initial mixture: this is apparent in Fig. 1 in a "bifurcation" of the $S-\tau^{1/2}$ curves at quite large τ, but with the system still far from a steady state. Under otherwise similar conditions a given separation factor is attained more rapidly the richer was the initial mixture in the enrichable isotope [281,282]. For example, the time required to reach $S = 10$ with $\gamma_0 = 1$ is only one-third of the time required when $\gamma_0 = 0$. These are obviously limiting cases for the isotopic composition of a mixture, for in real materials $0 < \gamma_0 < 1$.

The "mean time" t_S required for a steady state to be established is given by the formula [74]

$$t_s = \frac{L^2}{\left(\pi^2 + \frac{\lambda^2}{4}\right)D'} \qquad (19)$$

Since $\frac{1}{2}\lambda \ll \pi$, we have [68,74] $t_S = L^2/\pi^2 D'$; a steady state is actually established [74,246] in the time $t \simeq 4t_S$. The maximum separation factor which can be achieved in the steady state is determined solely by the length of the tube [281]:

$$S_{st} = e^{\lambda}. \qquad (20)$$

Equations (18) and (20) are valid in the absence of withdrawals. If enriched material is removed at a rate p (in $cm^3\ s^{-1}$) from the head of the cell, the separation factor S_p is given by the formula [96]

$$\ln\frac{S_p}{S} = -\frac{v_p}{v_{cc}}(S-1)\frac{\gamma(0,t)}{\gamma(L,t)}, \qquad (21)$$

where $v_p = p/A$ (cm s^{-1}) is the speed of withdrawal, d_{cc} is the speed of the countercurrent of electrolyte in the separating tube, and $\gamma(0, t)$ and $\gamma(L, t)$ are the mole fractions of enriched isotope at the instant of withdrawal t at the head and at the opposite end of the tube. By integrating the equation of transport with continuous withdrawal

$$v_p\gamma_p = v'\gamma - D'\frac{d\gamma}{dx}, \qquad (22)$$

where γ_p is the mole fraction of the isotope in the product, while the rate of withdrawal of the isotope is related to its actual speed v' along the separating tube (i.e. v' is the rate of electrical migration minus the rate of diffusion in the opposite direction) by the expression

$$v_p = v'\gamma + (v' + \Delta v')(1-\gamma) \qquad (23)$$

(it is obvious $\Delta v' = \Delta v$), Klemm [167] obtained the formula

$$L = \frac{D'}{2\Delta v\sqrt{b^2 + \frac{v_p\gamma_p}{\Delta v}}}\ln\left[\frac{\gamma_p - b - \sqrt{b^2 + \frac{v_p\gamma_p}{\Delta v}}}{\gamma_p - b + \sqrt{b^2 + \frac{v_p\gamma_p}{\Delta v}}}\cdot\frac{\gamma_0 - b - \sqrt{b^2 + \frac{v_p\gamma_p}{\Delta v}}}{\gamma_0 - b + \sqrt{b^2 + \frac{v_p\gamma_p}{\Delta v}}}\right], \qquad (24)$$

where $b = \frac{1}{2}(1 - v_p/\Delta v)$. Substituting selected values for γ_p and v_p in Eqn. (24), together with values of Δv and D' determined by the actual conditions under which the process is conducted, we can find the length of tube L which is necessary for the withdrawal at a rate v_p of a product enriched to γ_p.

Accumulation of the enriched isotope is most rapid in the absence of withdrawal at the closed end of the separating tube or—rather slower—in a small reservoir. The content of the isotope also increases with time in the adjacent region of the tube, but a specified separation factor is reached here with some delay, which is greater the further the point from the end of the tube. In other words, the region of enrichment gradually extends from the end of the tube to its midpoint, reaching the latter in time $t_{1/2} = L^2/\pi D'$; at the same time impoverishment of the mixture with respect to this isotope takes place in the other half of the tube. The distribution of isotopes along the tube at time t is given by formulae of type (15). In particular, in the steady state

$$\gamma(\xi, \infty) = \gamma_0 e^{\xi} \tag{25}$$

It is easily seen that Eqn. (20) is a particular case of (25).

By time t the region of enrichment has extended to a distance

$$x' = \sqrt{\pi D' t}, \tag{26}$$

from the end of the tube[281,282], provided that the tube has no reservoir at its head. The presence of a reservoir of reduced length L' has little effect[285] on x', which remains proportional to $(D't)^{1/2}$, the coefficient of proportionality being $\pi^{1/2} = 1.77$ or $8/3\pi^{1/2} = 1.5$ according as $L' \ll$ or $\gg (D't)^{1/2}$.

Expanding Eqn. (18) as a series and neglecting powers higher than the first, we obtain for small values of τ the relation[278]

$$\gamma = \gamma_0\left(1 + 2\frac{\Delta v}{v} \cdot \frac{vt}{\sqrt{\pi D' t}}\right) \tag{27}$$

where v is the mean velocity of ions of the element in an electric field of strength E. Thus in the initial stage of the process the accumulation of the isotope $N(\gamma - \gamma_0)$ over the initial quantity, where N is the total number of equivalents of the element in the region of enrichment x', is proportional to the migration path vt and inversely proportional to the diffusion path $(\pi D't)^{1/2}$.

The quantity $\Delta v/v$ in Eqn. (27)—the relative difference in rates of migration of the isotopic ions—is independent of the operating parameters of the process and is directly related to the mechanism of separation. It represents the theoretical efficiency of countercurrent electrical migration, and determines the single-stage separation factor by this method

$$1 + \frac{\Delta v}{v} = 1 + \frac{\Delta w}{w} = 1 + \varepsilon = \alpha, \tag{28}$$

where $w = v/E$ is the mobility of the ions, i.e. their velocity in an electric field $E = 1$ V cm^{-1}.

Expressing the enrichment factor ϵ in terms of the relative difference between the mobilities of the isotopic ions $\Delta w/w$—not the difference in their speeds $\Delta v/v$—makes it unnecessary to allow for the effect of the variable E and enables an objective characteristic of the method ϵ to be assigned to standard conditions. In this respect a still more useful characteristic is the mass effect suggested by Klemm[68,282]

$$\mu = \frac{\Delta w / w}{\Delta m / m}, \tag{29}$$

where $\Delta m = {}^{j}m - {}^{k}m$ and $m = \frac{1}{2}({}^{j}m + {}^{k}m)$, which enables the efficiency of the method to be assessed independently of the number of atomic mass units distinguishing the isotopes j and k. If j and k are respectively a light and a heavy isotope, we have $\Delta w = {}^{l}w - {}^{h}w > 0$ and $\Delta m = {}^{l}m - {}^{h}m < 0$, so that the mass effect is always negative.

Taking into account the quantity of electricity transported in time t through a cross-section of the separating tube

$$Q = \frac{NF}{x'} vt, \tag{30}$$

where F is Faraday's constant, we obtain from Eqns. (26) and (27) the expression

$${}^{jk}\varepsilon = \frac{\Delta^{jk} w}{w} = -\left(\frac{{}^{l}\gamma}{{}^{l}\gamma_0} - \frac{{}^{h}\gamma}{{}^{h}\gamma_0}\right)\frac{FN}{Q} \tag{31}$$

for the relative difference in the mobilities of the two isotopes[282]. A method has been published[8,192] for assessing the accuracy of the calculation of ϵ by means of Eqn. (31).

Equation (31) is easily converted into a form which is convenient for practical calculation of the mass effect[200]:

$$\mu = \frac{Fz}{MQ} \cdot \frac{m}{\Delta m} \cdot \frac{1}{\gamma_0(1-\gamma_0)} \sum_r G_r(\gamma_r - \gamma_0), \tag{32}$$

where z is the valency of the isotopic ions, M the molecular weight of the salt, r the serial number of one of the specimens into which the separating tube is cut after electrolysis has ceased and the melt has solidified (see subsection 2), G_r is the weight of salt in the rth specimen, and the summation is made over all specimens r in which isotopic analysis has detected enrichment with a given isotope. This formula (32) applies to elements consisting of two isotopes. If an element comprises n isotopes, the mass effect can be calculated for the jth and kth isotopes by means of the equation[214]

$${}^{jk}\mu = \frac{Fz}{MQ^{j}\gamma_0} \cdot \frac{m}{\Delta m} \sum_r \frac{G_r({}^{jk}R_r - {}^{jk}R_0)}{\sum_i^n {}^{ik}R_r}, \tag{33}$$

where ${}^{ik}R_r = ({}^{j}\gamma/{}^{k}\gamma)_r$ is the ratio of the contents of these isotopes in the rth specimen, and

$$[m = \sum_i^n {}^{i}\gamma_0 {}^{i}m --$$

is the atomic weight of the element.

The overall and the single-stage separation factors, S and α, are related by the formula

$$S = \alpha^q \tag{34}$$

where q is the number of theoretical plates realised in the region of enrichment. The function q in Eqn. (9) has this physical meaning. The quantities x' and q are interrelated by the height of an equivalent theoretical plate:

$$h = \frac{x'}{q} \tag{35}$$

According to Westhaver[66] the physical meaning of h in countercurrent electrical migration is the length of the separating tube in which the isotopic ratio ${}^{jk}R$ changes by a factor α. This author discussed in detail[66] theoretical methods for estimating h and D'. The practical calculation of h can be based on data obtained when a steady-state is reached. Since α differs very little from unity, it follows from Eqn. (34) that $\ln S = q\ln(1+\epsilon) = q\epsilon$, when substitution for q in (35) yields for the steady state

$$h = \frac{L\varepsilon}{\ln S_{st}} \tag{36}$$

It follows from Eqns. (14) and (20) that $L/\ln S_{st} = D'/\Delta v$, and substitution in (36) gives

$$h = \frac{D'\varepsilon}{\Delta v} = \frac{D'}{v} \tag{37}$$

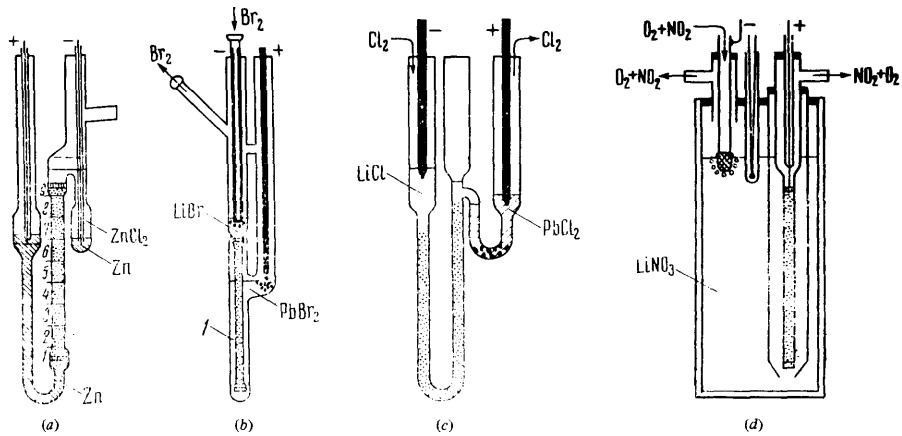

Figure 2. Cells used in the application of countercurrent electrical migration to the enrichment of: *a*) ^{35}Cl in molten $ZnCl_2$ (the numbering 1–9 indicates the specimens into which the separating tube is cut for chemical and isotopic analyses after the experiment)[8]; *b*) ^{7}Li in molten LiBr (*1* = boundary between LiBr and $PbBr_2$)[164]; *c*) ^{7}Li in molten LiCl;[162] *d*) ^{7}Li in molten $LiNO_3$.[192]

i.e. the height of an equivalent theoretical plate is smaller the smaller is D' and the greater the rate of migration of ions in the separating tube.

2. Apparatus and Method of Operation under Laboratory Conditions

Fig. 2 shows typical designs of cells for electrical migration under laboratory conditions. The cell is made of quartz or heat-resistant glass (Vycor, Supremax, Pyrex), the choice of material depending on the operating temperature and the corrosiveness of the molten salt. It consists mainly of a vertical cylindrical (*a*, *b*, *d*) or U-shaped (*c*) separating tube. Conical separating tubes have been suggested[192,203] to provide a better countercurrent and a higher current density transported by the enriched isotope; this increases the efficiency of separation of the isotopes provided that $(r_1r_2)^{1/2} < r$, where r_1 and r_2 are the radii of upper and lower portions of the conical tube, and r is the radius of a cylindrical tube of the same volume.

The separating tube is filled with a packing satisfying certain requirements—mechanical and thermal stability, chemical resistance to the molten salt, and the maximum possible thermal conductivity—in order to prevent mixing of the melt by convection currents. The packing materials usually employed are ground glass or quartz, from which the cell itself is made, and also alundum, steatite, zirconium oxide, zircon, and zirconyl phosphate. The packing should first have been carefully freed from traces of organic compounds and metallic particles by being boiled in acid or heated in a current of chlorine, washed with water, and dried. The free volume of a packed separating tube is 35–45% of the volume of the empty tube and depends on the uniformity of the particles with respect to shape and size, not on their coarseness. The "electrical free space" constitutes 70–80% of the geometrical free space, since the ions are unable to move in straight lines, but have to pass through pores between packing grains ("labyrinth effect"): in ignited asbestos, for example, the path traversed by the ions is on the average 30% longer than the straight line between the electrodes[14]. The efficiency of separation is independent of the material of the packing, but becomes higher as the latter becomes finer. Since at the experimental temperature the density of the packing may be comparable with that of the melt, the packing is placed between porous glass or quartz filters (frits) sealed into both ends of the separating tube, in order to prevent the packing from floating to the surface or being loosened by gases evolved from the melt with the formation of longitudinal channels. Details of the design of the cells and of the part played by the packing have been fully discussed by Lundén[8]. A theoretical analysis of the hydrodynamic flow of an electrolyte through a packed separating tube and of various effects on the separation factor was made by Westhaver[66].

A fundamentally different design of cell has also been proposed and studied for work with molten salts[20]: a horizontal separating tube without packing is divided by frits into a series of successive compartments, in which the melt mixes freely (Fig. 3). The advantages of such a design have been considered for aqueous solutions[27,91–93], and the conclusions reached are valid also for molten salts.

Intense movement of the liquid takes place in the separating tube during electrolysis. This results in a shift in the levels of the melt in the electrode compartments relative to their original position (Fig. 2*a*), and may even cause a break in contact between the salt and the anode[163]. Various methods are used to control the levels of the melt in the electrode compartments: the initial salt may be added to the anode compartment and excess of the melt overflows from the cathode compartment[200,219,233]; excess pressure is produced in the cathode compartment by means of an inert gas[160,214]; etc. With a correct choice of current density and in the absence of breaches in the packing, no displacement of the electrolyte relative to the cell is observed, although the components of the mixture undergo continuous separation as a consequence of mutual displacement of the molecules. This constitutes one of the advantages of the countercurrent method over

movement of a zone, e.g. in electrophoresis on a paper support: with a short distance between the electrodes the separable species, in overcoming the counterflow of electrolyte, traverse a very long path, which ensures high separation factors. Thus in an experiment with cadmium chloride in a tube ~ 20 cm long the displacement of the cations relative to the anions was estimated[217] to be 3 m, and in a prolonged experiment with thallium(I) chloride about 18 m[219].

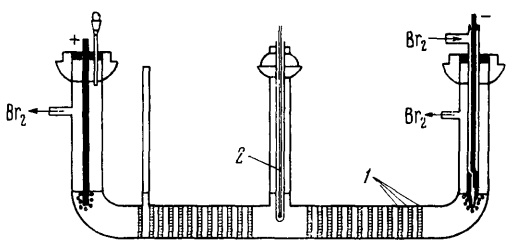

Figure 3. Horizontal cell[20] without packing: 1) porous sintered-glass discs; 2) thermocouple.

Electrical migration must be arranged in such a way that the components do not leave the separation zone, e.g. as a result of electrode reactions. This is ensured in two ways. The first method consists in neutralising the products of the electrode reaction and regenerating the original salt in the electrode compartment. Metals deposited on the cathode in molten halides are continuously oxidised by gaseous chlorine or by bromine or iodine vapour in a current of argon, entering the cathode compartment through either a special tube or a hollow cathode (special investigations have been made[8,20,163,184] to elaborate a cathode); a current of nitrogen dioxide, alone or mixed with oxygen, or of the vapours from fuming nitric acid is used for this purpose in molten nitrates. The quantity of oxidising gases supplied should always be considerably larger than stoichiometric to ensure saturation of the melt in the cathode compartment; otherwise, corrosive metals, especially alkali metals, will rapidly put the electrodes and the walls of the cell out of action. The results of many experiments have shown that the most corrosion-resistant materials for cathodes are graphite and carborundum with halides, and aluminium and stainless steel with nitrates; the most corrosion-resistant anodes are made of carbon and graphite for halides, and of platinum for nitrates, while gold anodes have been used with sulphates[193,236-238]. Data on the stability of various materials in molten salts and metals have been compiled in Ref. 286 and in standard tables[287].

Molten metal anodes can be used in the separation of isotopic anions, with tungsten wires as conducting electrodes (leads). Thus in the separation of chlorine isotopes[9,229,230] molten lead or zinc dissolves to form the corresponding chloride, so that chlorine does not leave the separation zone, and enrichment with the light isotope ^{35}Cl takes place gradually at the salt–metal interface. The same procedure is used in the separation of bromine isotopes[234,235]. If the opposite process—deposition of metal from the salt—takes place at the cathode, the molten salt remains held between two regions of molten metal—cathodic and anodic—and the only apparent result is the transport of metal from anodic to cathodic compartments (Fig. 2*a*), with no evident separation of isotopes. Liquid metals—lead, zinc, mercury—have sometimes been used as cathodes also in the separation of alkali-metal isotopes[8,193], but the alkali metal then underwent reduction and formed an alloy with the metal of the cathode, so that ions were removed irreversibly from the separation zone, and played no part in the subsequent process. Lundén has made a detailed study of this method[238,288,289].

The second method of retaining the components in the separation zone is to exclude any contact between the separable species and the electrode. This is accomplished by placing an ancillary salt, having the same gegenion as the working salt, between the latter and the electrode (Fig. 2*b*). A sharp boundary is formed between the two salts, which is especially noticeable when the salts differ in colour or have sufficiently differing refractive indices. The relative positions of the salts in the separating tube are determined by the ratio of their densities at the temperature of the experiment (to avoid mechanical mixing the denser salt should be below the boundary, which is the main factor governing the form of tube chosen) and by the relative mobilities of unlike ions (e.g. the salt having the more mobile cation should be located closer to the cathode). The common ion passes freely through the boundary, which is the only obstacle to the unlike ions: in fact, the more mobile the ions of the salt the higher its conductivity and the weaker the electric field on that side of the boundary; when, therefore, the "foreign" ion, which may be e.g. less mobile, penetrates the boundary into the zone occupied by the salt, it immediately begins to move more slowly than in its "own" salt, lags behind the ions of the first salt, and returns back through the boundary. However, this mechanism is not sufficiently effective with small differences in mobility between the ions, and the boundary between the salts remains blurred or "diffuse". If necessary the working salt can be bounded by other salts at both ends: relative densities and conductivities must satisfy the above requirements for both salt pairs forming the two boundaries. Conditions for the production of a boundary between molten salts and its behaviour have been surveyed[165]. A boundary is an excellent indicator of movement of the salts along the separating tube, and is often used to measure various characteristics of the salt systems.

Special precautions are necessary when filling the cell with the salts: no bubbles of air or other gases should remain in the separating tube; hygroscopic salts should absorb as little moisture as possible during filling; and the free surface of molten metal electrodes should not be oxidised before contact has been established with the molten salt. Filling is therefore conducted either under a vacuum or in an atmosphere of an inert gas; if necessary the initial position of the zone of the working salt in the separating tube is controlled by producing a difference in gas pressure between the electrode compartments.

The choice of conditions of electrolysis is dictated by the aims of the experiment. The design of the furnace should ensure that the thermal field inside it is as uniform as possible and is constant with time. The minimum working temperature is determined by the melting point of the most refractory of the salts used, and the maximum working temperature by the volatility of the salts and the temperature at which the glass of the cell begins to soften. In practice a vertical temperature gradient along the cell cannot be avoided, especially if the separating tube is not

immersed in a melt but is surrounded by air. Furthermore, the heating effect of the electric current produces a radial temperature gradient in the tube: special measurements have established that the difference in temperature between the centre of the tube and its outer wall may reach 200 deg in individual cases[231]. The electric field in the separating tube should be as strong as possible, but there is always an upper limit to the current, depending on the thermal conductivity of the salts and the materials of the cell: if the current density is too high, regions of local overheating appear in the packing, which may cause serious disturbances of the process and even the need to discontinue the experiment. In measurement of the electrical transport characteristics of salts the duration of an experiment is usually a few days, but with lithium salts 10–12 h is sufficient for isotopic effects to be measured by modern methods of analysis. Nevertheless, reliable means of measurement and automatic control have been developed which enable the process to be conducted continuously for several months or years in order to obtain the necessary quantity of enriched material.

The progress of electrical migration is monitored by means of electrical measuring instruments and also visually, by observing that no visible disturbances occur in the cell (a stationary boundary between the salts in the separating tube is often a convenient indication of the steady occurrence of the process), for which purpose the cell is placed in a vertical tubular electric furnace made of transparent fused quartz. The results of the separation are evaluated by studying the distribution of the components along the tube after the experiment. For this purpose the cold separating tube is divided into lengths of 1–1.5 cm, and chemical and isotopic analyses are made on every sample. Sometimes the accumulation of an isotope in the electrode compartment is observed by withdrawing after a certain time a sample of the molten salt for analysis.

3. Experimental Conditions for and Results of the Separation of Isotopes

Data on all published molten salt systems in which countercurrent electrical migration has been studied are compiled in Table 1. Certain data on electrical migration in solid salts, aqueous solutions, and liquid metals are included for comparison.

Table 1 shows that, for isotopes of the same element, the mass effect depends on the medium in which electrical migration is conducted: in solid and molten salts $\mu \simeq 10^{-2}$; in aqueous solutions it is usually 20–30% of its value in melts (for uranium isotopes the mass effect is larger in solutions than in melts, apparently because of the superimposition of the isotope effect of exchange between different species present in solution); in liquid metals $\mu \simeq 10^{-5}$; and in solid metals the mass effect is extremely small. Metals are clearly of no interest as media for the practical separation of isotopes. Solid salts will evidently also find no application, for it is impossible to accomplish a countercurrent process (but see Ref. 156 to 158). Solutions of salts in water and other solvents continually attract attention by the convenience and safety of their use for enrichment and by the simplicity of the apparatus, but a substantial defect is the considerable consumption of energy in the "useless" transport of the solvate sheaths together with the ions. Thus molten salts are the most suitable media for the separation of isotopes by the electrical migration of ions.

Despite several experimental difficulties (high temperature, restricted choice of materials resistant to the corrosive action of melts, and with several elements the absence of salts of sufficiently high electrical conductivity which do not undergo thermal decomposition), electrical migration in molten salts has definite advantages: maximum mass effects are accompanied by a far wider temperature range for molten salts, which makes artificial cooling of the separating tube unnecessary (with aqueous solutions this is required to avoid their boiling), while the heat produced by the passage of the electric current through the melt makes a substantial contribution to the thermal balance and may completely eliminate the need for additional heating of the melt[167]; a countercurrent of electrolyte is far easier to provide in molten salts than in solutions; and molten salts are liquids having the maximum concentration of separable isotopes (apart from liquid metals), which ensures a higher yield of product from apparatus of a given size.

4. Separation of Isotopes in Large-scale Plant

In laboratory apparatus, where working with small quantities of material involves a small consumption of energy, the tendency is to achieve maximum enrichment is as short time as possible, which determines the design of cells and the choice of experimental conditions. The organisation of large-scale production involves the solution of a large complex of engineering problems, consideration of which is beyond our scope, as well as economic problems. In the present subsection we shall deal only with a few questions of principle.

The design of industrial equipment is similar to that shown in Fig. 2*d*: vertical separating tubes, into which electrodes are inserted from above, are lowered into a molten-salt bath. The advantages of this design[192] are that the separating tube can be moved vertically to control the countercurrent of electrolyte (e.g. with very compact packing, of grain diameter < 0.1 mm, the rate of flow of the melt in the tube is so diminished that its level in the anode compartment should be 3–5 cm below the level of the melt in the bath in order to create additional hydrostatic pressure), the temperature gradient along the separating tube becomes negligible owing to the intense convection in the bath, and the separating tubes are easily replaceable and simple in construction. A substantial disadvantage, however, is the unavoidable diffusion of ions through the walls of the tube, intensified by the electric field (direct experimental evidence of such a process has been provided[101]), which may considerably diminish or even eliminate altogether the effect of separation of the isotopes, so that the choice of material for the separating tube and the thickness of its walls are of decisive importance. Thus in the separation of calcium isotopes the necessary enrichment was ensured only by use of tubes made of several varieties of alumina[213].

If light isotopes are to be concentrated, a cathode of suitable design is immersed in the electrode compartment of the separating tube, and several anodes are arranged symmetrically around the tube, in such a way that the bath forms the anode compartment of the installation[184]. When a steady state is reached, enriched material is withdrawn regularly from the cathode compartment of the tube, and an equivalent quantity of the initial salt is added to the

Table 1. Experimental conditions and results for the separation of isotopes by countercurrent electrical migration*.

Expt. No.	Isotopes and medium (Ref.1)	Construction of cell (Ref.2)	Electrodes and electrolytes (Ref.3)	Voltage, V	Current, mA	Quantity of electricity, C	Temp., °C	Duration, h	Isotope content before → after experiment (Ref.4)	α	−μ	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13
1	^{6}Li—^{7}Li MS	U, Supr 22, 5/4 quartz 0.1	— C | $PbCl_2$ | LiCl + KCl | $PbCl_2$ | C (Cl_2) + 98 mole %	62	500	$8.65\cdot10^4$	650	48	^{7}Li/^{6}Li 12.3 → 13.7/44.3	1.0208	0.135	159
2	^{6}Li—^{7}Li MS	U, Supr 27/5.5 quartz 0.13	— C (Cl_2) | LiCl | C (Cl_2) +	—	500	$1.82\cdot10^5$	650	101	% ^{6}Li 7.3 → 16.1/—	—	—	160
3	^{6}Li—^{7}Li MS	U, Supr 20/-	— C (Cl_2) | LiCl | $PbCl_2$ | C (Cl_2) +	—	730	$1.17\cdot10^6$	—	—	% ^{6}Li 7.3 → —/0.1 (2 cm^3)	—	—	162
4	^{6}Li—^{7}Li MS	U, Supr. 20/- ZrO_2 0.12—0.15	—C (Cl_2) | LiCl | LiCl + $PbCl_2$ | $PbCl_2$ | C (Cl_2) + 100 mole %	—	500	$3.96\cdot10^4$	650	22	% ^{6}Li 7.24 → —/3.81	1.0222	0.144	165
5	ditto	ditto	54 mole %	—	500	$8.32\cdot10^4$	650	46.6	% ^{6}Li 7.24 → —/4.68	1.0182	0.118	165
6	»	»	25 mole %	—	500	$3.96\cdot10^4$	650	22	% ^{6}Li 7.24 → —/1.77	1.0192	0.125	165
7	»	»	12.6 mole %	—	500	$2.27\cdot10^4$	650	12.6	% ^{6}Li 7.24 → —/3.20	1.0344	0.224	165
8	»	»	10.9 mole %	—	500	$1.98\cdot10^4$	650	11	% ^{6}Li 7.24 → —/1.39	1.0356	0.231	165
9	»	»	5.3 mole %	—	500	$1.80\cdot10^4$	650	10	% ^{6}Li 7.24 → —/5.78	1.0454	0.295	165
10	^{6}Li—^{7}Li MS	U, Supr.30/4 Al_2O_3 0.1	— C (Cl_2) | LiCl | C (Cl_2) +	—	—	$5.4\cdot10^4$	674	—	^{7}Li/^{6}Li 12.3 → —/17.4	1.0215	0.140	195
11	ditto	ditto	ditto	—	—	$7.2\cdot10^4$	732	—	^{7}Li/^{6}Li 12.3 → —/17.1	1.0194	0.126	195
12	»	U, quartz 30/4 Al_2O_3 0.1	»	—	—	$5.2\cdot10^4$	843	—	^{7}Li/^{6}Li 12.3 → —/16.6	1.0265	0.172	195
13	»	ditto	»	—	—	$5.8\cdot10^4$	895	—	^{7}Li/^{6}Li 12.3 → —/26.6	1.0293	0.190	195
14	^{6}Li—^{7}Li MS	V, Supr 30/8 Al_2O_3— 30/8	— C (Cl_2) | LiCl | C (Cl_2) +	100	2360	$3.74\cdot10^5$	650	44	% ^{6}Li 7.4 → 10.5/— (2.5 g)	—	—	184
15	ditto	ditto 30/18	ditto	100	7620	$1.83\cdot10^6$	650	67	% ^{6}Li 7.4 → 19.5/— (30 g)	—	—	184
16	»	» 30/12	»	100	4530	$3.96\cdot10^5$	650	24	% ^{6}Li 7.4 → 15.4/— (6 g)	—	—	184
17	»	» 30/15	»	100	6550	$2.74\cdot10^5$	650	116	% ^{6}Li 7.4 → 29.2/— (6 g)	—	—	184
18	»	» 30/30	»	100	13400	$2.63\cdot10^5$	650	55	% ^{6}Li 7.4 → 15.8/— (15 g)	—	—	184
19	^{6}Li—^{7}Li MS	V, Supr 25/3, 9 supr. 0.15–0.20	— C (Br_2) | LiBr | $PbBr_2$ | C (Br_2) +	110	239	$1.24\cdot10^4$	590	14.3	^{7}Li/^{6}Li 12.5 → —/45.30	1.0401	0.261	164
20	^{6}Li—^{7}Li MS	V, Supr 24/4 supr 0.15–0.20	— C (Br_2) | LiBr | $PbBr_2$ | C (Br_2) +	65	194	$4.9\cdot10^3$	565	7	^{7}Li/^{6}Li 12.32 → —/18.18	1.0214	0.139	173
21	ditto	ditto	ditto	155	239	$1.24\cdot10^4$	590	14.3	^{7}Li/^{6}Li 12.48 → —/45.30	1.0206	0.134	174
22	»	»	»	95	250	$1.48\cdot10^4$	565	164.7	^{7}Li/^{6}Li 12.09 → —/1162 ±26	—	—	174
23	^{6}Li—^{7}Li PC	U, Supr 24/4, 3 supr 0.20–0.25	— C | Pb | $PbBr_2$ | LiBr | $PbBr_2$ | C (Br_2) +	108	295	$8.56\cdot10^3$	580	81	^{7}Li/^{6}Li 12.28 → —/26.05	—	—	174
24	ditto	ditto	ditto	72	192	$3.66\cdot10^4$	560	53.1	12.35 → —/156.0	1.0242	0.157	173,174
25	»	»	»	120	172	$5.02\cdot10^4$	575	81	12.42 → —/41.24	1.0202	0.131	173,174
26	^{6}Li—^{7}Li MS	U, Pyrex 22/13 zircon 0.18	— C (Br_2) | LiBr | C (Br_2) +	20	480	$1.12\cdot10^5$	570	65	^{7}Li/^{6}Li 11.88 → —/14.54 (11.3 g)	1.0270	0.175	20
27	ditto	ditto	ditto	20	400	$1.10\cdot10^5$	570	77	11.84 → —/14.66 (10.2 g)	1.0263	0.171	20
28	^{6}Li—^{7}Li MS	U, Pyrex 16/- zircon 0.1	— C (Br_2) | LiBr + NaBr | C (Br_2) + 78 wt.%	25	600	$2.52\cdot10^6$	540	720	^{7}Li/^{6}Li 12.57 → 9.82/80.0 (7.6 cm^3) (5.3 cm^3)	—	—	178,180
29	ditto	ditto 26/8	— C (Br_2) | LiBr + KBr | C (Br_2) + 68 wt.%	70	700	$3.63\cdot10^6$	450	1008	^{7}Li/^{6}Li 11.7 → 6.6/3500 (8 cm^3) (1.14 cm^3)	—	—	178,180
30	^{6}Li—^{7}Li MS	U, Pyrex- zircon-	— C (Br_2) | LiBr + KBr | C (Br_2) +	—	—	—	500	4320	% ^{7}Li 92.7 → —/99.97	—	—	182
31	^{6}Li—^{7}Li MS	U, Pyrex 10/8 zircon 0.5	— C (Br_2) | LiBr + KBr | C (Br_2) + 70 mole %	—	165	$1.91\cdot10^5$	500	720	^{7}Li/Li^6 11.7 → —/22.4	—	—	183,186

Table 1 contd.

Expt. No.	Isotopes and medium (Ref.1)	Construction of cell (Ref.2)	Electrodes and electrolytes (Ref.3)	Voltage, V	Current, mA	Quantity of electricity, C	Temp., °C	Duration, h	Isotope content before → after experiment (Ref.4)	α	−μ	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13
32	^{6}Li—^{7}Li MS	U, Pyrex 21, 8/10 zircon 0.18	— C (Br_2) | LiBr + KBr | C (Br_2) + 51 wt.%	45	550	$4.32 \cdot 10^6$	450	2180	^{7}Li/^{6}Li 10.5, → 8/3000 (18.5 cm^3) (0.7 cm^3)	—	—	20
33	ditto	ditto 22/13	ditto	54	1600	$1.66 \cdot 10^7$	500	2880	0.50 → 0,33/35 (86 cm^3)	—	—	20
34	»	ditto	»	54	1600	$7.91 \cdot 10^6$	500	1200	1,94 → 0,053/40 (4 cm^3)	—	—	20
35	»	»	— C (Br_2) | LiBr + KBr | C (Br_2) + 50 wt.%	50	400	$5.72 \cdot 10^4$	450	40	12,07 → /13.68 (3.58 g)	1.0193	0.125	20
36	»	»	ditto	40	400	$9.38 \cdot 10^4$	450	65	11.85 → /13.72 (4.84 g)	1.0181	0.118	20
37	»	»	— C (Br_2) | LiBr + KBr | C (Br_2) + 57 wt.%	35	420	$1.32 \cdot 10^5$	570	88	11.70 → —/14.20 (6.22 g)	1.0200	0.130	20
38	^{6}Li—^{7}Li MS	V, Pyrex- ZrO_2-	— C (Br_2) | LiBr + KBr | C (Br_2) + 58.5 wt.%	—	165	$1.91 \cdot 10^5$	500	321.6	^{7}Li/^{6}Li 12.20 → —/46.9	—	—	197
39	^{6}Li—^{7}Li MS	H, Pyrex, 24 frits diam. 40 mm	— C (Br_2) | LiBr + KBr | C (Br_2) + 52.5 wt.%	39	8500	$2.34 \cdot 10^7$	510	1060	^{7}Li/^{6}Li 13.3 → 5.85/26 (212 g) (212 g)	—	—	20
40	^{6}Li—^{7}Li MS	U, Supr 24/4.3 supr 0.20–0.25	— C | Pb | PbI_2 | LiI | PbI_2 | C (I_2) +	112	191	$9.6 \cdot 10^3$	470	14.0	^{7}Li/^{6}Li 12.35 → — /22.14	1.0235	0.153	173,174
41	ditto	ditto	ditto	160	183	$8.11 \cdot 10^3$	475	12,3	ditto → — /18,01	1.0126	0,082	174
42	ditto	ditto 22/3.4	ditto	140	73	$8.10 \cdot 10^3$	480	30,8	ditto → — /26,14	1.0225	0.146 / 0,15[5]	174
43	^{6}Li—^{7}Li MS	Quartz membrane 0.2 mm thick	— Pt | KBr + NaBr | SiO_2 | LiBr | Pt (Br_2) +	30	2.5	225	770	5	^{7}Li/^{6}Li 14,4 → 13.3 / —	—	0.5[6]	181
44	ditto	ditto	ditto	5	2.2	40	810	5	ditto → 13.2 / —	—	0.5[6]	181
45	ditto	»	—Pt|KNO_3+$NaNO_3$| SiO_2| $LiNO_3$ |Pt(NO_3+O_2)+	2500	0.03	8	350	72	^{7}Li/^{6}Li 12,1 → 11.1 / —	—	0.5[6]	181
46	ditto	»	ditto	35	0.07	12	510	48	ditto → 11.05 / —	—	0.5[6]	181
47	^{6}Li—^{7}Li MS	V, Supr 26/4.5 quartz 0.1–0.12	— Fe (NO_2 + O_2) | $LiNO_3$ | Pt (NO_3 + O_2) +	76	173	$2.99 \cdot 10^4$	300	48	% ^{6}Li 7.40 → — /6.09	1.0087	0.057	163
48	^{6}Li—^{7}Li MS	V, Supr 22/4 quartz 0.2–0.25	— Fe (NO_2 + O_2) | $LiNO_3$ | Pt (NO_3 + O_2) +	150	243	$6.55 \cdot 10^4$	270	74	% ^{6}Li 7.40 → 7.68/6.05	1.0084	0.055	196
49	ditto	ditto	ditto	—	—	$2.03 \cdot 10^4$	320	28.8	—	1.0139	0,0906	196
50	»	»	»	—	—	$8.82 \cdot 10^3$	315	12.1	—	1.0119	0,0774	196
51	»	»	»	—	—	$2.04 \cdot 10^4$	320	21.2	—	1.0131	0.0848	196
52	»	»	»	—	—	$1.97 \cdot 10^4$	313	23.4	—	1.0135	0.0875	196
53	»	»	»	—	—	$1.72 \cdot 10^4$	326	23.2	—	1.0121	0.0789	196
54	»	»	»	—	—	$1.88 \cdot 10^4$	412	24.1	—	1.0127	0.0826	196
55	»	»	»	—	—	$1.75 \cdot 10^4$	429	24.0	—	1.0136	0.0880	196
56	»	»	»	—	—	$1.74 \cdot 10^4$	487	24.0	—	1.0070	0.0456	196
57	»	»	»	—	—	$7.56 \cdot 10^4$	339	9.5	—	1.0099	0.0643	196
58	»	»	»	—	—	$7.06 \cdot 10^3$	411	9.7	—	1.0138	0.0897	196
59	»	»	»	—	—	$4.61 \cdot 10^3$	488	6.5	—	1.0132	0.0856	196
60	^{6}Li—^{7}Li MS	U,quartz -/18 quartz 0.85	— Fe (NO_2 + O_2) | $LiNO_3$ | Rh (NO_2 + O_2) +	34	380	$5.5 \cdot 10^5$	280	402	^{7}Li/^{6}Li 12.69 → — /1349	—	—	161
61	ditto	U, quartz -/9 Al_2O_3 1.0	ditto	125	1000	$1.2 \cdot 10^5$	280	200	12.69 → 11.11/21.22	—	—	161
62	^{6}Li—^{7}Li MS	V, Vycor 12/4 quartz 0.1–0.15	— Fe (NO_2 + O_2) | $LiNO_3$ | Pt (NO_2 + O_2) +	60	60	$1.03 \cdot 10^4$	265	48	^{7}Li/^{6}Li 12.31 → — /28.80	1.0120	0.0782	192
63	ditto	ditto	ditto	40	100	$1.77 \cdot 10^4$	310	48	12.54 → — /30.34	1.0110	0.0713	192
64	»	»	»	48	90	$1.70 \cdot 10^4$	340	52	12.54 → — /21.62	1.0110	0.0712	192
65	»	»	»	42	95	$1.69 \cdot 10^4$	365	50	12.53 → — /26.06	1.0113	0.0733	192

Table 1 contd.

Expt. No.	Isotopes and medium (Ref.1)	Construction of cell (Ref.2)	Electrodes and electrolytes (Ref.3)	Voltage, V	Current, mA	Quantity of electricity, C	Temp., °C	Duration, h	Isotope content before → after experiment (Ref.4)	α	−μ	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13
66	^{6}Li—^{7}Li MS	V, Vycor 12/4 quartz 0.1–0.15	— Fe ($NO_3 + O_2$) | $LiNO_3$ | Pt ($NO_3 + O_2$) +	45	100	$1.75 \cdot 10^4$	365	47	12.40 → — /28.70	1.0112	0.0726	192
67	»	»	»	42	90	$1.64 \cdot 10^4$	415	52	12,53 → — /25,78	1.0103	0,0668	192
68	»	»	»	80	80	$1.37 \cdot 10^4$	460	48.5	12,31 → — /20.71	1.0103	0,0671	192
69	»	U, quartz 9/4 ZrPh 0.1–0.15	»	40	130	$1.16 \cdot 10^4$	300	25	12.40 → — /17.26	1.0089	0.0578	192
70	»	ditto	»	40	120	$1.29 \cdot 10^4$	290	30	12.40 → — /14.97	—	—	192
71	»	V, Vycor 12/4 quartz 0.1	»	85	59	$9.72 \cdot 10^4$	320	465	12.47 → — /473	—	—	192
72	»	ditto 12/5	»	100	72	$2.37 \cdot 10^5$	310	912	12.47 → — /250	—	—	192
73	^{6}Li—^{7}Li MS	U, Supr 24/4.2 supr 0.15–0.20	—Fe ($NO_3 + O_2$) | $LiNO_3$ | $RbNO_3$ | Pt($NO_3 + O_2$)+	—	207	$7.95 \cdot 10^4$	450	106.8	^{7}Li/^{6}Li 11.45 → — /15.24	1.0084	0.055	179
74	^{6}Li—^{7}Li MS	M, Pyrex 30/7 steatite 0.25–0.50	— Al (HNO_3) | $LiNO_3$ | Pt ($NO_3 + O_2$) +	20	50	$4.32 \cdot 10^4$	290	240	—	1.0046	0.030	171
75	ditto	ditto	ditto	80	200	$2.94 \cdot 10^5$	290	408	—	1.0088	0.057	171
76	»	» 3.5/5	»	23	250	$1.30 \cdot 10^5$	290	144	—	1.0035	0.023	171
77	»	» 27/12	»	38	260	$1.64 \cdot 10^5$	290	175	—	1.0087	0.057 0.050[9]	171 171
78	^{6}Li—^{7}Li MS	—	— Fe (HNO_3) | $LiNO_3$ | Pt ($NO_3 + O_2$) +	—	300	$7,77 \cdot 10^4$	280	72	^{7}Li/^{6}Li 11.35 → 10.8/11,95	—	—	187
79	^{6}Li—^{7}Li MS	— 25/— zircon —	—Ta (HNO_3) | $LiNO_3 + KNO_3$ | Pt ($NO_3 + O_2$) + 75 wt.%	88	450	$1.17 \cdot 10^6$	330	720	^{7}Li/^{6}Li 11.8 → — /28,2 (2.9 cm^3)	—	—	188,190
80	ditto	ditto	—Ta (HNO_3) | $LiNO_3 + KNO_3$ | Pt ($NO_3 + O_2$) + 41 wt.%	92	500	$1.30 \cdot 10^6$	340	720	ditto /27,2 (2.9 cm^3)	—	—	188,190
81	^{6}Li—^{7}Li SS	V, steel 5/10 in H_2 atm	— Zn | LiH | Fe +	30	900	$6.6 \cdot 10^3$	600	2	^{7}Li/^{6}Li 12.48 → — /12.71	1,00616	0.04	239
82	^{6}Li—^{7}Li SS	U, Vycor 30/10.4	— Mo | Zn | Li_2SO_4 | Au ($SO_3 + O_2$) +	—	255	$4.57 \cdot 10^3$	630	5	^{7}Li/^{6}Li 12.63 → — /13.08	1,0215	0.140	236,237
83	ditto	ditto	ditto	—	775	$8.40 \cdot 10^3$	620	3	ditto → — /13.25	1,0228	0,148	236,237
84	»	»	»	—	695	$1.26 \cdot 10^4$	600	5	ditto → — /13.64	1,0249	0.162	236,237
85	^{6}Li—^{7}Li SS	ditto 30/7.4	— Mo | Zn | Li_2SO_4 | Au ($SO_3 + O_2$) +	—	345	$1,37 \cdot 10^4$	600	11	ditto → — /13,71	1.0168	0,109	236,237
86	ditto	ditto	ditto	—	560	$2.0 \cdot 10^4$	605	10	ditto → — /13,98	—	—	236,237
87	»	»	»	—	475	$1,89 \cdot 10^4$	660	11	ditto → — /14,10	1.0191	0,124	236,237
88	»	»	»	—	430	$1.54 \cdot 10^4$	715	10	ditto → — /14,12	1.0215	0,140	236,237
89	»	»	»	—	615	$1,99 \cdot 10^4$	740	9	ditto → — /15,04	1.0225	0,146	236,237
90	»	»	»	—	485	$5,68 \cdot 10^3$	790	3.25	ditto → — /13.53	1.0169	0.110	236,237
91	»	»	»	—	610	$1.32 \cdot 10^4$	790	6	ditto → — /13.96	1.0222	0,144	236,237
92	^{6}Li—^{7}Li MS	V, Supr 21/4.5 supr 0.20–0.25	— Mo | Zn | $Li_2SO_4 + K_2SO_4$ | Pt ($SO_3 + O_2$) + 89.6 mole %	60	145	$6.84 \cdot 10^3$	685	13,1	—	1.00134	0.087	193,194
93	ditto	ditto	80.4 mole %	100	215	$1,95 \cdot 10^3$	590	2.53	—	—	—	193,194
94	»	»	80.4 mole %	140	175	$4,79 \cdot 10^3$	635	9.50	—	1,00120	0.078	193,194
95	»	»	80.4 mole %	160	125	$3,32 \cdot 10^3$	760	7.50	—	1.00260	0.169	193,194
96	»	»	81.0 mole %	110	180	$2,69 \cdot 10^3$	625	4,10	—	1.00182	0.118	193,194
97	»	Pyrex 0.20–0.25	81.1 mole %	110	280	$2,75 \cdot 10^3$	635	2.75	—	1.00228	0.148	193,194
98	»	Supr 0.20–0.25 ditto	79.8 mole %	35	200	$5.61 \cdot 10^3$	735	7,72	—	1.00194	0.126	193,194
99	»	»	79.9 mole %	45	180	$5.14 \cdot 10^3$	745	7.98	—	1.00115	0.075	193,194
100	»	»	79.9 mole %	60	215	$4,69 \cdot 10^3$	835	6.00	—	1.00238	0.155	193,194

Table 1 contd.

Expt. No.	Isotopes and medium (Ref.1)	Construction of cell (Ref.2)	Electrodes and electrolytes (Ref.3)	Voltage, V	Current, mA	Quantity of electricity, C	Temp., °C	Duration, h	Isotope content before → after experiment (Ref.4)	α	−μ	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13
101	$^6Li—^7Li$ MS	Supr 0.20–0.25	59.8 mole %	70	200	$6.81\cdot10^3$	735	9.42	—	1.00177	0.115	193, 194
102	ditto	ditto	40.8 mole %	70	200	$7.36\cdot10^3$	745	10.20	—	1.00211	0.137	193, 194
103	$^6Li—^7Li$ AQ	H, Pyrex 75/16 paper membranes	— Pt (H_2) | CH_3COOLi | Pt (O_2) + 0.007*N*	2500	90	$3.25\cdot10^5$	41	1000	% ^6Li 7.31 → 7.61/ —	—	—	93
104	$^6Li—^7Li$ AQ	U, Pyrex 20/6 sand 0.03–0.04	— Pt (H_2) | HCl | LiCl | $CuCl_2$ | Pt (Cl_2) + 9*N*	150	110	—	37	140	% ^6Li 7.5 → 11.35/ —	1.0033	—	75
105	$^6Li—^7Li$ AQ	H, Pyrex 65/40 80 nylon membranes	— Pt (H_2) | CH_3COOLi | Pt (O_2) + 0.05*N*	1350	900	$2.55\cdot10^6$	40	786	$^7Li/^6Li$ 12.50 → 9.76/ —	1.00086	—	102
106	$^6Li—^7Li$ LM	H, steel 20/0.7 —	— Fe | Li | Fe +	—	37 amp	$1.65\cdot10^7$	300	159	% ^6Li 7.5 → — /9.4	—	$3.5\cdot10^{-5}$	248
107	$^{22}Na—^{23}Na$ MS	V, Pyrex 17/4 quartz 0.1–0.2	— Al ($NO_2 + O_2$) | $NaNO_3$ | Pt ($NO_2 + O_2$) +	45	80	$5.76\cdot10^3$	340	20	—	1.0023	0.051	192, 198
108	ditto	ditto	ditto	82	90	$2.22\cdot10^4$	380	67	—	1.0017	0.039 / 0.045[a]	192, 198
109	$^{39}K—^{41}K$ MS	U, Supr 22.5/4 quartz 0.1	— C | $PbCl_2$ | LiCl + KCl | $PbCl_2$ | C (Cl_2) + 2 mole %	62	500	$8.65\cdot10^4$	650	48	$^{41}K/^{39}K$ 0.0715 → — /0.0885	1.016	0.32	159
110	$^{39}K—^{41}K$ PC	U, Vycor 30.5 Al_2O_3 0.1	— SiC (Cl_2) | KCl | C (Cl_2) +	—	—	$9.72\cdot10^4$	824	—	—	1.0036	0.071	200
111	ditto	ditto	ditto	—	—	$1.26\cdot10^5$	882	—	—	1.0040	0.080	200
112	»	»	»	—	—	$1.26\cdot10^5$	893	—	—	1.0041	0.082	200
113	»	»	»	—	—	$7.05\cdot10^4$	918	—	—	1.0040	0.080	200
114	»	»	»	—	—	$8.45\cdot10^4$	943	—	—	1.0038	0.076	200
115	»	»	»	—	—	$7.5\cdot10^4$	1015	—	—	1.0046	0.091	200
116	$^{39}K—^{41}K$ MS	U, Pyrex 21.8/10 zircon 0.18	— C (Br_2) | LiBr + KBr | C (Br_2) + 49 wt.%	45	550	$4.32\cdot10^6$	450	2180	$^{39}K/^{41}K$ 15.0 → 17/6.5	—	—	20
117	$^{39}K—^{41}K$ MS	V, Supr 22/4.1 quartz 0.20–0.25	— Al ($NO_2 + O_2$) | KNO_3 | Pt ($NO_2 + O_2$) +	82	100	$5.26\cdot10^4$	360	146	% ^{41}K 6.7 → 6.68/7.64	1.00184	0.036	199
118	$^{39}K—^{41}K$ MS	V, Supr 22/4 quartz 0.20–0.25	—Al($NO_2 + O_2$) | $KNO_3 + KNO_2$ | Pt(NO_2+O_2)+	—	87.5	$4.72\cdot10^4$	360	149.5	—	1.0019	0.038	201
119	ditto	ditto	ditto	—	99.5	$8.53\cdot10^4$	360	248.0	—	1.0019	0.038	201
120	»	»	»	—	233	$2.43\cdot10^4$	354	29.0	—	1.0022	0.044	201
121	»	»	»	—	206	$3.54\cdot10^4$	370	47.8	—	1.0021	0.042	201
122	»	»	»	—	202	$3.38\cdot10^4$	375	46.5	—	1.0017	0.034	201
123	»	»	»	—	206	$1.78\cdot10^4$	388	24.0	—	1.0025	0.050	201
124	»	»	»	—	198	$2.55\cdot10^4$	442	35.7	—	1.0023	0.046	201
125	»	»	»	—	222	$2.56\cdot10^4$	454	32.1	—	1.0023	0.046	201
126	»	»	»	—	197	$4.10\cdot10^4$	470	57.0	—	1.0029	0.058	201
127	»	»	»	—	192	$2.88\cdot10^4$	496	41.6	—	1.0028	0.057	201
128	»	»	»	—	200	$2.02\cdot10^4$	541	28.0	—	1.0035	0.070	201
129	»	»	»	—	161	$1.35\cdot10^4$	562	23.3	—	1.0033	0.065	201
130	»	»	»	—	228	$2.46\cdot10^4$	586	30.0	—	1.0035	0.070	201
131	$^{39}K—^{41}K$ MS	V, Vycor 24/4 quartz 0.1–0.15	— Al ($NO_2 + O_2$) | KNO_3 | Pt ($NO_2 + O_2$) +	148	98	$3.37\cdot10^4$	388	100	$^{39}K/^{41}K$ 13.85 → — /8.57	1.0021	0.042	192
132	$^{39}K—K^{41}$ MS	V, Vycor 24/4 quartz 21/4	— Al ($NO_2 + O_2$) | KNO_3 | Pt ($NO_2 + O_2$) +	190	120	$7.63\cdot10^4$	380	177.5	13.86 → — /8.23	1.0020	0.040	192
133	ditto	ditto 14.6/4	ditto	145	150	$8.46\cdot10^4$	380	149	13.9 → — /5.22	1.0020	0.040	192
134	»	U, quartz 15/4 ZrPh 0.1–0.15	»	120	80	$2.06\cdot10^4$	380	70	13.85 → — /13.07	1.0017	0.034	192
135	»	ditto 9.5/4	»	45	90	$1.90\cdot10^4$	380	65	13.85 → — /12.68	1.0018	0.036	192

Table 1 contd.

Expt. No.	Isotopes and medium (Ref.1)	Construction of cell (Ref.2)	Electrodes and electrolytes (Ref.3)	Voltage, V	Current, mA	Quantity of electricity, C	Temp., °C	Duration, h	Isotope content before → after experiment (Ref.4)	α	−μ	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13
136	^{39}K—^{41}K MS	V, Vycor 14/4 quartz 0.1–0.15	—Al(NO_3+O_2) | $KNO_3+K_2SO_4$ | Pt(NO_3+O_2)+	55	130	$1.85\cdot10^4$	390	42	$^{39}K/^{41}K$ 13.85 → — /13.53	1.0027	0.054	192
137	ditto	ditto	ditto	95	55	$1.52\cdot10^4$	390	171	ditto /13.36	1.0021	0.042	192
138	»	»	»	80	50	$9.4\cdot10^3$	390	60	» /13.36	1.0018	0.036	192
139	^{39}K—^{41}K AQ	H, Pyrex 7/14 pyrex 0.15	— Pt (H_2) | KCl | Pt (Cl_2) + 0.898*N*	93	500	$1.81\cdot10^5$	27	450	$^{39}K/^{41}K$ 14.2 → 24.0/—	1.00385	0.077	60
140	^{39}K—^{41}K AQ	H, Pyrex 122/22 sand 0.15	— Pt (H_2) | H_2SO_4 | K_2SO_4 | Pt (O_2) + 1.083*N*	800	500	—	50	335	$^{39}K/^{41}K$ 14.2 → 17.4/—	1.0029	0.058	60
141	^{39}K—^{41}K AQ	V, Pyrex 20/6 sand 0.03–0.04	— Pt (H_2) | KCl | $CuCl_2$ | Pt (Cl_2) + 3*N*	—	—	—	—	—	—	1.0025	0.050	77
142	^{39}K—^{41}K LM	V, Pyrex 20/0.6	— W | K | W +	5.3	8250	$1.05\cdot10^7$	140	355	% ^{41}K 6.695 → 7.025/6.30	—	$9\cdot10^{-6}$	250
143	^{85}Rb—^{87}Rb MS	U, quartz 30/5 Al_2O_3 0.1	— SiC (Cl_2) | RbCl | C (Cl_2) +	—	—	$5.76\cdot10^4$	757	—	—	1.00121	0.052	200
144	ditto	ditto	ditto	—	—	$1.28\cdot10^5$	812	—	—	1.00109	0.047	200
145	»	»	»	—	—	$8.64\cdot10^4$	827	—	—	1.00119	0.051	200
146	»	»	»	—	—	$5.11\cdot10^4$	830	—	—	1.00114	0.049	200
147	»	»	»	—	—	$9.28\cdot10^4$	840	—	—	1.00135	0.058	200
148	»	»	»	—	—	$7.76\cdot10^4$	924	—	—	1.00132	0.057	200
149	»	»	»	—	—	$7.24\cdot10^4$	976	—	—	1.00140	0.060	200
150	^{85}Rb—^{87}Rb MS	U, quartz 39/5 Al_2O_3 0.1	— SiC (Br_2) | RbBr | C (Br_2) +	—	—	$5.26\cdot10^4$	745	—	—	1.00165	0.071	200
151	ditto	ditto	ditto	—	—	$7.20\cdot10^4$	768	—	—	1.00170	0.073	200
152	»	»	»	—	—	$4.57\cdot10^4$	852	—	—	1.00184	0.079	200
153	^{85}Rb—^{87}Rb MS	U, quartz 39/5 Al_2O_3 0.1	— SiC (Br_2) | RbBr | C (Br_2) +	—	—	$5.90\cdot10^4$	929	—	—	1.00168	0.072	200
154	»	ditto	ditto	—	—	$5.80\cdot10^4$	946	—	—	1.00184	0.079	200
155	^{85}Rb—^{87}Rb MS	U, Supr 24/4.2 supr 0.15–0.20	—Fe (NO_3+O_2) | $LiNO_3$ | $RbNO_3$ | Pt(NO_3+O_2)+	—	207	$7.95\cdot10^4$	450	106.8	$^{85}Rb/^{87}Rb$ 2.62 → 3.21/—	1.0011	0.05	179
156	^{85}Rb—^{87}Rb MS	U, Supr 22/4 quartz 0.20–0.25	—Al (NO_3+O_2) | $RbNO_3$ | Pt (NO_3+O_2) +	—	150	$4.68\cdot10^4$	354	120.7	$^{85}Rb/^{87}Rb$ 2.62 → — /2.47	1.00079	0.0345	202
157	ditto	ditto	ditto	—	150	$1.86\cdot10^4$	346	38.0	ditto → — /2.54	1.00079	0.0345	202
158	^{85}Rb—^{87}Rb MS	U, Pyrex 10/4 quartz 0.1–0.15	— Al (NO_3+O_2) | $RbNO_3$ | Pt (NO_3+O_2) +	80	120	$1.93\cdot10^5$	360	40	$^{85}Rb/^{87}Rb$ 2.612 → — /2.469	1.00064	0.028	192
159	ditto	ditto 13/4	ditto	60	80	$1.37\cdot10^4$	360	48	2.597 → — /2.380	1.00093	0.040	192
160	»	» 18/4	»	125	55	$1.75\cdot10^4$	360	77	2.597 → — /2.351	1.00068	0.029	192
161	^{85}Rb—^{87}Rb MS	V, quartz 16/5 quartz 0.075	— Al (HNO_3) | $RbNO_3$ | Pt (NO_3+O_2) +	120	120	$3.14\cdot10^5$	375	727	$^{85}Rb/^{87}Rb$ 2.60 → — /2.015	—	—	203
162	ditto	ditto 12/4–7	ditto	115	42.5	$6.35\cdot10^4$	365	415.5	ditto → — /2.126	—	—	203
163	»	V, quartz 16/4–9 quartz 0.075–0.1	»	141	125	$1.53\cdot10^5$	365	346	» → — /1.968	—	—	203
164	»	ditto	»	150	160	$2.52\cdot10^5$	365	442	» → — /1.807	—	—	203
165	^{85}Rb—^{87}Rb AQ	H, Pyrex 100/16 paper membranes	— Pt (H_2) | RbOH | Pt (O_2) + 0.006*N*	2300	110	$7.9\cdot10^4$	80	200	% ^{85}Rb 72.2 → 73.8/ —	—	—	92
166	^{85}Rb—^{87}Rb AQ	U, Pyrex 20/6 sand 0.03–0.04	— Pt (H_2) | HCl | RbCl | $CuCl_2$ | Pt (Cl_2) + 3*N*	—	—	—	—	—	—	1.0011	—	77
167	^{133}Cs—^{137}Cs MS	V, Vycor 11/4 quartz 0.1–0.15	— Al (NO_3+O_2) | $CsNO_3$ | Pt (NO_3+O_2) +	100	80	$6.3\cdot10^3$	450	23.5	—	1.00081	0.0218	192
168	ditto	ditto 9/5	ditto	55	130	$3.26\cdot10^4$	450	71	—	1.00115	0.031	192
169	^{63}Cu—^{65}Cu MS	V, Supr 17/3.8 quartz 0.15–0.20	— C (Cl_2) | LiCl + KCl | CuCl | $PbCl_2$ | C (Cl_2) +	54	194	$4.87\cdot10^4$	535	70	% ^{63}Cu 68.94 → — /65.1	1.0028	0.080	204

Table 1 contd.

Expt. No.	Isotopes and medium (Ref.1)	Construction of cell (Ref.2)	Electrodes and electrolytes (Ref.3)	Voltage, V	Current, mA	Quantity of electricity, C	Temp., °C	Duration, h	Isotope content before → after experiment (Ref.4)	α	−μ	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13
170	^{63}Cu—^{65}Cu MS	V, Supr 17/4.1 quartz 0.1–0.15	— C (Cl_2) | LiCl + KCl | **CuCl** | $PbCl_2$ | C (Cl_2) +	49	196	$5.65\cdot10^4$	530	80	% ^{63}Cu 68.94 → — /64.4	—	—	204
171	^{63}Cu—^{65}Cu AQ	H, Pyrex 10/10 sand 0.15–0.25	— Pt (H_2) | H_2SO_4 | **$CuSO_4$** | Cu + 0.923*N*	—	200	$2.8\cdot10^5$	29	429	$^{63}Cu/^{65}Cu$ 2.2045 → 2.2408/ —	1.00069	0.022	62
172	^{63}Cu—^{65}Cu AQ	V, Pyrex 1.5/1.2 sand 0.03–0.04	—Pt(H_2) | HCl | $MgCl_2$ | **$CuCl_2$** | $CdCl_2$ | Pt(Cl_2)+ 8.70*N*	—	25	—	50	35.3	$^{63}Cu/^{65}Cu$ 2.33 → — /2.08	1.0013	—	79
173	^{107}Ag—^{109}Ag MS	U, Supr 20/- supr 0.1–0.12	— C (Cl_2) | LiCl | **AgCl** | C (Cl_2) +	48	300	$4.89\cdot10^4$	650	50	$^{107}Ag/^{109}Ag$ 1.08 → 1.130/ —	1.00118	0.064	205
174	^{107}Ag—^{109}Ag SS	H, Pyrex 65/4 —	— Ag | α-**AgJ** | C (I_2) +	—	250	$1.8\cdot10^4$	230	20	% ^{109}Ag 48 → — /51	1.002	0.11	71.72
175	^{24}Mg—^{26}Mg MS	U, quartz 30/4 A_2O_3 0.1	— C (Cl_2) | **$MgCl_2$** | C (Cl_2) +	—	262	$6.12\cdot10^4$	790	64.8	% ^{26}Mg 10.74 → — /12.50	1.00816	0.102	206.207
176	ditto	ditto.	ditto	—	288	$5.22\cdot10^4$	790	50.4	ditto /11.98	1.00825	0.103	206,207
177	^{24}Mg—^{26}Mg AQ	H, Pyrex 12/3 sand 0.1	— Pt (H_2)/HBr | **$MgBr_2$** | Pt (Br_2) + 4.65*N*	150	670	$3.2\cdot10^6$	25	1326	$^{24}Mg/^{26}Mg$ 0.1435 → — /0.1495	1.0009	0.0113	89
178	^{24}Mg—^{26}Mg AQ	V, Pyrex 1.5/1.2 sand 0.03–0.04	—Pt (H_2)/HCl | **$MgCl_2$** | $CuCl_2$ | $CdCl_2$ | Pt (Cl_2)+ 8.95*N*	—	25	—	50	35.6	$^{24}Mg/^{26}Mg$ 0.1435 → — /0.184	1.0031	—	79
179	^{40}Ca—^{48}Ca MS	U, quartz 30/4 A_2O_3 0.1	— C (Cl_2) | **$CaCl_2$** | C (Cl_2) +	—	210	$5.8\cdot10^4$	850	76.8	% ^{48}Ca 0.187 → — /0.281	1.0093	0.052	206,207
180	ditto	ditto	ditto	—	125	$8.78\cdot10^5$	850	720	То же /0.294	1.0090	0.050	206,207
181	^{40}Ca—^{48}Ca MS	U, quartz 30/4 A_2O_3 0.1	— C (Br_2) | **$CaBr_2$** | C (Br_2) +	—	205	$5.32\cdot10^4$	850	72	% ^{48}Ca 0.187 → — /0.481	1.0115	0.063	206,207
182	^{40}Ca—^{46}Ca MS	U, quartz 15/29 ZrO_2 —	— C (Br_2) | **$CaBr_2$** | C (Br_2) +	—	—	—	775	720	% ^{46}Ca 0.0032 → — /0.0064	—	—	213
183	ditto	V, Al_2O_3 15/29 ZrO_2 —	ditto	—	—	—	775	720	ditto /0.016 (200 g)	—	—	213
184	^{40}Ca—^{44}Ca MS	U, quartz 20/17 A_2O_3 —	— C (Br_2) | **$CaBr_2$** + KBr | C (Br_2) + 50 mole %	14	400	$3.39\cdot10^6$	765	2352	$^{44}Ca/^{40}Ca$ 0.0216 → 0.0170/0.0261	—	—	209
185	ditto	U, quartz 17/14 zircon–	ditto	37	1000	$4.23\cdot10^6$	765	1176	0.0217 → 0.0173/0.0381	1.0057	0.06	209
186	ditto	ditto	»	78	2700	$5.14\cdot10^6$	765	528	0.0213 → 0.0194/0.0401	1.0057	0.06	209
187	^{40}Ca—^{44}Ca MS	U, quartz 12/6 zircon 0.15	— C (Br_2) | **$CaBr_2$** + LiBr | C (Br_2) +	—	1000	$3.9\cdot10^5$	—	100	% ^{44}Ca 2.06 → — /3.5	1.0057	0.060	211
188	ditto	ditto	— C (Br_2) | **$CaBr_2$** + $SrBr_2$ | C (Br_2) +	—	1000	$2.9\cdot10^5$	—	80	% ^{44}Ca 2.06 → — /3.7 % ^{48}Ca 0.185 → — /0.46	— —	— —	211 211
189	^{40}Ca—^{44}Ca MS	U, quartz 26/3.5 Al_2O_3 0.1	— C (I_2) | **CaI_2** | C (I_2) +	150	205	$4.85\cdot10^4$	880	66	$^{40}Ca/^{44}Ca$ 0.0213 → — /0.0270	1.0067	0.072	214
190	ditto	ditto	ditto	168	235	$5.54\cdot10^4$	880	65.5	ditto /0.0248	1.0073	0.077 0.0745[9]	214 214
191	^{84}Sr—^{88}Sr MS	U, quartz 30/4 Al_2O_3 0.1	— C (Cl_2) | **$SrCl_2$** | C (Cl_2) +	—	250	$8.65\cdot10^4$	1000	96	$^{88}Sr/^{84}Sr$ 147.12 → — /214.46	1.00167	0.036	206,207
192	^{130}Ba—^{138}Ba MS	U, quartz 30/4 Al_2O_3 0.1	— C (Cl_2) | **$BaCl_2$** | C (Cl_2) +	—	318	$8.78\cdot10^4$	1080	76.8	$^{138}Ba/^{130}Ba$ 688.67 → — /875.99	1.00116	0.0195	206,207
193	ditto	ditto	ditto	—	260	$7.2\cdot10^4$	1075	76.8	688.65 → — /718.11	1.00111	0.0186 0.019[10]	206,207 206
194	^{64}Zn—^{66}Zn MS	V, Supr 18/4.1 supr 0.15–0.20	— C | Pb | $PbCl_2$ | **$ZnCl_2$** | C (Cl_2) +	300	230	$5.96\cdot10^4$	650	72	$^{64}Zn/^{66}Zn$ 1.76 → 2.62/ —	1.00239	0.0776	215
195	^{64}Zn—^{66}Zn MS	V, Supr 23/3.75 quartz 0.15–0.20	— C | Pb | $PbBr_2$ | **$ZnBr_2$** | C (Br_2) +	415	140	$2.9\cdot10^4$	500	57.5	$^{64}Zn/^{66}Zn$ 1.76 → 2,22/ —	1.00343	0.11	216
196	^{64}Zn—^{68}Zn LM	H, Pyrex 20/0.55	— W | **Zn** | W +	—	10,5amp.	$9.95\cdot10^6$	510	254	$^{64}Zn/^{68}Zn$ 2,655 → — /2,75	—	$0.58\cdot10^{-8}$	255
197	^{106}Cd—^{116}Cd MS	U, Supr 13/4 quartz 0.1	— C | $PbCl_2$ | LiCl | **$CdCl_2$** | C (Cl_2) +	95	550	$9.0\cdot10^4$	700	50	$^{106}Cd/^{116}Cd$ 0.205 → 0,308/ —	1.006	0.067	217
198	^{106}Cd—^{116}Cd MS	V, Supr 24/4 supr 0.15–0.20	— C (Br_2) | **$CdBr_2$** | C (Br_2) +	—	253	$1.18\cdot10^4$	610	13	$^{106}Cd/^{116}Cd$ 0.16 → 0.192/ —	1.00505	0.0560	218

Table 1 contd.

Expt. No.	Isotopes and medium (Ref.1)	Construction of cell (Ref.2)	Electrodes and electrolytes (Ref.3)	Voltage, V	Current, mA	Quantity of electricity, C	Temp., °C	Duration, h	Isotope content before → after experiment (Ref.4)	α	−μ	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13
199	^{106}Cd—^{116}Cd MS	V, Supr 24/4 supr 0.15–0.20	— C (Br_2) | **$CdBr_2$** | C (Br_2) +	—	225	$5.42\cdot10^4$	620	67	^{106}Cd/^{116}Cd 0.16 → 0.427/ —	1.00662	0,0735	218
200	^{106}Cd—^{116}Cd MS	ditto	— Cd (Br_2) | **$CdBr_2$** | C (Br_2) +	—	320	$5.77\cdot10^4$	620	50	^{106}Cd/^{116}Cd 0.16 → 0.402/ —	1.00628	0.0697	218
201	ditto	U, Supr 28/4 supr 0.10–0.12	— C (Br_2) | LiBr | **$CdBr_2$** + **Cd** | C (Br_2) +	—	200	$3.62\cdot10^4$	630	50	ditto → 0.256/ —	1.00720	0.0800 0.075[11]	218 218
202	^{110}Cd—^{114}Cd MS	U, Supr 24/4 **Al_2O_3** 0.1	— W | Cd | **CdI_2** | C (I_2) +	278	230	$1.20\cdot10^5$	580	135	^{114}Cd/^{110}Cd 2,33 → — /3,25	1.00272	0.0762	214
203	ditto	ditto	ditto	268	225	$1.01\cdot10^5$	580	125	ditto → — /2.78	1.00266	0,0745	214
204	»	»	»	265	250	$7.20\cdot10^4$	580	84	ditto → — /2,62	1.00281	0.0786 0.0764[12]	214 214
205	^{106}Cd—^{116}Cd LM	H, Pyrex 20/0.55	— W | **Cd** | W +	—	12.5 amp	$1.6\cdot10^7$	540	360	^{116}Cd/^{106}Cd 6.14 → 6,73/5.43	—	$1.24\cdot10^{-6}$	255
206	^{113}In—^{115}In LM	V, quartz 20/0.987	— W | **In** | W +	—	16,3 amp	$2.0\cdot10^7$	820	360	^{115}In/^{113}In 22,00 → 22,19/21,36	—	$6\cdot10^{-6}$	260
207	^{113}In—^{115}In SM	V, Pyrex 20/0.566	— W | **In** | W +	—	9,1 amp	$2.5\cdot10^7$	123	768	—	—	$<5\cdot10^{-7}$	260
208	^{203}Tl—^{205}Tl MS	U, Supr 27/4 supr 0.3	— C | Tl | **TlCl** | **$ZnCl_2$** | C (Cl_2) +	244	250	$1.7\cdot10^4$	530	109	^{205}Tl/^{203}Tl 2.45 → — /2.81	1.0004	0,04	219
209	^{203}Tl—^{205}Tl MS	U, Supr 20/4 **Al_2O_3** 0.1	— C (Cl_2) | LiCl | **TlCl** | **$ZnCl_2$** | C (Cl_2) +	—	325	$1.16\cdot10^5$	680	98.4	% ^{205}Tl 29,59 → — 28.53	1.00035	0,0353	221
210	^{203}Tl—^{205}Tl MS	U, Supr 20/4 **Al_2O_3** 0.1	— C (Cl_2) | LiCl | **TlCl** | $ZnCl_2$ | C (Cl_2) +	—	380	$1.99\cdot10^5$	665	158.4	29.55 → — /28,25	1.00036	0.0366	221
211	ditto	ditto	— W | Tl | **TlCl** | $ZnCl_2$ | C (Cl_2) +	—	325	$1.14\cdot10^5$	555	96,5	29.62 → — /27,70	1.00041	0.0411	221
212	»	»	ditto	—	200	$1.58\cdot10^5$	535	214	29,49 → — /26,28	1.00042	0.0419	221
213	»	»	»	—	100	$1.64\cdot10^5$	475	455	29,54 → — /26.59	1.00045	0,0459	221
214	^{203}Tl—^{205}Tl MS	V,Vycor 13/4 quartz 0.1–0.15	— Al (NO_3 + O_2) | **$TlNO_3$** | Pt (NO_3 + O_2) +	100	102	$3.72\cdot10^4$	219	100	—	1,00031	0,032	222
215	ditto	ditto	ditto	127	70	$1.69\cdot10^4$	219	74,5	—	1,00031	0.032	222
216	»	»	»	90	90	$1.56\cdot10^4$	219	50	^{205}Tl/^{203}Tl 2.382 → — /2,540	1.00037	0,038	222
217	»	»	»	117	90	$1.59\cdot10^4$	219	50	—	1.00037	0,038	222
218	^{112}Sn—^{124}Sn MS	V, Pyrex 20/4 pyrex 0,2–0,3	— Mo | Sn | **$SnCl_2$** | $ZnCl_2$ | C (Cl_2) +	80	194	$4.51\cdot10^4$	590	64	^{112}Sn/^{124}Sn 0.163 → — /0.104	1.0064	0 065	223
219	ditto	ditto	ditto	90	210	$4.26\cdot10^4$	340	56	ditto → — /0.107	1.0065	0,066	223
220	»	U, Pyrex 12/4 pyrex 0,2–0,3	— Mo | Pb | $PbCl_2$ | LiCl + + KCl | **$SnCl_2$** | $ZnCl_2$ | C(Cl_2)+	110	188	$4,5\cdot10^4$	540	66	ditto → 0.227/—	1.0062	0.063	223
221	»	ditto	ditto	105	202	$3,85\cdot10^4$	450	53	ditto → 0,253/—	1.0065	0.066	223
222	^{112}Sn—^{124}Sn MS	U, Pyrex 20/4 pyrex 0.2–0.3	—SiC(Br_2) | LiBr+KBr | **$SnBr_2$** | $ZnBr_2$ | C(Br_2)+	110	154	$4.24\cdot10^4$	470	76	^{112}Sn/^{124}Sn 0.16 → 0.288/ —	1.0071	0.072	224
223	^{112}Sn—^{124}Sn MS	V, Pyrex 20/4 pyrex 0.2–0.3	— Mo | Sn | **SnI_2** | ZnI_2 | C (I_2) +	94	179	$2.06\cdot10^4$	470	32	^{112}Sn/^{124}Sn 0.16 → — /0.083	1.0079	0,080	224
224	^{112}Sn—^{124}Sn MS	U, Pyrex 17.7/4 pyrex 0.32–0.35	—SiC(Cl_2)|LiCl+KCl|**$SnCl_2$**+$PbCl_2$|$ZnCl_2$|C(Cl_2)+ 11.40 mole %	256	240	$1.19\cdot10^5$	575	161	—	—	0 012[13]	225
225	ditto	U, Pyrex 14,5/4 pyrex 0.35–0.4	58.83 mole %	224	150	$8.17\cdot10^4$	565	146	—	—	0,012[13]	225
226	»	ditto 17.8/4	78.84 mole %	196	200	$5.8\cdot10^4$	570	180	—	—	0,012[13]	225
227	^{112}Sn—^{124}Sn LM	H, Pyrex 20/0.55	— W | **Sn** | W +	—	10,3 amp	$1.52\cdot10^7$	285	408	^{124}Sn/^{112}Sn 6,19 → 7,22/5,43	—	$1,13\cdot10^{-5}$	255
228	^{204}Pb—^{206}Pb MS	V, Supr 0.22/3.8 supr 0.15–0.20	—C (Cl_2) | LiCl+KCl | **$PbCl_2$** | $ZnCl_2$ | C (Cl_2) +	110	220	$1.86\cdot10^5$	640	236	^{204}Pb/^{206}Pb 0,0570 → 0.0612/ —	1.000227	0,0233	226
229	^{206}Pb—^{208}Pb MS	V, Supr 17/- supr 0.20–0.25	— C (Cl_2) | LiCl+KCl | **$PbCl_2$** | $ZnCl_2$ | C (Cl_2) +	110	226	$1,38\cdot10^5$	530	169	^{08}Pb/^{206}Pb 2.148 → — /2.272	1.000232	0,0240	226

Table 1 contd.

Expt. No.	Isotopes and medium (Ref.1)	Construction of cell (Ref.2)	Electrodes and electrolytes (Ref.3)	Voltage, V	Current, mA	Quantity of electricity, C	Temp., °C	Duration, h	Isotope content before → after experiment (Ref.4)	α	−μ	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13
230	^{206}Pb—^{208}Pb MS	U, Supr 24/4 supr 0.20–0.25	— C | Pb | $PbBr_2$ | LiBr | $PbBr_2$ | C (Br_2) +	—	172	$7.42 \cdot 10^4$	590	120	$^{208}Pb/^{206}Pb$ 2.21 → 2.098/ —	1.000396	0.041	227
231	^{206}Pb—^{208}Pb MS	U, Supr 17/4 Al_2O_3 0.1	— W | Pb | PbI_2 | C (I_2) +	180	450	$1.15 \cdot 10^5$	600	81	$^{208}Pb/^{206}Pb$ 2.07 → — /2.17	1.000728	0.0753	214
232	ditto	ditto 24/4	ditto	285	425	$1.24 \cdot 10^5$	600	82	ditto → — /2.15	1.000685	0.0708 0.0731[14]	214 214
233	^{235}U—^{238}U MS	U, quartz 15/7.4 quartz 0.5–0.6	— C (Cl_2) | UCl_4 | C (Cl_2) +	65	130	$5.43 \cdot 10^4$	615	115	% ^{235}U 0.7205 → 0.7241/ —	1.00036	0.032	228
234	^{235}U—^{238}U AQ	H, Pyrex 20/30 pyrex 0.135	— Pt (H_2) | HCl | UCl_4 + UO_2Cl_2 | Pt (Cl_2) + 0,10*M* 0,10*M*	40	82	$4.16 \cdot 10^5$	18	1408	% ^{235}U 0.7111 → 0.7171/ —	1.0012	0.0945	64
235	^{234}U—^{238}U AQ	V, Pyrex 1.5/1.2 sand 0.03–0.04	—Pt(H_2)| HCl | UO_2Cl_2|$CdCl_2$+Cd(OH)$_2$|Pt(Cl_2)+	—	10	—	60	72	% ^{234}U 0.006 → 0.00602/—	1.0009	—	81
236	^{35}Cl—^{37}Cl MS	U, quartz 60/5 Al_2O_3 0.1	+ C (Cl_2) | KCl | KBr | SiC (Br_2) —	—	—	$3.64 \cdot 10^4$	825	—	—	1.00345	0.062	200
237	ditto	ditto	ditto	—	—	$3.24 \cdot 10^4$	938	—	—	1.00340	0.061	200
238	»	»	»	—	—	$3.6 \cdot 10^4$	974	—	—	1.00328	0.059	200
239	^{35}Cl—^{37}Cl MS	U, quartz 60/5 Al_2O_3 0.1	+ C (Cl_2) | RbCl | RbBr | SiC (Br_2) —	—	—	$4.68 \cdot 10^4$	781	—	—	1.00628	0.113	200
240	ditto	ditto	ditto	—	—	$3.42 \cdot 10^4$	881	—	—	1.00628	0.113	200
241	»	»	»	—	—	$4.0 \cdot 10^4$	959	—	—	1.00750	0.135	200
242	^{35}Cl—^{37}Cl MS	U, Supr 20.5 supr 0.1–0.12	+ Zn | $ZnCl_2$ | W —	415	215	$1.54 \cdot 10^5$	600	198	% ^{37}Cl 24.6 → — /17.55	1.00241	0.043	230
243	^{35}Cl—^{37}Cl MS	—	+ Cd | $CdCl_2$ + Cd | $CdCl_2$ | Cd —	—	—	—	—	—	—	1.00189	0.034	232
244	^{35}Cl—^{37}Cl MS	U, Supr 20/5.5 Al_2O_3 0.1	+ Tl | TlCl | Tl —	100	450	$8.0 \cdot 10^4$	565	50	% ^{37}Cl 24.6 → — 19.45	1.00433	0.078	231
245	ditto	ditto	ditto	100	350	$1.73 \cdot 10^5$	560	141.5	ditto → — /8.4	1.00472	0.085	231
246	»	»	»	100	500	$1.54 \cdot 10^5$	730	89	» → — /17.55	1.00310	0.056	231
247	»	»	»	100	500	$1.54 \cdot 10^5$	690	89	» → — /16.50	1.00305	0.055	231
248	»	»	»	100	500	$1.23 \cdot 10^5$	565	69	» → — /16.79	1.00422	0.076	231
249	»	U, Supr 30/5 Al_2O_3 0.1	»	100	600	$1.15 \cdot 10^6$	565	624	% ^{35}Cl 75.4 → 98.4 (0.57 *z*)	—	—	231
250	^{35}Cl—^{37}Cl MS	U, Supr 20/5.5 supr 0.1–0.12	+ Pb | $PbCl_2$ | W —	130	523	$3.17 \cdot 10^5$	520	168.5	% ^{37}Cl 24.6 → — /14.1	1.0029	0.052	229
251	^{35}Cl—^{37}Cl MS	U, Supr 8.25/5.5 supr–	+ C (Cl_2) | $PbCl_2$| Pb —	110	400	—	520	73	% ^{37}Cl 24.6 → — /30.2	1.0020	0.036	233
252	^{35}Cl—^{37}Cl AQ	H,Pyrex 10/20 sand 0.15–0.20	+ Pt (O_2) | NaOH | NaCl | Pt (H_2) — 1,782*N*	80	500	$8.5 \cdot 10^5$	50	474	$^{35}Cl/^{37}Cl$ 3.12 → — /4.18	1.00207	0.037	61
253	^{35}Cl—^{37}Cl AQ	V, Pyrex 2.1/1.2 sand 0.03–0.04	+Pt(O_2) | LiOH | LiCl |$Li_2Cr_2O_7$|Li_2SO_4|Pt(H_2)— 7,5*N*	—	11	—	50	12.3	% ^{37}Cl 24.6 → — /26.6	1.0022	—	80
254	ditto	ditto 1.1/1.2	+Pt(O_2)| NaOH|NaCl |$Na_2Cr_2O_7$|Na_2SO_4|Pt(H_2)— 5,4*N*	—	20	—	50	6.8	ditto → — /28.8	1.0021	—	80
255	ditto	» 1.2/0.7	+Pt (Cl_2) | HCl | $H_2Cr_2O_7$ | H_2SO_4 | Pt (H_2) — 10*N*	—	60	—	50	7.4	ditto → — /26.5	1.0015	—	80
256	^{79}Br—^{81}Br MS	U, quartz 60/5 Al_2O_3 0.1	+ C (Cl_2) | RbCl | RbBr | SiC (Br_2) —	—	—	$4.68 \cdot 10^4$	800	—	—	1.00275	0.110	200
257	ditto	ditto	ditto	—	—	$3.42 \cdot 10^4$	889	—	—	1.00312	0.125	200
258	»	»	»	—	—	$2.95 \cdot 10^4$	935	—	—	1.00290	0.116	200
259	»	»	»	—	—	$4.0 \cdot 10^4$	967	—	—	1.00278	0.111	200

Table 1 contd.

Expt. No.	Isotopes and medium (Ref.1)	Construction of cell (Ref.2)	Electrodes and electrolytes (Ref.3)	Voltage, V	Current, mA	Quantity of electricity, C	Temp., °C	Duration, h	Isotope content before → after experiment (Ref.4)	α	−μ	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13
260	^{79}Br—^{81}Br MS	U, Supr 21/4.4 supr 0.1-0.12	+ Zn | $ZnBr_2$ | W −	400	171	$2.11 \cdot 10^5$	650	337	$^{79}Br/^{81}Br$ 1.024 → — /1.298	1.000875	0.035	235
261	ditto	ditto 20/3.9	ditto	—	159	$1.77 \cdot 10^5$	610	308	ditto → — /1.307	1.000875	0.035	236
262	^{79}Br—^{81}Br MS	U, Pyrex 20/5 pyrex 0.1-0.12	+ Pb | $PbBr_2$ | W −	182	447	$3.0 \cdot 10^5$	400	187	% ^{79}Br 50.414 → — /56.500	1.00111	0.044	234

[1]Isotopes for which the mass effect has been calculated. The abbreviations have the following significance: MS = molten salts; SS = solid salt; AQ = aqueous solution; LM = liquid metal; SM = solid metal.

[2]The structural characteristics of the cell are given in the sequence—form and material of separating tube, dimensions of tube (length (cm) in numerator, internal diameter (mm) in denominator) and material and grain-size (mm) of packing. Abbreviations: U = U-shaped tube of type illustrated in Fig. 2*c*; V = vertical tube as shown in Figs. 2*a*, 2*b*, and 2*d*; H = horizontal cell as in Fig. 3; Supr = Supremax glass; ZrPh = zirconyl phosphate.

[3]"Head" electrode on left-hand side (negative in the separation of isotopic cations, positive in the separation of anions). The salt containing the isotopes to be separated is printed in bold type; its content in the initial mixture or the concentration of the solution is indicated underneath.

[4]Results of isotopic analysis before → after experiment (in the numerator for the cathodic end of the separation zone, in the denominator for the anodic end): the values given are those which differ to the maximum extent from the initial values (for example, if maximum enrichment with a given isotope is observed not in an electrode compartment but in the adjacent portion of the separating tube, the latter value is cited). The quantity of enriched salt (in g or cm^3) is given in parentheses if electrical migration was conducted for preparative purposes.

[5]Mean value of μ for Expts. 40 and 42.

[6]Value of μ for Expts. 43–46 calculated in Ref. 279.

[7]Mean value of μ for Expts. 74–77.

[8]Mean value of μ for Expts. 107 and 108.

[9]Mean value of μ for Expts. 189 and 190.

[10]Mean value of μ for Expts. 192 and 193.

[11]Mean value of μ for Expts. 198–201.

[12]Mean value of μ for Expts. 202–204.

[13]Mean value of μ for Expts. 224–226.

[14]Mean value of μ for Expts. 231 and 232.

bath. When heavy isotopes are to be concentrated, on the other hand, the bath forms the cathode compartment, and enriched material is withdrawn from the upper space, not occupied by the packing, of the tube (the anode compartment)[20,213]. If, however, both cathodic and anodic separating tubes are immersed in the bath, both light and heavy isotopes can be concentrated in the same installation; an electrode at zero potential should be lowered into the bath to prevent disturbance of the electrical conditions in the individual tubes and the bath as a whole. Klemm[172] described the mode of operation of such an installation for separating the isotopes of lithium, in which the ratio of the numbers of cathodic and anodic tubes was 1 : 2, the quantity of material enriched with the light isotope ^{6}Li to 90 at.% was 8.2% of the total quantity of salt removed from the separating tubes, whereas 91.8% of the whole salt was enriched to 99.974 at.% with the heavy isotope ^{7}Li.

The choice of optimum dimensions for the separating tube is governed by the relation between the required separation factor S and the rate v_p of removal of the product from the plant, together with the mechanical and thermophysical properties of the materials of which the plant is made. Thus S is proportional to the current density, i.e. inversely proportional to the diameter of the tube; and the permissible rate of withdrawal, which is still insufficient to cause serious disturbance of the steady state, is directly proportional to the diameter of the separating tube. In the separation of lithium isotopes in the molten chloride with $S = 3-4$ and a very small withdrawal the optimum tube diameter has been estimated[184] as 10–15 mm; but with considerable withdrawal (several grams of lithium chloride per day) and $S = 2$, the diameter must be increased to 30 mm.

From Eqn. (24) and the requirement of minimum energy consumption Klemm[167] found that the optimum conditions for the concentration of ^{7}Li from 92.7% to 99.974% ($S = 310$) were a separating tube 22.8 cm long with the product removed at a rate of 2.8 cm day^{-1}. The electrical energy consumed was 11 kW h per gram of lithium enriched with ^{7}Li. The energy consumption for the concentration of ^{6}Li from 7.3% to 90% was[172] 60 kW h g^{-1}. Neubert and Klemm[208] calculated the energy consumption and the cost for calcium chloride enriched with the ^{48}Ca isotope: a single value of the separation factor, which must be achieved by electrical migration in order that the total cost of the product should be a minimum, corresponds to each value of the sum of overhead expenses in preliminary enrichment with ^{46}Ca by electrical migration followed by complete enrichment on an electromagnetic separator. In the equipment of Ménès et al.[211] 25 kW h of electrical energy was consumed per gram of calcium in which the initial content of ^{46}Ca had been doubled. Westhaver[66] estimated energy consumptions in the separation of potassium isotopes in aqueous solution: enrichment with ^{41}K from 14.2% to 21.3% in a tube 4.6 cm long requires 14 kW h g^{-1} potassium.

Equation (37) shows that the chief parameter of an actual tube as a separating device[74] is the ratio D'/v, so that its diminution is one of the most important engineering problems. Experience of the operation of large-scale installations[20,167,184,192] shows that under optimum conditions D' does not exceed D more than 3–4 fold: i.e. it is of the order of 10^{-4} cm^2 s^{-1}. Since the mobility of ions in a molten salt is $\sim 10^{-4}$ cm^2 V^{-1} s^{-1}, the quantity h is around 2–3 mm with a field of 3–5 V cm^{-1} in the tube: i.e. the dimensions of separating devices of this kind can be considerably smaller than in other methods for the separation of isotopes.

IV. APPLICATION OF ELECTRICAL MIGRATION TO THE STUDY OF THE STRUCTURE AND TRANSPORT PROPERTIES OF MOLTEN SALTS

1. Measurement of Ionic Mobilities by Countercurrent Electrical Migration

A cell with a separating tube can be used not only for applied purposes—for the separation of isotopes—but also as a scientific research tool. A large proportion of the experiments reflected in Table 1 were undertaken with the aim of measuring the relative difference in mobility between isotopic ions, a quantity which is necessary for theoretical conclusions and generalisations with respect to both the structure of the medium in which the ions move, in particular molten salts, and the mechanism of the actual movement of the ions.

Table 1 shows that the mass effect has a tendency to decrease with increase in the atomic weight of the separable element, which can be expressed by the empirical formula[290]

$$\mu_+ = \mu' \left(1 + \frac{m_+}{M}\right)^{-1} \qquad (38)$$

where μ' is a constant, $M = km_-$, and m_+ and m_- are the masses of the cations and anions forming the salt. Klemm[279,208], having published a summary of measurements of μ_+ for seventeen metal halides in the molten state, noted an interesting regularity: the mass effects of isotopic cations of salts having a layer lattice in the solid state conformed closely to the curve described by Eqn. (38) with $\mu' = -0.15$ and $k = 2.1$; but for cations of salts not having a layer lattice the appropriate values were -0.079 and 2.1 respectively. Both curves are shown in Fig. 4, from which it is evident that all halides have values of μ_+ grouped about these curves. Attempts to select other values of μ' and k had only partial success[8,200,227].

Klemm's suggestion[208]—that if the above rule is valid magnesium and cadmium bromides, the corresponding iodides, and the iodides of calcium, zinc, and lead, which have a laminar structure in the solid state, should when molten have values of μ_+ close to curve A, while those of strontium and barium bromides should be close to curve B—has since been verified for CaI_2, CdI_2, PbI_2,[214] and $CdBr_2$,[218] and also for $SnCl_2$,[223] $SnBr_2$,[223] and SnI_2.[224] The results made a more careful formulation of the rule necessary[214], the two types of salts being delimited by an empirical curve (the broken curve C in Fig. 4), for which an analytical expression was not found.

Experimental values of μ_+ for alkali-metal and thallium nitrates are also plotted in Fig. 4. Lundén and Ekhed[196] found that the variation in μ_+ for the alkali-metal nitrates is best represented by the equation

$$-\mu_+ = 0.0848\,(1 + m_+/46)^{-1}, \qquad (39)$$

provided that values of μ_+ are taken at temperatures 5% above the absolute melting points of the corresponding nitrates. It is evident that μ_+ for thallium(I) nitrate does not obey the rule. It is noteworthy that values of μ_+ for solid lithium sulphate and lithium hydride fit well on curve A.

Attempts to find a similar relation for isotopic anions were undertaken[229,235] in the absence of sufficient experimental results. Similar series of salts in the order of diminishing μ_-—RbCl > TlCl > KCl > $PbCl_2$ > $CdCl_2$ > > $ZnCl_2$ and RbBr > $PbBr_2$ > $ZnBr_2$—can be distinguished from the results in Table 1. If this type of relation does

exist for anions, it is obviously more complicated. In any case, the rule formulated by Herzog and Klemm[231]—that the isotope effect in ionic mobilities is larger the greater the number of the heaviest possible gegenions surrounding the separable isotopic ions in the melt—is well satisfied for cations, and with large exceptions for anions.

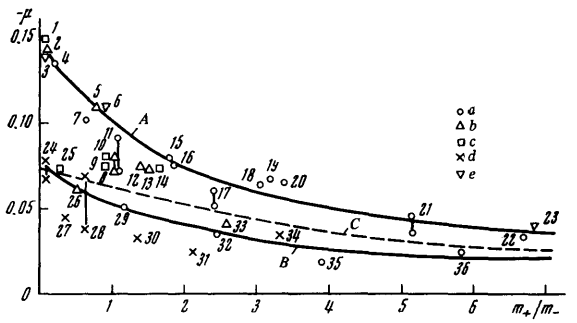

Figure 4. Graphical expression of Klemm's "halide rule"[279,208], where the curves represent: *A*) $\mu = 0.15(1 + m_+/2.1m_-)^{-1}$; *B*) $\mu = 0.079(1 + m_+/2.1m_-)^{-1}$; *C*) boundary between salts having layer and coordinated lattices in the solid state. The experimental points correspond to: *a*) molten chlorides; *b*) molten bromides; *c*) molten iodides; *d*) molten nitrates; *e*) solid salts: 1) LiI; 2) LiBr; 3) Li_2SO_4; 4) LiCl; 5) $ZnBr_2$; 6) α-AgI; 7) $MgCl_2$; 8) RbBr; 9) CdI_2; 10) SnI_2; 11) KCl; 12) $CdBr_2$; 13) $SnBr_2$; 14) PbI_2; 15) CuCl; 16) $ZnCl_2$; 17) RbCl; 18) AgCl; 19) $CdCl_2$; 20) $SnCl_2$; 21) TlCl; 22) UCl_4; 23) LiH; 24) $LiNO_3$; 25) CaI_2; 26) $CaBr_2$; 27) $NaNO_3$; 28) KNO_3; 29) $CaCl_2$; 30) $RbNO_3$; 31) $CsNO_3$; 32) $SrCl_2$; 33) $PbBr_2$; 34) $TlNO_3$; 35) $BaCl_2$; 36) $PbCl_2$.

Correlations of μ_+ with ionic radii are clearer than with ionic masses. For nitrates Okada and Saito[192,222] suggested a linear relation between μ_+ and r_+, but the empirical formula

$$-\mu_+ = 1/(20.9r_+ - 2.4) \qquad (40)$$

derived by Lundén and Ekhed[196] is a far better description of such correlation, which applies also to thallium(I) nitrate. With nitrates this formula (40) is satisfied better than (39)[196], and a still better correlation

$$-\mu_+ = 1/(9.91 + 1.51V_+) \qquad (41)$$

exists between μ_+ and the volume V_+ of the cation: thus the deviation in experimental values of μ_+ for the lithium isotopes from those calculated by means of Eqns. (39)–(41) is respectively 53%, 1%, and 0.4%. For halides Klemm[279] found that μ_+ is correlated more closely with r_+/r_- than with m_+/m_-.

The temperature variation of the mass effect has been studied for several salts. A linear relation is obtained in all cases, expressed by empirical formulae of the type

$$-\mu = a[1 + b(t - t_0)] \qquad (42)$$

where a and b are constant coefficients and t_0 (°C) is a fixed temperature. Table 2 gives values of these three parameters together with the temperature range for which formulae (42) have been derived. The mass effect is seen to decrease with temperature for thallium and chlorine isotopes in thallium(I) chloride and for tin and lead isotopes in tin(II) and lead(II) chlorides respectively; it is almost independent of temperature for lithium isotopes in solid lithium sulphate, chlorine isotopes in rubidium chloride, and bromine isotopes in the bromide; and in the remaining cases it increases with temperature. There are several discrepancies in the results of different workers: for example, μ_+ for lithium isotopes in the nitrate has been found to increase[196] and to decrease[14,172] with temperature (in Ref. 14 the coefficients in Eqn. (42) were not calculated). Lundén and Ekhed[196] suggested several reasons for such discrepancies, but also emphasised the strong influence of difficulty controllable parameters on experiments, which diminished reliability of the results.

Table 2. Values of the constant a, b, and t_0 in Eqn. (42). Elements for whose isotopes this relation has been found are indicated by **bold type** in the formulae of the salts.

No.	Molten salt	a	b	t_0	Temp. range, °C	Ref.
1	**Li**Cl	0.111	+0.00237	610	670—900	195
2	**Li**NO_3	0.0718± ±0.0007	−0.00067± ±0.00024	360	265—460	192
3	**Li**NO_3	0.0860± ±0.0012	+0.00023 ±0.00024	375	313—488	196
4	^{6}LiCl—^{7}LiCl*	0.335	+0.000412	610	620—780	195, 291
5	^{6}LiNO_3—^{7}LiNO_3*	0.167	+0.000976	254	280—440	195
6	Li_2SO_4	0.139± ±0.009	−0.0003± ±0.0006	600	600—790	236—238
7	Li_2SO_4—K_2SO_4**	0.129	+0.000735	625	625—835	193
8	KNO_3	0.0385± ±0.0012	+0.00324± ±0.00039	337	354—586	201
9	KCl	0.071	+0.0013	820	820—1020	200
10	KCl	0.062	−0.0001	820	820—980	200
11	RbCl	0.048	+0.0012	750	750—980	200
12	RbCl	0.109	+0.0013	790	790—960	200
13	RbBr	0.072	+0.0003	740	740—950	200
14	RbBr	0.115	+0.0001	800	800—970	200
15	TlCl	0.045	−0.001	470	470—680	221
16	TlCl	0.077	−0.00192	565	565—730	231
17	$SnCl_2$	0.069	−0.0003	340	340—590	223
18	$PbCl_2$***	0.024	−0.033	530	530—640	226

*Calculated by authors from measurements of ratio of electrical conductivities for isotopically pure lithium salts.
**Calculated by Reviewer from results of Expts. 96–98 and 100 in Table 1.
***Calculated by Reviewer from results of Expts. 228 and 229 in Table 1.

Mass effects for the isotopes of five elements (shown in **bold type**) have been measured in the molten salt mixture **Li**Cl–KCl,[159] **Li**Br–NaBr and **Li**Br–KBr,[20,178,180,182,183,186,197] Li_2SO_4–K_2SO_4,[193,194] **Li**NO_3–Li_2SO_4,[192] **Li**Cl–$PbCl_2$,[165] $SnCl_2$–$PbCl_2$,[225] $CdBr_2$–Cd,[218] and $CdCl_2$–Cd.[232] In most cases measurements were made in a narrow range of compositions, which is probably why no clear dependence of μ on the chemical composition of the melt could be detected. The work of Chemla et al. showed that variation in the content of lithium and potassium bromides in the separating tube during electrical migration had no apparent effect on the separation of lithium and potassium isotopes. On the other hand, Klemm and Monse[165] studied the composition variation of μ in the **Li**Cl–$PbCl_2$ system, and showed that the mass effect of lithium isotopes remains almost unchanged over the range 100–25 mole % of lithium chloride, but increases sharply at lower contents of this

salt (Table 1, Expts. 4–9), and $-\mu_+ = 0.296$ at 5.3 mole % LiCl. This rule is fully consistent with the value $-\mu_+ = 0.32$ for potassium isotopes in a mixture of 2 mole % of the chloride with lithium chloride[159] (Expt. 109). The abnormally high value of $-\mu_+ = 0.261$ obtained by Lundén[164] for lithium isotopes in the bromide (Expt. 19) is explained by considerable contamination of the lithium bromide melt with other salts, as has been established by control experiments[173,174] (Expts. 20–25). This relation is probably widespread: Klemm[216] showed that the mass effects in the diffusion of hydrogen in solid palladium, of lithium in molten lead, and of copper in solid silver sulphide are respectively −0.45, −0.47, and −0.44, of the order of ten times the values of μ for these cations in molten salts. A common feature of all these processes is the dilute state of the separable species. Nevertheless, over the range 10–80 mole % of tin(II) chloride in lead(II) chloride the tin isotopes have[225] $-\mu_+ = 0.012$ (Expts. 224–226), which is one-fifth of the mass effect in pure tin(II) chloride.

Klemm and Monse[165] proposed a method for measuring the absolute difference in mobility between the isotopic lithium ions in the $LiCl-PbCl_2$ system. The formula used for the calculations was

$$\Delta^{lk}w = -\frac{\varkappa}{Q}\left(\frac{{}^{l}N}{{}^{l}c} - \frac{{}^{k}N}{{}^{k}c}\right) = -\frac{\varkappa x' A}{Q}\left(\frac{{}^{l}\gamma}{{}^{l}\gamma_0} - \frac{{}^{k}\gamma}{{}^{k}\gamma_0}\right) \qquad (43)$$

where $\varkappa$ is the electrical conductivity, ${}^{j}c$ and ${}^{k}c$ are the molar concentrations of the components in the initial molten salt, and ${}^{j}N$ and ${}^{k}N$ are the numbers of moles of the components in the enrichment zone x' after the passage of Q coulombs of electricity through it, the remaining symbols having the same significance as in Eqn. (31). Variation in the mole fraction of lithium chloride from 1.0 to 0.053 is accompanied by an increase in $\Delta^{67}w$ from 3.93×10^{-5} to 7.10×10^{-5} $cm^2\ V^{-1}\ s^{-1}$.

Countercurrent electrical migration has proved extremely fruitful in studies of the transport properties not only of isotopic ions but also of ions of different elements in mixtures of molten salts. It has been used to measure the relative mobilities of Li^+ and Pb^{2+} in $LiCl-PbCl_2$;[165] Li^+, Na^+, and K^+ in various mixtures of their bromides[20,23,178,180] and nitrates[23,188,190,292,293]; Na^+, K^+, and Rb^+ in mixtures of their nitrates[294]; Li^+ and K^+ in $Li_2SO_4-K_2SO_4$;[193] Li^+, K^+, and Ag^+ in $LiNO_3-KNO_3-AgNO_3$;[294] Li^+ and Ca^{2+} in $LiNO_3-Ca(NO_3)_2$;[294] Li^+ and Ag^+ in $Li_2SO_4-Ag_2SO_4$;[193] Ca^{2+}, Sr^{2+}, and Ba^{2+} in mixtures of their bromides[211,295]; Li^+, K^+, and Ca^{2+} in mixtures of their bromides[211]; Sn^{2+} and Pb^{2+} in $SnCl_2-PbCl_2$;[225] Cl^- and NO_3^- in $AgCl-AgNO_3$;[296] NO_3^- in $LiNO_3-KNO_3$;[297] Cd dissolved in $CdCl_2$[232] and in $CdBr_2$;[218] and also Pb dissolved in $PbCl_2$.[298] The technique of measuring transport numbers of ions in individual melts was developed by Fischer and Klemm[299], and their temperature dependence in thallium(I) chloride and zinc chloride was measured. A general phenomenological theory of the measurement of transport in molten salts by this method was put forward by Klemm[300].

2. Measurement of Ionic Mobilities by the Electrical Migration of a Zone

The electrical migration of ions can be investigated also without production of a countercurrent of electrolyte, by the use of the classic principle of paper electrophoresis[301]. Fig. 5 illustrates the experimental arrangement[14] for molten salts: inside a tubular electric furnace *1* is fixed, in an exactly horizontal position, an asbestos strip *2* (typical dimensions 600 × 12 × 0.3 mm), the ends of which dip into small baths *3* and *4* containing melts of the same salt together with conducting electrodes *5* and *6*. The asbestos strip has previously been washed in acids, ignited, and impregnated with the molten salt solvent.

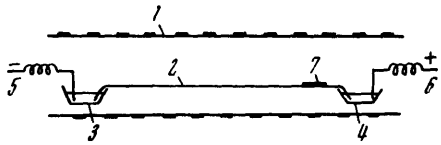

Figure 5. Experimental arrangement for studying electrical zone migration[14].

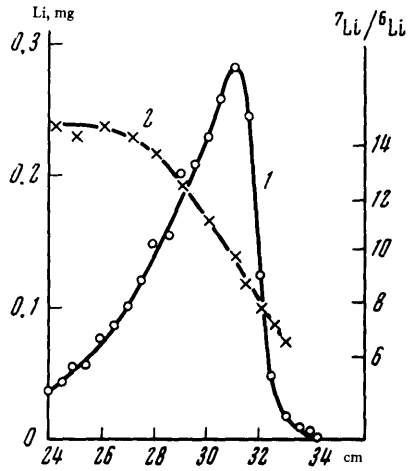

Figure 6. Distribution along migration path of zone after completion of experiment[12] for: 1) concentration of lithium; 2) isotope ratio $^7Li/^6Li$.

The method of investigation consists in applying to one end of the asbestos strip a few milligrams of the salt containing the isotopes, and passing through the system a constant current, under whose influence the initial spot (zone) of the salt *7* moves along the strip. If the zone contains radioactive isotopes, its movement can be followed conveniently by means of a counter. Owing to the difference between the mobilities of isotopic ions, their concentrations within the zone undergo redistribution in the direction of migration: the more mobile light isotopes accumulate at the forward edge of the zone, and the slower heavy isotopes at the rear. The experiment is continued for 2–4 h, after which the asbestos strip with the solidified salts is cut, in the region occupied by the zone, into transverse bands about 5 mm wide, in each of which the isotopic composition of the test element is determined, and if necessary a chemical analysis of the salt mixture is made. Typical results for the electrical migration of a zone in molten salts are illustrated in Fig. 6.

The phenomenological theory of electrical zone migration is simpler than that of countercurrent migration.

Chemla[10,13] showed that movement of the zone in the direction of the electrical field and extension of its boundaries by diffusion can be regarded to a first approximation as mutually independent processes. Substitution of variables $y = x - t\Delta v$ in Eqn. (7) then leads to the equation of Fick's law

$$\frac{\partial \gamma}{\partial t} = D\frac{\partial^2 \gamma}{\partial y^2}, \qquad (44)$$

in which the coefficient of molecular diffusion D (not the coefficient of mixing D') is used. In fact diffusion and electrical migration are not independent processes: Arnikar[48,49,302] showed that the final distribution of the components in electrical zone migration is not identical with their distribution in pure diffusion. The difference between the actual distribution curve for lithium isotopes along the zone and the symmetrical Gaussian curve is readily seen from Fig. 6. In order to calculate the relative difference between the mobilities of the isotopic ions we construct concentration distribution curves for each isotope along the zone, using curves *1* and *2* in Fig. 6. The curves obtained for the distribution of the isotopes are similar to curve *1* for the distribution of the element, but their maxima are displaced a distance $\Delta x'$, and it is easy to show that

$$\frac{\Delta w}{w} = \frac{\Delta x'}{x'} \qquad (45)$$

where x' is the distance traversed by the whole zone. This formula has been discussed critically[14,303]. Experimental conditions and measurements of the mobilities of isotopic ions by electrical zone migration in molten salts are collected together in Table 3, which includes for comparison some data on aqueous solutions with various kinds of paper as support.

Like countercurrent migration, zone migration is widely used to measure the electrical transport parameters of ions in molten salts. Besides asbestos, glass-fibre cloth and plates of sintered alumina powder are employed as substrates. This method has been used to measure the mobilities and the transport numbers of ions of alkali metals, silver, and thallium in pure alkali-metal nitrates[11,12,243,303-312] and in their mixtures[313-315], alkaline-earth metal ions in alkali-metal nitrates[11,12,303,313,314,316] and their mixtures with alkaline-earth metal nitrates[317,318], ions of multivalent metals—copper, zinc, cadmium, cobalt, chromium, cerium, lead, and thorium—in alkali-metal nitrates[313,314,319], in potassium thiocyanate[319], and in LiCl–KCl eutectic[313,320], and chloride, bromide, and nitrate anions in alkali-metal nitrates[11,12,243,303,306,315]. Radioactive isotopes have been widely used in these investigations as tracers in following the movement of the zone along the migration path.

3. Comparison of the Two Methods of Electrical Migration —Frame of Reference

Comparison of Tables 1 and 3 shows fairly close agreement between values of the mass effect determined by electrical zone and countercurrent migration for isotopes in the same salt. Lundén[321] made a detailed comparison of results obtained by the two methods for molten nitrates. Nevertheless, Table 3 shows that the mass effect varies in complicated fashion with the mass of the element, with the composition of the solvent medium impregnating the asbestos support, and also with the temperature. The effects of all these factors on the mobility of isotopic ions are closely interrelated, so that all the experimental results accumulated up to the present time (Tables 1–3) must be taken into account in order to establish general rules. Attempts at the interpretation of experimental results in the light of individual measurements (often only the interpreter's own) are considered below.

Table 3. Experimental conditions of and results obtained by electrical zone migration.

No.	Working salt	Solvent medium*	Potential gradient, V cm^{-1}	Path of zone, cm	Temp., °C	α	$-\mu$	Ref.
1	$LiNO_3$	$NaNO_3$+KNO_3	10	26.0	250	1.0137	0.089	14
2	ditto	ditto	10	23.4	300	1.0102	0.067	14
3	»	»	6	21.0	350	1.0090	0.0585	14
4	»	»	10	31	350	1.014	0.091	11, 12
5	»	»	16	20	300	1.03	0.19	240
6	$LiNO_3$	10% soln. NH_4NO_3	1.5	—	room.[4]	1.0036	0.023	10, 13, 45
7	ditto	ditto	4	56	room.[4]	1.0038	0.024	139
8	$NaNO_3$	$NaNO_3$+KNO_3	14	35	300	1.010	0.10	12, 241
9	ditto	$LiNO_3$	10	30	305	1.0040	0.046	243
10	»	ditto	10	30	355	1.0058	0.067	243
11	»	$NaNO_3$	10	30	358	1.0070	0.080	243
12	»	KNO_3	10	30	358	1.0088	0.101	243
13	»	$CsNO_3$	10	30	435	1.0057	0.0655	243
14	»	$NaNO_3$+KNO_3**	10	30	355	1.0071	0.0815	243
15	»	$NaNO_3$+KNO_3***	10	30	355	1.0080	0.092	243
16	»	$NaNO_3$+KNO_3	10	30	255	1.0053	0.061	243
17	$NaNO_3$	$NaNO_3$+KNO_3	10	30	304	1.0060	0.069	243
18	ditto	ditto	10	30	340	1.0076	0.086	243
19	»	»	10	30	374	1.0090	0.104	243
20	»	»	10	30	404	1.0076	0.086	243
21	»	»	10	30	434	1.0073	0.084	243
22	$NaNO_3$	0.04% soln. NaCl	12.5	—	room.[4]	1.003	0.035	138
23	ditto	soln. $NaNO_3$	17.5	—	1	1.0029	0.038	140
24	»	ditto	17.5	—	26	1.0048	0.055	140
25	»	»	17.5	—	38	1.0065	0.075	140
26	»	»	17.5	—	49	1.0083	0.095	140
27	KNO_3	$NaNO_3$+KNO_3	10	40	350	1.00274	0.0548	14
28	$RbNO_3$	$NaNO_3$	9.1	42	350	1.00158	0.0691	10, 12, 14, 242
29	$RbNO_3$	soln. $NaNO_3$	17.5	—	3	1.0011	0.047	141
30	ditto	ditto	17.5	—	28.5	1.0014	0.060	141
31	»	»	17.5	—	48	1.0017	0.073	141
32	$CsNO_3$	$NaNO_3$+KNO_3	10	41	350	1.0027	0.060	13, 14
33	ditto	$NaNO_3$	10	40	350	1.0036	0.080	10
34	»	soln. $NaNO_3$	—	40	35	1.0097	—	12

*The $NaNO_3$ + KNO_3 mixture always contains 45 wt.% $NaNO_3$.
**The mixture contains 75 wt.% $NaNO_3$.
***The mixture contains 25 wt.% $NaNO_3$.

In the comparison of mass effects obtained by different methods and the assessment of their reliability, it must be borne in mind that any determination of a velocity presupposes agreement on the frame of reference: in the present case this is an object, selected inside or outside the electrolyte, relative to which the speed of the ion is measured. A "convenient"[295] system is one in which the separation factor α is independent of the electric field strength in the electrolyte. Different frames of reference are chosen[279] depending on the medium in which the ions migrate: in solids the surface or the stationary crystal lattice is selected, in solutions the solvent, in molten salts the centre of gravity of the oppositely charged ions, and in liquid metals the flux of conduction electrons. In pure molten salts the choice is a fundamental question, involving controversy about the advisability of applying the concept of transport number to such salts[18,300,322-324]. If the gegenions are chosen as reference, the transport number of the test ions is unity: i.e. they alone are regarded as current carriers and move within the melt, while the gegenions are at rest (this gives rise to the concept of a quasi-crystalline lattice in molten salts).

Physically, however, it is also possible that both cations and anions may move relative to the walls of the vessel, which may also be chosen as stationary frame of reference: in such case both types of ions have fractional transport numbers. The possibility of displacement of the melt as a whole relative to the walls makes incorrect measurement of these quantities highly probable. The use of a porous diaphragm—packing in the separating tube or an asbestos support—tends to diminish the probability of such displacement, in the ideal case to zero (Eqn. 3).

Measurement of transport numbers and ionic mobilities relative to these two frames of reference—gegenions inside the molten salt and a porous diaphragm outside the salt—yields different values for these quantities, which Klemm [19,300] proposed calling "internal" and "external" respectively. Formula (29), which is a definition of the mass effect, shows that the choice of frame of reference affects only the one quantity

$$w = \frac{\sum_i {}^i w {}^i\gamma}{\sum_i {}^i\gamma} \qquad (46)$$

the mean mobility of the isotopic ions to be separated. According to this the internal mobilities of ions should exceed in absolute magnitude the external values, and therefore the internal mass effects, measured by counter-current electrical migration, should be smaller than the external mass effects, measured by electrical zone migration under identical conditions. Comparison of the values of μ for alkali-metal nitrates in Tables 1 and 3 shows general conformity to this principle.

4. Structure of Molten Salts and Mechanism of Ionic Migration

Among the numerous theoretical papers on the inner structure of molten salts and the mechanism of the movement of ions in them under the influence of an electric field, we shall consider only those relating to the problem of the mobility of isotopic ions and their separation. The reasons for the occurrence of an isotope effect in electrical migration have not been established unambiguously. Investigators usually choose the most soundly based (in their opinion) model for the structure of a molten salt and for intermolecular interaction, and compare with experimental results the macro-values calculated on the basis of this micro-model.

To explain the differences in the mobilities of isotopic ions in molten salts we suppose that the element can exist in several states (as free ions, ion-pairs, etc.). The mole fraction of the element in state l is $\Gamma_l = C_l/C$, where C is the molar concentration of the element in the melt, C_l is the concentration of a species in state l, and $\sum_l \Gamma_l = 1$. The mole fraction of the ith isotope in this state is ${}^i\gamma_l = {}^iC_l/C_l$, and $\sum_i {}^i\gamma_l = 1$. The mobility of the ith isotope in the electric field is

$${}^i w = \frac{\sum_l \Gamma_l {}^i\gamma_l {}^i w_l}{\sum_l \Gamma_l {}^i\gamma_l}. \qquad (47)$$

If the equilibrium constant for the exchange of isotopes j and k between states l and m

$${}^{jk}K_{lm} = \frac{{}^i\gamma_l {}^k\gamma_m}{{}^i\gamma_m {}^k\gamma_l} \qquad (48)$$

differs from unity, the difference between the mobilities of the two isotopes in the electric field is [325]

$$\Delta^{jk} w = {}^j w - {}^k w = \sum_l \Gamma_l \left[{}^j w_l - {}^k w_l + \left(w_l - \sum_r \Gamma_r w_r \right) ({}^{jk}K_{lm} - 1) \right]. \qquad (49)$$

Since the mobility of the element as a whole is composed of the mobilities of its species in different states $w = \sum_r \Gamma_r w_r$, it follows from formulae (29) and (49) that [290]

$$\mu \frac{\Delta_m}{m} = \frac{\Delta w}{w} = \sum_l \Gamma_l \frac{\Delta w_l}{w} + \sum_l \Gamma_l \left(\frac{w_l}{w} - 1 \right) ({}^{jk}K_{lm} - 1). \qquad (50)$$

Numerical estimates showed Klemm [215,231,290] that the effect of the isotope exchange equilibrium between different states is not significant in molten salts: i.e. the second summation in Eqn. (50) could be neglected. However, the precisely opposite view is also held [243]: isotopic exchange actually makes the chief contribution to $\Delta w/w$, and the first summation in formula (50) is negligible in comparison with the second.

If the "self-transport number" T is defined as the ratio of external u to internal w ionic mobilities of the element [19]

$$T = \frac{u}{w}, \qquad (51)$$

we can rewrite Eqn. (50), on the assumption that the second summation is close to zero, in the form

$$\mu = T \sum_l \frac{\gamma_l u_l}{\gamma u} \cdot \frac{\Delta u_l}{u_l} \cdot \frac{m}{\Delta m}, \qquad (52)$$

since $\Delta u_1 = \Delta w_1$. Only two states of the species—mobile and stationary—need be distinguished in ionic liquids [261,262]. In terms of the theory of rate processes, activated ions—i.e. those occupying interstitial sites, sites adjacent to holes, etc. in the quasi-crystalline lattice—can be regarded as mobile [167]. Thus mobile ions migrate through the quasi-crystalline lattice formed by the stationary species, by making spontaneous jumps between adjacent equilibrium positions with an average frequency z_S (s^{-1}). [216] This is proportional to the thermal vibration frequency ν of the ions, which is in turn proportional to $m'^{-1/2}$, where $m' = mM/(m+M)$, in which m is the mass of the ion making a jump and M is the total mass, arbitrarily concentrated at a point and vibrating together with the ion, of particles which surround this ion immediately before the jump [290]. Since the summation in Eqn. (52) is made only over the mobile states $l = b$, it follows that

$$\Delta u_l/u_l = \Delta u_b/u_b = \Delta\nu/\nu = -\tfrac{1}{2}\Delta m'/m',$$

and formula (52) becomes

$$\mu = -\frac{1}{2} T \frac{\Delta m'}{m'} \cdot \frac{m}{\Delta m} \sum_b \frac{\gamma_b u_b}{\gamma u}. \qquad (53)$$

The mean rate of migration u_b of mobile ions is proportional to their total number of jumps per second: $z = z_S + z_i$, where z_i is the frequency of jumps induced by processes in the immediate environment of the ion, e.g. by jumps by adjacent ions. Therefore

$$\sum_b \frac{\gamma_b u_b}{\gamma u} = \frac{\gamma_s u_s + \gamma_i u_i}{\gamma u} = \frac{z_s + z_i}{z}.$$

If we bear in mind that the frequency of induced jumps is independent of the mass of the isotopic ions and, passing from finite differences Δm and $\Delta m'$ to infinitesimals dm and dm', differentiate Eqn. (53), we obtain

$$\mu = -\frac{1}{2} T \frac{z_s}{z} \left(1 + \frac{m}{M} \right)^{-1}. \qquad (54)$$

Thus a theoretical basis has been found for formula (38), and the constant it contains μ' is interpreted as $-\frac{1}{2}Tz_S/z$.

It is also useful to introduce the concept of the intrinsic mobility w_0 of an isotopic ion—its mobility in the isotopically pure compound—when the molten salt contains only this isotope of the given element. Since $w = \Lambda/F$, where Λ is the equivalent conductance of the molten salt and F is Faraday's constant, the ratio of the intrinsic mobilities of two isotopic ions is equal to the ratio of the equivalent conductances of the isotopically pure molten salts, and since the difference between the molar volumes of such salts can be neglected[195], this ratio is equal to the ratio of their conductivities κ, which can be found experimentally. Values of this parameter have now been determined for the systems $^6LiCl-^7LiCl$,[195,291] $^6LiNO_3-^7LiNO_3$,[195] and $^6Li_2SO_4-^7Li_2SO_4$.[326]

In the absence of any interaction between the moving ions the mass effect attains the limiting value[279] of $\mu = -0.5$. But in an actual substance this interaction cannot be neglected. Even in an ionic gas, which may be so degenerate that only two-body collisions need be considered, and the effect of the charges of surrounding ions, i.e. the ionic atmosphere, can be neglected, the intrinsic mobility of the ions depends on the reduced mass of the component cations and anions of this gas[25,200]:

$$w_0 = A\left(\frac{m_+ \cdot m_-}{m_+ + m_-}\right)^{-1/2}, \qquad (55)$$

where A is a factor which is independent of the masses. The intrinsic mass effect then becomes

$$\mu_0 = \frac{\Delta w_0}{w_0} \Big/ \frac{\Delta m}{m} \approx \frac{\partial \ln w_0}{\partial \ln m} = -\frac{1}{2}\left(1 + \frac{m_+}{m_-}\right)^{-1}. \qquad (56)$$

Calculation by means of Eqn. (56) of μ_0 for lithium chloride, nitrate, and sulphate yields respectively −0.42, −0.45, and −0.47, whereas the corresponding values measured in the molten salt are −0.35, −0.18, and −0.28.[195,326] This indicates that the mass of the anions has a stronger effect on the intrinsic mobility of the cations in molten salts than in an ionic gas. The ratio $n = \mu_0/\mu$ is interpreted[195,326,327] as the mean number of cations involved in the elementary step of electrical migration by being bound into a single group. For the above lithium salts it has the values 2.39, 2.56, and 2.0. Whether these numbers can be linked with the number of spontaneous and induced jumps by ions and in what way is still being examined more closely; in any case these results reflect the fact that the ions in molten salts cannot move independently of each other.

Ionic conductivity, migration, and diffusion data do not yet enable us to suggest a more detailed model for the structure of molten salts. Thus Klemm[300] showed, when considering the phenomenology of the transport of ions in pure molten salts, that it was impossible to choose the best among models presupposing that a molten salt consists of two components (cations and anions), three components (cations, anions, and a quasi-crystalline lattice), or four components (cations, anions, lattice, and neutral complexes). Lundén[328] found that parameters calculated specially for molten alkali-metal nitrates on a basis of all three models agreed qualitatively with the experimental results. Attempts to apply similar models to solutions of cadmium in cadmium chloride[232] and of lead in lead(II) chloride[298] also showed the impossibility of selecting one of them unambiguously on the basis solely of data on the transport properties of the molten salts.

The theoretical concepts used to explain the temperature dependence of the mass effect have been modified and refined as experimental data have accumulated[25,167,200,231,279,303]. A model was suggested[25] taking into account the most recent measurements of the mass effect at different temperatures. With rise in temperature the structure of an ionic melt passes successively through three different stages (Fig. 7): a quasi-crystalline structure—a lattice with a few free ions within—predominates at low temperatures (stage I); then the lattice breaks down into electrically charged polyionic groups (stage II); and at very high temperatures the melt consists mainly of neutral ion-pairs with a small proportion of free ions (stage III). The situation is less favourable for a large mass effect in the second stage than in stages (I) and (III), in which a larger number of mobile groups of ions are present. Experimental results show larger mass effects in solid than in molten salts, and the above estimates indicate that they should also be larger in an ionic gas than in a melt. Thus on passing from a solid through the melt to the gas the mass effect has a tendency to pass through a minimum (the smooth variation in the function may be disturbed abruptly at the melting point and the boiling point[200]).

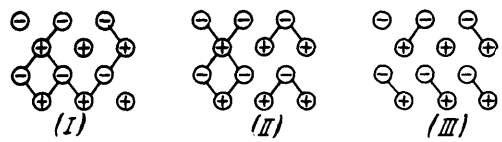

Figure 7. Model of change in structure of molten salt with rise in temperature[25].

From a comparison of this model with Table 2 it may be supposed that, for example, molten thallium(I) and lead(II) chlorides are located somewhere between stages (I) and (II), and molten alkali-metal halides somewhere between stages (II) and (III). The contribution of quantum-mechanical effects to isotopic differences in the mobilities of light elements such as lithium can be neglected at high temperatures[195,200], but in lithium nitrate electrical migration takes place at relatively low temperatures, and these effects may be appreciable: hence the difference between the temperature dependence of μ_+ for this salt and for other alkali-metal salts. The variation of the mass effect for sodium isotopes in the $NaNO_3-KNO_3$ eutectic (Expts. 16–21, Table 3), which is "unusual" in terms of this model, is explained[243] by the predominant effect at low temperatures of the proportion of combined displacements of ions, which increases with temperature, and by the predominant effect at high temperatures of the isotopic exchange constant (48) between ions and neutral complexes, which decreases with temperature. On the whole these views evidently do not contradict a three-stage model, and the above categorical statements on the relative contributions of the first and second summations in Eqn. (50) to the mass effect are refined. The most correct hypothesis is apparently that the separation of isotopes in the electrical migration of ions takes place by several parallel mechanisms[279], whose relative contributions to the overall effect varies with temperature.

APPENDIX

Since this paper was submitted for publication a monograph [329] and several papers have appeared on the electrical migration of ions in molten salts [330-339], aqueous solutions [340], and solid salts [341].

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Thermogalvanic Cells with a Single Fused Salt

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This paper reviews the theory of thermogalvanic cells with metal or halogen electrodes and a single fused salt, and analyses the results of experimental studies of thermogalvanic cells (including those obtained in the author's laboratory). Some examples of the application of thermopotentials in studies of the physical chemistry of fused salts are discussed. 47 references.

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1. INTRODUCTION

Two identical reversible electrodes held at different temperatures and connected by a fused electrolyte containing the potential-determining ions will generate a thermo-e.m.f whose magnitude depends first and foremost on the temperature difference and on the nature of the element. A thermogalvanic element of this type is usually characterised by the temperature coefficient of its thermo-e.m.f., for which we shall use the term "thermopotential". Equivalent terms often used in the literature include "thermo-electric power" and "Seebeck coefficient". When a cell of this type is short-circuited, current flows in a direction such that the electrode reaction at the hotter electrode is continuously absorbing heat, and vice-versa. Hence, the only driving force for the generation of electrical energy is the transfer of heat from the hotter to the cooler region.

The study of thermoelectric phenomena in fused salts includes a wide range of problems of great theoretical and practical importance. During the past decades, a great deal of work has been done on non-isothermal fused electrolyte systems because of the possibility of finding useful applications in the field of thermo-electricity and also in order to increase our understanding of the transfer of heat and electricity in ionic melts. Studies of thermogalvanic cells enable us to characterise the electrode reaction at the electrode–fused salt interface and give some insight into the structure of ionic melts. Enough experimental information on thermogalvanic cells with a single fused salt is available for a general analysis of the thermoelectric effect and its components as a function of the nature and the state of aggregation of the electrodes and the electrolyte. The thermogalvanic cells with a single fused salt which have been studied up to the present are listed in Table 1.

Table 1. Thermogalvanic cells with a single fused salt.

Thermogalvanic cell	Temp., °C	Thermopotential, mV deg^{-1}	Ref.
Graphite, Cl_2 | LiCl | Cl_2, graphite	700—1100	—0.540	1
	650—850	—0.534	2
Graphite, Cl_2 | NaCl | Cl_2, graphite	820—990	—0.45	3
	900—1300	—0.48 ÷ —0.415	1
	850	—0.483	3
Graphite, Cl_2 | KCl | Cl_2, graphite	850—1200	—0.475 ÷ —0.420	1
	800	—0.504	2
	830	—0.40	3
Graphite, Cl_2 | RbCl | Cl_2, graphite	750	—0.544	2
Graphite, Cl_2 | CsCl | Cl_2, graphite	700	—0.533	2
Cu | CuCl | Cu	462—588	—0.436	4
	450—590	—0.42	5
Cu | CuBr | Cu	620	—0.47	6
	500—700	—0.48	5
Cu | CuI | Cu	610—710	—0.510	6
	610—700	—0.53	5
Ag | AgF | Ag	435—550	—0.38	5
	500—900	—0.664	7
	500—900	—0.665	1
Graphite, Cl_2 | AgCl | Cl_2, graphite	430—680	—0.667	2
	470—645	—0.695	8
Ag | AgCl | Ag	455—650	—0.41	9
	490—590	—0.42	10
	500—900	—0.375	7
	470—570	—0.400	8
	500—625	—0.404 ÷ —0.396	11
	455—570	—0.44	5
Graphite, Br_2 | AgBr | Br_2, graphite	480—670	—0.701 ÷ 0.633	12
Ag | AgBr | Ag	450—550	—0.456	10
	450—600	—0.440	13
	450—550	—0,6	5
Ag | AgI | Ag	564—624	—0.498	10
	560—650	—0.490	6
	560—600	—0.52	5
Ag | $AgNO_3$ | Ag	230—375	—0.344	15
	210—310	—0.33	3
	239—311	—0.306	16
	215—347	—0.322 ÷ —0.331	14

Table 1 contd.

Thermogalvanic cell	Temp., °C	Thermopotential, mV deg^{-1}	Ref.
Ag | Ag_2SO_4 | Ag	657—750	—0.310	17
Graphite Cl_2 | $ZnCl_2$ | Cl_2, graphite	440—600	—0.65 ÷ —0.73	18
$Zn_{sol.}$ | $ZnCl_2$ | $Zn_{sol.(liq.)}$	347—580	+0.053 ÷ —0.035	18
$Zn_{liq.}$ | $ZnCl_2$ | $Zn_{liq.}$	450—600	+0.05 ÷ —0.03	18
	428—550	+0.032 ÷ —0.02	20
$Zn_{liq.}$ | $ZnBr_2$ | $Zn_{liq.}$	420—600	—0.05	19, 21
	428—548	—0.04	20
$Zn_{liq.}$ | ZnI_2 | $Zn_{liq.}$	439—530	—0.119 ÷ —0.094	20
Graphite Cl_2 | $CdCl_2$ | Cl_2, graphite	580—720	—0.714	22
$Cd_{liq.}$ | $CdCl_2$ | $Cd_{liq.}$	580—720	—0.146	23
$Cd_{liq.}$ | $CdBr_2$ | $Cd_{liq.}$	620—720	—0.135	23
$Cd_{liq.}$ | CdI_2 | $Cd_{liq.}$	400—600	—0.118	23
$Sn_{liq.}$ | $SnCl_2$ | $Sn_{liq.}$	263—463	—0.03 ÷ —0.04	22
	230—520	—0.014	20
$Sn_{liq.}$ | $SnBr_2$ | $Sn_{liq.}$	244—440	+0.04	20
$Sn_{liq.}$ | SnI_2 | $Sn_{liq.}$	339—455	—0.05 ÷ —0.04	20
	550	—0.587	2
Graphite Cl_2 | $PbCl_2$ | Cl_2, graphite	530—630	—0.620	24
	525—675	—0.006	3
$Pb_{liq.}$ | $PbCl_2$ | $Pb_{liq.}$	530—630	—0.008	24
	519—650	—0.013	20
$Pb_{liq.}$ | $PbBr_2$ | $Pb_{liq.}$	420—680	—0.037 ÷ —0.041	3
	421—506	—0.02	20
$Pb_{liq.}$ | PbI_2 | $Pb_{liq.}$	438—478	+0.04	20

2. MODEL OF THE THERMOGALVANIC CELL AND LOCATION OF THE THERMOPOTENTIAL

The location of the thermopotential in a thermogalvanic cell consisting of two identical, reversible solid electrodes can be described by the model shown in Fig. 1. (The two electrodes are immersed in the same fused salt, containing ions of this metal in a single state of oxidation.) If T_2 and T_1 differ by 1°, the thermo-e.m.f. measured between the electrodes is equal to the thermopotential of the cell. The thermopotential is the algebraic sum of five quantities: the potential steps (having opposite signs) at the electrode—melt interfaces at temperatures T_2 and T_1, the potential differences in the metallic conductors due to the temperature differences $(T_2 - T_0)$ and $(T_1 - T_0)$, also having opposite signs, and the potential difference due to the temperature difference within the electrolyte.

To simplify the theoretical analysis of the thermopotential, we shall assume a temperature distribution within the cell as shown in Fig. 1: each electrode will be treated as if it were in an isothermal region. Our experiments were designed to produce a temperature distribution of this type. A thermogalvanic cell consisting of two halogen electrodes on an indifferent carrier (for example, graphite) and a suitable salt can be represented by an analogous model.

In the case of a thermogalvanic cell with two liquid metal electrodes (M_I) to which contact is made with solid electronic conductors (M_{II}), a correction must be made to the measured thermopotential for the thermopotential of the couple M_I/M_{II}. The potential gradient in the liquid metal is ignored because it is much smaller than the thermopotential for a temperature difference of the order of one degree.

3. RELATION BETWEEN THE THERMOPOTENTIAL AND THE TEMPERATURE COEFFICIENT OF THE E.M.F. OF THE ISOTHERMAL CHEMICAL CELL

Reinhold[25], in his work on thermogalvanic cells with solid electrolytes, first pointed out that the measured thermopotentials can conveniently be tested against the temperature coefficient of the appropriate isothermal chemical cell. The relationship between these quantities can easily be derived analytically[8], and it also follows from the diagram of Fig. 2.

Adding all the e.m.f.'s in this circuit, and equating to zero, we obtain the following expression:

$$\left(\frac{dE}{dT}\right)_{X_2} - \left(\frac{dE}{dT}\right)_{M} = \left(\frac{dE}{dT}\right)_{chem} - \left(\frac{dE}{dT}\right)_{M-C}. \quad (1)$$

The thermopotentials $(dE/dT)_{X_2}$ and $(dE/dT)_M$ are given a sign corresponding to the polarity of the "hot" electrode, and the thermopotential of the pair M—C is given a sign corresponding to the polarity of the metal with respect to graphite. We shall consider a few examples of the application of Eqn. (1).

For the thermogalvanic cell $Ag_{T_2}|AgCl_{melt}|_{T_1}Ag$ we have the following thermopotential: $(dE/dT)_{Ag} = -0.400 \times 10^{-3}$ V deg^{-1}; for the cell $Cl_2T_2|AgCl_{melt}|_{T_1}Cl_2$ we have $(dE/dT)_{Cl_2} = -0.695 \times 10^{-3}$ V deg^{-1}; for the

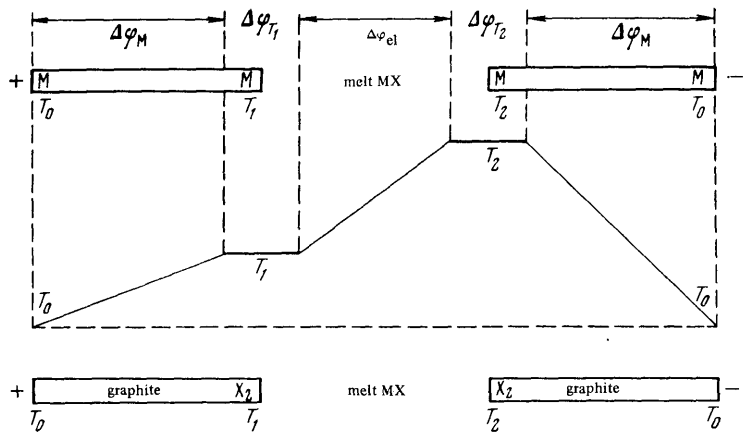

Figure 1. Model of a thermogalvanic cell and location of the thermopotential.

Ag—C thermocouple we have $(dE/dT)_{Ag-C} = +1 \times 10^{-6}$ V deg^{-1}.[8] Inserting these values into Eqn. (1) we obtain $(dE/dT)_{chem.\ calc.} = -0.285 \times 10^{-3}$ V deg^{-1}. The most reliable measurements of the e.m.f. of the chemical cell $Ag|AgCl_{melt}|Cl_2$, reported by different workers, lead to the following values for the temperature coefficient of the e.m.f.: 0.292×10^{-3} V deg^{-1},[26] 0.289×10^{-3} V deg^{-1},[27] and 0.294×10^{-3} V deg^{-1}.[8] Thus, the agreement between the measured temperature coefficient and the value calculated from the thermopotentials is within experimental error.

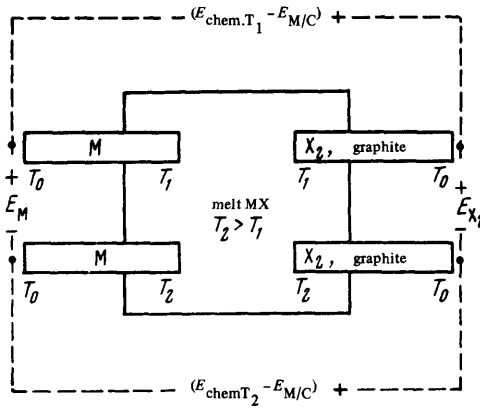

Figure 2. Relationship between the e.m.f.'s of the thermogalvanic cells and the e.m.f. of the isothermal chemical cell with a single fused salt.

The experimentally measured thermopotential for the thermogalvanic cell $Pb_{liq.}\,T_2|PbCl_2 melt|T_1\,Pb_{liq.}$ is $(dE/dT)_{Pb} = -0.008 \times 10^{-3}$ V deg^{-1}, for the cell $Cl_2T_2|PbCl_2 melt|T_1Cl_2$ we find $(dE/dT)_{Cl_2} = -0.620 \times 10^{-3}$ V deg^{-1}, and for the Pb—C couple $(dE/dT)_{Pb-C} = +0.001 \times 10^{-3}$ V deg^{-1}.[24] From Eqn. (1) we obtain $(dE/dT)_{chem.\ calc.} = -0.61 \times 10^{-3}$ V deg^{-1}. Direct measurements of the e.m.f. of the chemical cell $Pb|PbCl_2 melt|Cl_2$ gave the following values of the temperature coefficient: -0.60×10^{-3} V deg^{-1} [28] and -0.62×10^{-3} V deg^{-1}.[29]

For the thermogalvanic cell $Cd_{liq.}\,T_2|CdCl_2 melt|T_1\,Cd_{liq.}$ we find $(dE/dT)_{Cd} = -0.146 \times 10^{-3}$ V deg^{-1}; for the cell $Cl_2T_2|CdCl_2 melt|T_1Cl_2$, $(dE/dT)_{Cl_2} = -0.714 \times 10^{-3}$ V deg^{-1}; for the $Cd_{liq.}$—C couple, $(dE/dT)_{Cd-C} = -0.0075 \times 10^{-3}$ V deg^{-1}.[22] Hence $(dE/dT)_{chem.\ calc.} = -0.575 \times 10^{-3}$ V deg^{-1}, whereas the experimentally measured value[30] is -0.568×10^{-3} V deg^{-1}. For fused zinc chloride[18] the thermopotential difference[30] is -0.700×10^{-3} V deg^{-1}; the thermopotential of the $Zn_{liq.}$—C couple is $+0.005 \times 10^{-3}$ V deg^{-1}. Hence $(dE/dT)_{chem.\ calc.} = -0.695 \times 10^{-3}$ V deg^{-1}. From the measured e.m.f.'s of the cell $Zn_{liq.}|ZnCl_2 melt|Cl_2$, the temperature coefficient is given as -0.695×10^{-3} V deg^{-1},[29] -0.697×10^{-3} V deg^{-1},[31] and -0.700×10^{-3} V deg^{-1}.[32] The agreement between calculation and experiment is good.

4. THERMOPOTENTIAL EQUATION

We shall derive an equation for the thermopotential by considering the components of this potential, as shown in Fig. 1.

According to Wagner[33], the thermopotential can be divided into two components: a heterogeneous thermoelectric effect, arising from the electrochemical reaction at the electrode—electrolyte boundary, and a homogeneous thermoelectric effect, due to the temperature gradient in the electrolyte and in the electrodes.

For the thermogalvanic cell $M_{T+dT}|MX_{melt}|T^M$, the heterogeneous thermoelectric effect $(dE/dT)_M^{het}$ can be expressed as the difference between the potential steps at the electrode—electrolyte interface: $(dE/dT)_M^{het} = \Delta\varphi_{T+dT} - \Delta\varphi_T$. The passage of one Faraday of electricity through the electrode—electrolyte interface alters the free energy of the system, as a result of the reaction $M \rightarrow M^+ + e$, by an amount $\Delta G = F \cdot \Delta\varphi$. Hence, for the whole cell, $F \cdot (dE/dT)_M^{het} = \Delta G_{T+dT} - \Delta G_T = -\Delta S$, where ΔS is the entropy change attending the reaction. Expressing ΔS as the difference $\Delta S = \bar{S}_{M^+} + \bar{S}_e^M - S_M$, we obtain

$$F \cdot \left(\frac{dE}{dT}\right)_M^{het} = S_M - \bar{S}_{M+} - \bar{S}_e^M \qquad (2)$$

where S_M is the absolute entropy of the metal at temperature T, $\bar{S}_{M^+}$ is the partial entropy of the M^+ ion in the electrolyte, and $\bar{S}_e^M$ is the partial entropy of an electron in the metal.

The homogeneous thermoelectric effect, as a component of the thermopotential, can itself be expressed as the resultant of two effects: one due to the temperature gradient in the electrolyte and one due to the temperature gradient in the metal:

$$F \cdot \left(\frac{dE}{dT}\right)_M^{hom} = \overset{*}{S}_i - \overset{*}{S}_e^M \qquad (3)$$

where $\overset{*}{S}_i$ is the entropy of transfer in the electrolyte, $\overset{*}{S}_e^M$ is the entropy of transfer of an electron in the metal. By adding Eqns. (2) and (3) we obtain the equation for the thermopotential of a thermogalvanic cell with metallic electrodes:

$$F \cdot \left(\frac{dE}{dT}\right)_M = S_M - \bar{S}_{M+} + \overset{*}{S}_i - (\bar{S}_e + \overset{*}{S}_e)^M \quad . \qquad (4)$$

Similarly, for a thermogalvanic cell with halogen electrodes we obtain

$$F\left(\frac{dE}{dT}\right)_{X_2} = \bar{S}_{X^-} - \frac{1}{2}S_{X_2} + \overset{*}{S}_i - (\bar{S}_e + \overset{*}{S}_e)^c \qquad (4')$$

where S_{X_2} is the absolute entropy of the halogen, $\bar{S}_{X^-}$ is the partial entropy of the halide ion. Thermopotential equations have been derived also from irreversible thermodynamics[34,35].

5. HETEROGENEOUS COMPONENT OF THE THERMOPOTENTIAL

In the calculation of the heterogeneous component of the thermopotential of a thermogalvanic cell with metallic electrodes the partial entropy of electrons in the metal [Eqn. (2)] is much smaller than the other components and can be ignored[36].

The absolute entropy S_M of the metal at the temperature T for which the thermopotential is measured can be found in standard thermodynamic tabulations[37,38]. The difficulty arises in computing the partial entropy of the ion. In 1929 Wagner had suggested taking the partial entropy of an ion in a uni-univalent electrolyte as one-half of the entropy of the salt[33]. A more valid method, put forward by Pitzer[39], takes into account the mass (M) of both the cation and the anion: Pitzer's equation is

$$\bar{S}_{M+} = \frac{1}{2}\left(S_{MX} + \frac{3}{2} R \ln \frac{M_M}{M_X}\right) \quad (5)$$

Eqn. (5) gives the best results with alkali metal halides, but it can be used (with some reservations) with other uni-univalent electrolytes as well.

Having evaluated the heterogeneous component, we can now calculate an approximate value of the homogeneous component of the thermopotential.

Since the heterogeneous effect is the entropy of the electrode reaction, it also gives a measure of the heat of the electrode reaction when multiplied by the absolute temperature (local Peltier effect). Evidently, the magnitude and sign of the thermal effect must be determined by the difference between the entropy of the metal and the partial entropy of the metal ion.

6. ENTROPY OF TRANSFER IN THE SALT

As the diagram of the thermogalvanic cell (Fig. 1) shows, a potential gradient $\nabla\varphi_i$ arises in the electrolyte as a result of the presence of a temperature gradient. The work done by the passage of one Faraday of electricity through the electrolyte ($F \cdot \nabla\varphi$) appears in the form of heat absorbed or evolved by the electrolyte, depending on the direction of the current and on the sign of the potential gradient $\nabla\varphi_i$. This thermal effect, known as the heat of transfer, corresponds to the Thomson effect. The heat of transfer, divided by the temperature, defines a new parameter: the entropy of transfer in the salt, denoted by $\overset{*}{S}_i$. Naturally, for a given temperature gradient, the magnitude and sign of the potential gradient in the electrolyte ($\nabla\varphi_i$) must be a function of the nature of the fused electrolyte: for example, for a symmetrical electrolyte like KCl having a cation and an anion of comparable mobility the potential gradient will be small, and conversely for a unipolar cationic conductor like AgCl the potential gradient will be quite large. If the conductivity type in the fused electrolyte is a sensitive function of temperature, the potential gradient will also change with temperature.

Thus, the entropy of transfer in the electrolyte is a direct measure of the structural features of the fused salt. Since the entropy of transfer [see Eqns. (4) and (4')] is defined as a difference, its confidence limits are set by the uncertainty in the heterogeneous component of the thermopotential.

Physically, the entropy of transfer in the salt ($\overset{*}{S}_i$) is a manifestation of the migration of ions accompanying the passage of current through the electrolyte. If the heterogeneous component of the thermopotential is known with sufficient accuracy, the calculated entropy of transfer can be related to transport phenomena in the fused electrolyte (conductivity, self-diffusion, transport number), and can be treated as a structural characteristic determined by the nature of the chemical bond. The discontinuous change in transfer parameters which occurs at the melting point is reflected in a sharp change in the entropy of transfer.

The entropies of transfer of uni-univalent fused electrolytes are compared in Table 2. It can be seen that alkali metal chlorides have a small entropy of transfer: in other words, their thermopotential is determined mainly by the heterogeneous component, and only Joule heat is evolved by the passage of current through these electrolytes. For the most symmetrical of these electrolytes (KCl) the entropy of transfer is almost zero. In fused copper and silver halides the entropy of transfer is appreciable, not surprisingly since their structure is more complex than that of the alkali metal halides. In fused silver nitrate and silver sulphate the calculated $\overset{*}{S}_i$ values are +7.5 e.u. (at 550°K) and +7.7 e.u. (at 950°K) respectively, showing that the presence of a complex anion leads to anomalous $\overset{*}{S}_i$ values. This effect may be ascribed to a significant potential gradient in a direction opposite to that of the thermo-e.m.f. of the cell.

Table 2. Entropy of transfer in single fused salts.

Electrolyte	Temp., °K	Entropy of transfer, e.u.	Reference	Electrolyte	Temp., °K	Entropy of transfer, e.u.	Entropy of transfer, e.u.
LiCl	1100	—1.0	1	CuI	900	—6.0	6
NaCl	1300	—0.3	1	AgF	800	—3.5	5
KCl	1300	—0.2	1	AgCl	900	—3.4	8
RbCl	1000	—1.5	2	AgBr	900	—4.2	13
CsCl	950	—1.7	2	AgI	900	—5.4	6
CuCl	900	—3.5	4	$AgNO_3$	550	+7.5	14
CuBr	900	—5.1	6	Ag_2SO_4	930	+7.7	17

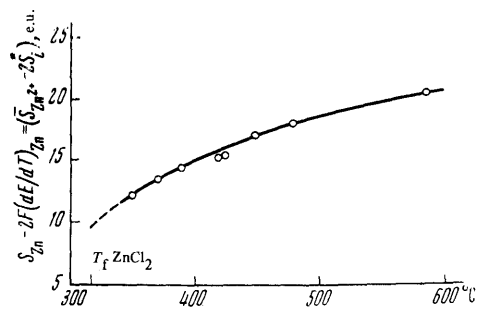

Figure 3. Variation of $(\bar{S}_{Zn^{2+}} - 2\overset{*}{S}_i)$ with temperature for the thermogalvanic cell $Zn_{T_2}|ZnCl_2|_{T_1}Zn$.

The entropy of transfer of bivalent metal salts may be discussed by considering a thermogalvanic cell with fused zinc chloride and liquid zinc electrodes. Inserting known values of S_{Zn} and $(dE/dT)_{Zn}$ into the thermopotential equation we can obtain the algebraic sum $(\bar{S}_{Zn^{2+}} - 2\overset{*}{S}_i)$: this quantity is found to increase by more than 11 e.u. over the temperature range between the melting point of $ZnCl_2$ and 600° (Fig. 3). The contribution of $\bar{S}_{Zn^{2+}}$ to this increase cannot be more than a few entropy units, since the entropy of zinc chloride increases by approximately 8.7 e.u. in this temperature range and the partial entropy of the zinc ions can only account for a fraction of this increase. It follows that the entropy of transfer in fused zinc chloride

is a fairly large quantity which decreases with temperature (in absolute value). Thus, the quantity $\overset{*}{S}_i$ may be added to the list of strongly temperature-dependent properties of fused $ZnCl_2$ (electrical conductivity, viscosity, self-diffusion[40,41]). The lack of constancy of $\overset{*}{S}_i$ is consistent with the polymeric network model of the structure of zinc chloride, which has been postulated[42] on the basis of Raman scattering studies.

At temperatures close to the melting point, the dissociation of zinc chloride with formation of simple ions is negligible, owing to polymerisation. Few current carriers are present, and fairly large potential gradients can develop. On raising the temperature the polymers are broken down and a simpler structure begins to appear, tending towards the structure of ionic melts (for which the entropy of transfer is small).

A more detailed analysis of the entropy of transfer is not justified as long as only tentative values of this parameter are available.

7. DEPENDENCE OF THE THERMOPOTENTIAL AND ITS COMPONENTS UPON THE STATE OF AGGREGATION OF THE ELECTRODES AND THE ELECTROLYTE

In the majority of thermogalvanic cells with a single fused salt (Table 1) the thermopotential has a negative sign and is almost independent of temperature. A barely significant change of thermopotential with temperature has been observed in sodium and potassium chloride[1], zinc and tin iodide[20], and lead bromide[3]. Measurements[18] on the cell $Zn_{liq.\,T_2}|ZnCl_{2melt}|_{T_1}Zn_{liq.}$, which were subsequently confirmed[20], indicate a more substantial and complicated temperature dependence of the thermopotential. Between 420 and 600° the thermopotential of fused zinc chloride changes sign (from positive to negative), showing a discontinuity at the melting point of zinc (Fig. 4).

Changes in thermopotential with temperature are due to structural changes in the fused electrolyte, and should therefore be observed in all electrolytes over a sufficiently wide range of temperature.

We shall discuss the discontinuous change in thermopotential accompanying a change in the state of aggregation of the electrodes for the particular case of the thermogalvanic cell consisting of fused zinc chloride with zinc electrodes. Applying Eqn. (4) to the cell

$$\underset{T_0}{W}\ \ldots\ W\,|\,\underset{T}{Zn}_{liq.(sol.)}\,|\,ZnCl_{2\,melt}\ \ldots\,|\,\underset{T+dT}{Zn}_{liq.}\,|\,W\ \ldots\ \underset{T_0}{W}$$

we can write

$$2F\left(\frac{dE}{dT}\right)_{Zn\,liq.} = -\Delta S + 2(\bar{\bar{S}}_e^{Zn\,liq.} - \bar{\bar{S}}_e^{W}) - 2\overset{*}{S}_e^{Zn\,liq.} + 2\overset{*}{S}_i$$

where $\Delta S = S_{Zn(liq.)} - \bar{S}_{Zn^{2+}} - 2\bar{S}_e^{Zn(liq.)}$, $(\bar{\bar{S}}_e^{Zn(liq.)} - \bar{\bar{S}}_e^{W})$ is the thermopotential of the Zn(liq.)/W couple, $\overset{*}{S}_e^{Zn(liq.)}$ is the entropy of transfer of electrons in liquid zinc, $\overset{*}{S}_i$ is the entropy of transfer in the salt.

After simplification we arrive at the expression

$$2F\left(\frac{dE}{dT}\right)_{Zn\,liq.} = S_{Zn\,liq.} - \bar{S}_{Zn^{2+}} - 2s_e^{W} + 2\overset{*}{S}_i$$

Similarly, for the cell with solid zinc, we can write

$$2F\left(\frac{dE}{dT}\right)_{Zn\,sol.} = S_{Zn\,sol.} - \bar{S}_{Zn^{2+}} - 2s_e^{W} + 2\overset{*}{S}_i$$

The difference between these equations is

$$2F\left[\left(\frac{dE}{dT}\right)_{Zn\,liq.} - \left(\frac{dE}{dT}\right)_{Zn\,sol.}\right] = S_{Zn\,liq.} - S_{Zn\,sol.} = \Delta S_{f(Zn)}$$

Thus, the difference in thermopotential between two cells measured close to and on either side of the melting point of zinc gives the entropy of melting of zinc.

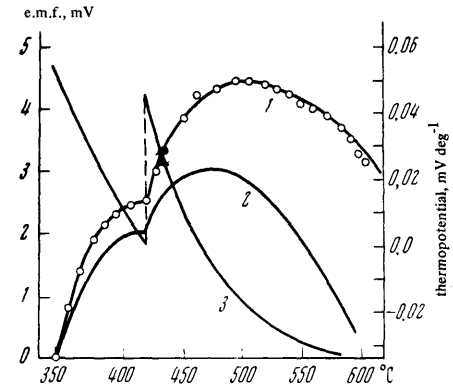

Figure 4. *1*) e.m.f. of the thermogalvanic cell $W\,|\,Zn_{T_2}\,|\,ZnCl_{2melt}\,|\,_{T_1}Zn\,|\,W$ against temperature of the "hot" electrode; *2*) ditto, for the thermogalvanic cell $Zn_{T_2}\,|\,ZnCl_{2melt}\,|\,_{T_1}Zn$; *3*) variation of thermopotential with temperature.

In our approximate, graphical determination, the jump in thermopotential at the melting point (see Fig. 4) is 0.05—0.052 mV deg^{-1}, giving an entropy of melting of 2.3—2.4 e.u. The tabulated value[43], obtained from calorimetric measurements of the heat of melting, is 2.48 e.u.

Table 3.

Electrolyte	T, °C	$F\left(\frac{dE}{dT}\right)_{Ag}$ e.u. crystal	$F\left(\frac{dE}{dT}\right)_{Ag}$ e.u. crystal	$\Delta F\left(\frac{dE}{dT}\right)_{Ag}$ e.u.	$(\bar{S}_{Ag^+})$melt − $-(\bar{S}_{Ag^+})$cryst. e.u.	$\overset{*}{S}_{i\,cryst} - \overset{*}{S}_{i\,melt}$
AgCl	455	−14.10	−9.30	−4.8	(+2.2)	(−7.0)
AgI	558	−11.30	−11.30	0	(+1.35)	(−1.35)
$AgNO_3$	210	−5.45	−7.35	+1.9	(+2.86)	(−0.96)

Writing Eqn. (4) for the liquid and the solid electrolyte, and subtracting the two expressions, we obtain

$$F\cdot\left[\left(\frac{dE}{dT}\right)_M^{liq.} - \left(\frac{dE}{dT}\right)_M^{cryst.}\right] = (\overset{*}{S}_i^{liq.} - \overset{*}{S}_i^{cryst.}) - (\bar{S}_{M^+}^{liq.} - \bar{S}_{M^+}^{cryst.})$$

Evidently, since $\bar{S}_{M^+}^{liq.} > \bar{S}_{M^+}^{cryst.}$, the second term on the right-hand side is negative. In absolute value, $\overset{*}{S}_i^{cryst.} > \overset{*}{S}_i^{liq.}$, and therefore the first term is positive (since $\overset{*}{S}_i > 0$). The combined effect of these two terms may be a decrease or an increase in thermopotential at the transition from crystalline to fused electrolyte. As a special case, the

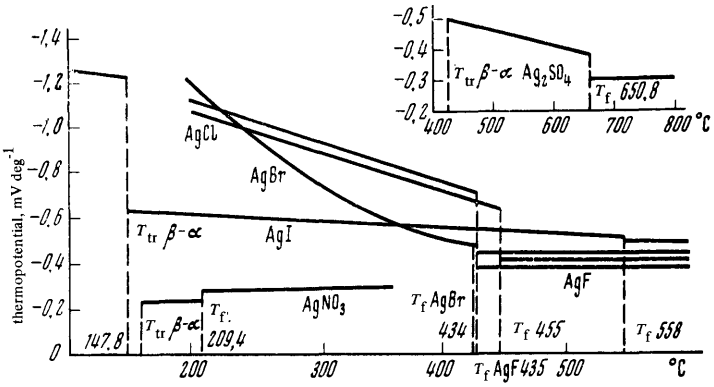

Figure 5. Temperature dependence of the thermopotential of the thermogalvanic cell $Ag_{T_2}|AgX|_{T_1}Ag$ (X = F, Cl, Br, I, NO_3, SO_4), from published data.

thermopotential may remain constant at the melting point of the electrolyte.

The measurements on thermogalvanic cells with AgCl, AgI, and $AgNO_3$ electrolytes, summarised in Table 3, provide examples of each type of thermopotential change at the melting point of the electrolyte.

Though the total thermo-effect can show different types of change at the melting point of the crystalline electrolyte, the entropy of transfer decreases in every case, because unipolar conduction (in the crystal) is replaced by mixed conduction (in the melt).

Fig. 5 shows thermopotential curves for cells with metallic (silver) electrodes and silver salt electrolytes over a wide temperature range. The curves have been compiled from published data.

New data on the entropy of transfer in solid and in fused salts are needed in order to provide more accurate values of ΔS_i^*, the change in entropy of transfer at the melting point, a very important parameter which reflects structural changes in the salt on melting. The first measurements of this type, reported by French workers[47], are consistent with a discontinuous change in the chemical bond of silver halides at the melting point.

8. APPLICATIONS OF THE THERMOPOTENTIAL

Leaving aside the possible application of thermogalvanic cells as converters of thermal into electrical energy, we can list some applications of thermo-e.m.f.'s in the study of the electrochemistry of fused salts.

Thermogalvanic corrosion. If the temperature of the surface of a reversible metal electrode is not uniform, a thermo-e.m.f. is developed between regions at different temperatures. Thermogalvanic corrosion is the result of current flow through this short-circuited thermogalvanic cell: the hotter regions are dissolved anodically, and metal is deposited on the cooler regions (usually in the form of dendrites). Thermogalvanic corrosion is often observed in practice.

Local Peltier effect. Electrolysis under isothermal conditions is accompanied by the absorption of heat in the regions where metal is dissolving anodically and heat evolution where metal is cathodically deposited. Hence, the passage of current through an isothermal electrode—fused electrolyte—electrode system converts it into a non-isothermal system: the temperature of the anode decreases, and that of the cathode increases with respect to the temperature in the bulk of the electrolyte. This phenomenon has been observed experimentally during the anodic dissolution and cathodic deposition of copper in a melt of cuprous chloride[46].

The sign and magnitude of the thermal effect accompanying, say, the anodic dissolution of a metal can be obtained from the measured thermopotential or calculated from the difference between the entropy of the metal and the partial ionic entropy of the same metal. Three cases are possible: the entropy of the metal and the partial entropy of the ion are approximately equal (resulting in a negligible thermal effect); the entropy of the metal is significantly smaller than the partial entropy of the ion (resulting in a large and positive thermal effect, i.e. heat absorption); the entropy of the metal is significantly larger than the partial entropy of the ion (resulting in a large and negative thermal effect, i.e. heat evolution). The thermal effect for cathodic reactions has the opposite sign.

Instances of all three cases are found in the calculations for systems with uni-univalent electrolytes summarised below.

$Cu_{sol.}|CuCl_{liq.}$ System

M.p. CuCl = 703°K; $S_{CuCl(liq.)}$ at 703°K is 36.9 e.u.[44]; S_{Cu} at 703°K is 13.2 e.u.[44]; $\bar{S}_{Cu^+}$ = 19.3 e.u.; ΔS = +6.1 e.u.; $T\Delta S$ = +4.3 kcal g-equiv^{-1}

$Ag_{sol.}|AgCl_{liq.}$ System

M.p. AgCl = 728°K; $S_{AgCl(liq.)}$ at 728°K is 39.8 e.u.[44]; S_{Ag} at 728°K is 15.8 e.u.[44]; $\bar{S}_{Ag^+}$ = 21.5 e.u.; ΔS = +5.7 e.u.; $T\Delta S$ = +4.15 kcal g-equiv^{-1}

$Li_{liq.}|LiCl_{liq.}$ System

M.p. LiCl = 880°K; $S_{LiCl(liq.)}$ at 880°K is 33.5 e.u.[44]; $S_{Li(liq.)}$ at 880°K is 15.7 e.u.[44]; $\overline{S}_{Li^+}$ = 14.3 e.u.; ΔS = −1.4 e.u.; $T\Delta S$ = −1.2 kcal g-equiv^{-1}

$Na_{liq.}|NaCl_{liq.}$ System

M.p. NaCl = 1073°K; $S_{NaCl(liq.)}$ at 1073°K is 40.8 e.u.[37]; S_{Na} at 1073°K is 23 e.u.[37]; $\overline{S}_{Na^+}$ = 19.8 e.u.; ΔS = −3.2 e.u.; $T\Delta S$ = −3.5 kcal g-equiv^{-1}

$K_{gas}|KCl_{liq.}$ System

M.p. KCl = 1043°K; b.p. K = 1030°K; $S_{KCl(liq.)}$ at 1045°K is 42.2 e.u.[37]; S_K at 1043°K is 44.87 e.u.[44]; $\overline{S}_{K^+}$ = 21.1 e.u.; ΔS = −23.77 e.u.; $T\Delta S$ = −24.8 kcal g-equiv^{-1}

$Rb_{gas}|RbCl_{liq.}$ System

M.p. RbCl = 995°K[45]; b.p. Rb = 952°K; $S_{RbCl(liq.)}$ at 995°K is 44.3 e.u.[45]; $S_{Rb(gas)}$ at 995°K is 48 e.u.[37,43,38]; $\overline{S}_{Rb^+}$ = 23.5 e.u.; ΔS = −24.5 e.u.; $T\Delta S$ = −24.4 kcal g-equiv^{-1}

$Cs_{liq.}|CsCl_{liq.}$ System

M.p. CsCl = 918°K; S_{CsCl} = 45 e.u.[45]; $S_{Cs(liq.)}$ at 918°K is 30.3 e.u.[37,43,38]; $\overline{S}_{Cs^+}$ at 918°K is 24 e.u.; ΔS = 5.9 e.u.; $T\Delta S$ = −5.4 kcal g-equiv^{-1}

It can be seen from these results that for solid metals the heat of anodic dissolution is appreciable, and its sign corresponds to absorption of heat; on the other hand, when the metal is in the vapour state its ionisation involves the evolution of a large amount of heat. When the state of aggregation of a metal electrode changes, a discontinuity occurs in the thermal effect. For liquid metals the thermal effect is small: this observation is consistent with the absence of chemical polarisation during the cathodic deposition of liquid metals. The small cathodic polarisation observed when solid metals are deposited is most probably a thermo-e.m.f. arising because of the difference in temperature between the polarised electrode and the reference electrode.

Electrocrystallisation of metals. The cathodic deposition of metals under non-isothermal conditions (i.e. in the presence of a temperature gradient) gives different types of deposit depending on the direction of the thermal field. In one direction, the operation of the short-circuited thermogalvanic cells assists the formation of a dendritic deposit, in the other direction it opposes dendrite formation. Of course, this effect is appreciable only when the thermopotential of the cell is fairly large.

Temperature coefficient of the electrode potential. The temperature coefficient of the e.m.f. of an isothermal chemical cell is the algebraic sum of the temperature coefficients of the two electrode potentials. Hence we can write

$$\Delta S = S_{MX} - S_M - \frac{1}{2}S_{X_2} = \left(\overline{S}_{X^-} - \frac{1}{2}S_{X_2}\right) - (\overline{S}_{M^+} - S_M)$$

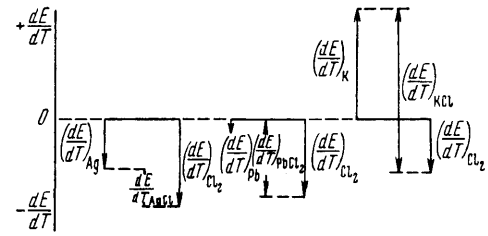

Figure 6. Temperature coefficient of the e.m.f. of a chemical cell as the algebraic sum of the temperature coefficients of the electrode potentials.

The terms in brackets (the heterogeneous components of the thermopotentials) are proportional to the temperature coefficients of the electrode potentials, which are added or subtracted (depending on their sign). Three possible cases are shown schematically in Fig. 6. For fused AgCl the temperature coefficient of the e.m.f. of the chemical cell $Ag|AgCl_{liq.}|Cl_2$ is equal to the difference between the temperature coefficients of the electrode potentials; for fused $PbCl_2$, $(dE/dT)_{PbCl_2}$ is equal to the temperature coefficient of the potential of the chlorine electrode; for fused KCl, $(dE/dT)_{KCl}$ is equal to the sum of the temperature coefficients of the electrode potentials.

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Further work on thermogalvanic cells with one-component electrolytes should be aimed at the following objectives. The experimental measurements should be extended to salts on which no data are yet available (in particular, bromides and iodides, and also fused oxides); there is also a need for a method of direct experimental measurement of the local Peltier effect (the heterogeneous component of the thermopotential), in order to obtain more precise data on partial ionic entropies and on the entropy of transfer in the salt (the homogeneous component of the thermopotential). Only then will it be possible to seek a quantitative relationship between the entropy of transfer and other kinetic parameters of the salt. The comparative studies of thermoelectric phenomena in crystals and in their melts should also continue, in order to throw new light on the nature of the melting process in crystalline salts.

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Infrared Spectroscopy of Nucleic Acids

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The review deals with infrared and Raman spectroscopic data for DNA, RNA, and their components and with the assignment of the infrared bands to the vibrations of individual bonds. An approach to a theoretical treatment of the normal vibrations of the nucleic acid skeleton is described. The applications of infrared spectroscopy to the study of the specificity of the interaction of the heterocyclic bases, the secondary structure of nucleic acids, and their interactions with proteins, metal ions, and certain biologically active substances is considered.
The bibliography includes 218 references.

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I. INTRODUCTION

The vigorous development of molecular biology has been accompanied by a large-scale application of physical and physicochemical methods in the investigation of the composition and structure of biologically important compounds. Infrared spectroscopy is acquiring increasing importance among these methods. The infrared spectroscopic method has been successfully employed to solve various structural and physicochemical problems in molecular biology, including the recognition of compounds with weak structural characteristics, the determination of the structural formulae of biologically important compounds, and the study of the steric configuration of biopolymers.

The infrared spectra of biologically important compounds such as aminoacids, peptides, heterocyclic bases of nucleic acids, lipids, steroids, and vitamins and also the spectra of biopolymers—proteins, nucleic acids, and polysaccharides—are being investigated at the present time. Major advances have been achieved in the study of the structure of polypeptides and proteins with theoretical analysis of the normal vibrations. However, for nucleic acids a complete description of the normal vibrations is still lacking, most probably due to the complexity of their molecular structure. Therefore the fundamental bands in the infrared spectra of the bases, polynucleotides, and nucleic acids have been interpreted by a semiempirical method based on the study of the absorption by individual atomic groups in the low-molecular-weight components. This reduces the reliability of the conclusions arrived at and, what is most important, limits the information which may be derived from the infrared spectra.

Nucleic acids consist of highly polymerised unbranched molecules the main valence chain of which comprises alternating phosphoric acid and sugar units; purine and pyrimidine bases are attached to the sugar residues (Fig. 1)†. The molecular structure of nucleic acids and also of synthetic polynucleotides is now fairly well known, as can be seen from the numerous papers, reviews, and monographs [1-9].

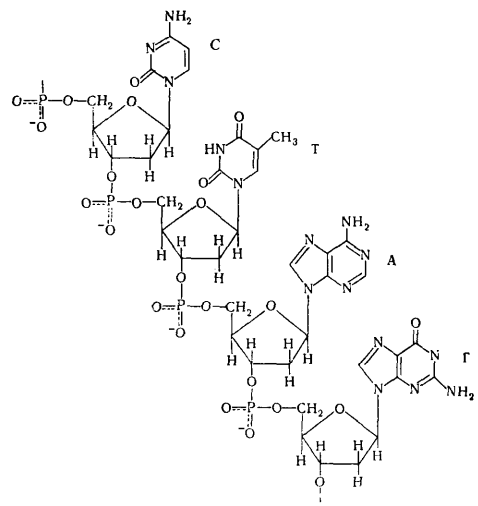


Figure 1. Schematic representation of the primary structure of the DNA chain.

There are no reviews on the infrared spectroscopy of nucleic acids in the Soviet literature. Abroad a review was published in 1965 by Shimanouchi et al. [10], in which the authors considered mainly the results of their own infrared spectroscopic studies on nucleotides, sugars, phosphates, synthetic polynucleotides, DNA, and RNA, while during the preparation of the present review Tsuboi [11] published a review on the infrared spectroscopic studies on the structure of nucleic acids. During recent years very many studies on the infrared spectra of nucleic acids, not included in the above reviews, have been published.

†The following abbreviations have been adopted: A = adenine, G = guanine, T = thymine, C = cytosine, U = uracil, I = inosine, GMP = guanosine monophosphate, poly-A = polyriboadenylic acid, poly-(G/C) = double helix of polyguanylic and polycytidylic acids.

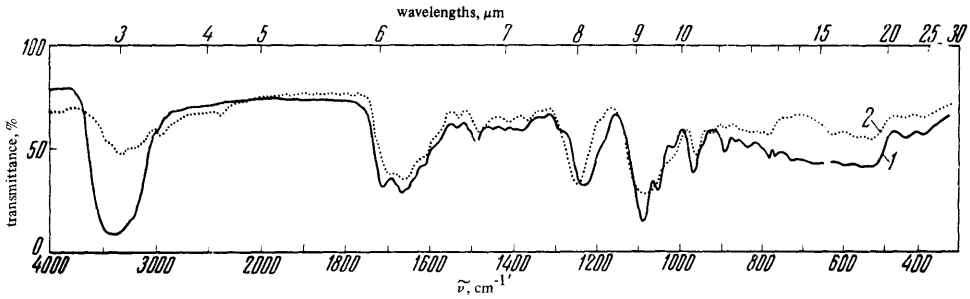


Figure 2. Infrared spectrum of the sodium salt of DNA for 75% (curve *1*) and 0% (curve *2*) relative moisture constants. Calf thymus DNA; $\tilde{\nu}$—vibration frequency (wave-number).

II. VIBRATIONAL SPECTRA OF NUCLEIC ACIDS

The infrared spectrum of DNA was described for the first time in 1948–1953 by Blout and coworkers for solid specimens in the range 4000–700 cm^{-1} [12,13] and for solutions in D_2O in the range 1750–1500 cm^{-1}. [14,15] Non-oriented DNA films and non-polarised radiation were employed in these investigations. The spectra of non-oriented DNA films were first published by Fraser [16] in 1951, but he did not take into account the effect of the moisture content of the specimens on the spectra. Subsequently a number of workers [10,17-23] studied the vibrational spectra of nucleic acids in the range 4000–400 cm^{-1} using all the possibilities of the method at present available.

The infrared spectrum of DNA [10] shown in Fig. 2 is comparatively simple: it consists of a fairly "diffuse" pattern, the majority of the bands of which are diffuse and only a few are fairly distinct. Numerous bands have become appreciably broadened and overlap with those adjoining them.

Three regions may be arbitrarily distinguished among the groups of absorption bands in the spectrum: 4000 to 2000 and 1700–1500 cm^{-1}, usually attributed to the vibrations of the bases and the CH groups of deoxyribose in DNA, and 1300–1000 cm^{-1} attributed to the vibrations of the sugar and the phosphate groups in the DNA molecular skeleton. The assignment of the bands in the infrared spectrum of DNA to the individual bonds of the skeleton and the DNA bases is given in Tables 1 and 2; for the majority of the bands, with the exception of those in the region 3500–2000 cm^{-1} and at 1705, 1220, and 1084 cm^{-1}, the assignment must be regarded as only approximate.

One should also bear in mind that the vibrations of the double bonds in the rings of the bases are strongly coupled. In the spectra of deuterated DNA, a shift of the majority of the bands towards lower frequencies is observed owing to the H–D isotope exchange in the NH_2 and NH groups of the bases [10,18].

The form of the infrared spectrum of DNA changes somewhat as the moisture content of the specimen is varied (Fig. 3)—a number of bands are displaced and the spectrum becomes systematically improved with increase of the relative moisture content to 92% [17,19] (a particular moisture content is achieved usually by placing the DNA film in a hermetically sealed chamber over a saturated solution of a particular salt or by blowing through the chamber a gas with a specified moisture content). Many bands become narrower, the degree of overlapping diminishes, and the overall diffuse background of the spectrum becomes less pronounced. A similar pattern

Table 1. Skeletal vibration bands in the infrared spectra of nucleic acids.

Group	No. of groups	Intensity	Expected vibration wave-number, cm^{-1}	Wave-number in spectrum, cm^{-1} of DNA	of RNA	of poly-adenylic acid
References			24–26	10, 17, 18	27	28
	1	s.	ν_{as} 1220	1230 ⊥	1225 ⊥	1240 ⊥
		s.		1224 ∥		
			ν_s 1085	1084—89 ⊥	1084 ∥	1090 ∥
—C—O—P	2	s.	ν 1100	1053 ⊥	1070 ∥	—
		s.	$\nu \sim 900$	965 ⊥	937 ⊥	920 ∥
—O—P—O—	1	med.	ν_{as} 820	820 ∥	810 ⊥	820
		w.	ν_s 760—750	784 ∥		
—C—O—C— rings	1	s.	ν_{as} 1100—1070	1050 ⊥		
				1024 ∥		
		s.	ν_s 940—910	970 ⊥	990 ⊥, 960 ∥	990 ⊥, 965 ∥
		w.	γ 650—600			645 ∥, 630 ∥
		s.	ν_{as} 2970—2920	2900		
		s.	ν_s 2860—2850	2800		
	2	w.	δ 1465—1445	1450 ⊥		
		w.	$\omega \sim 1380$	1301 ⊥		
		w.	r 825—800	825 ∥	890 ∥	880 ∥
					860 ⊥	860 ∥
		s.	ν 3630			
—OH	1	s.	δ 1250	—	1250 ⊥	
		w.	β 750—650		780, 730	780 ∥
	1	s.	$\nu_{degener}$ 1125—1085		1130—1120 ⊥	1116 ⊥
				—		1130 ∥
			$\nu_s \sim 800$		810 ⊥	820 ⊥
	3	m.	ν 2980—2890	2850		
		w.	δ 1440—1400	1410 ⊥	1400 ⊥	1420 ⊥
		w.	β 900—650			
—C—C ring	2	w.	ν 955	915	910	

Note. ∥, ⊥ -polarisation; s = strong (intense); m = medium; w = weak; ν—stretching vibration; δ—in-plane vibration; ρ—out-of-plane vibration; r—rocking vibration; ω—fanwise deformation vibration; γ—ring deformation vibrations.

is observed in the study of the vibrational spectra of amorphous synthetic polymers [36,37] and this suggests that the above spectroscopic behaviour is due to an appreciable structural imperfection of the test material. This conclusion is partly confirmed by an examination of the infrared spectrum of the double helix of polyriboadenylic acid (poly-A) [28] shown in Fig. 4. Simple elimination of the irregularity in the alternation of bases appreciably improves the spectroscopic pattern.

The polarisation of the infrared absorption bands of DNA also depends on the moisture content, the dichroism of the majority of the bands being shown fairly distinctly,

although it does not lead to an appreciable improvement of the quality of the spectrum (Fig. 3). The dichroic ratio of many bands usually increases with the relative moisture content of crystalline DNA specimens.

Table 2. Vibration bands of the bases in the infrared spectra of nucleic acids.

Group	Type of vibration	Expected wavenumber, cm^{-1}	Intensity	Wave-number in spectrum, cm^{-1}						
				C	U	T	A	G	DNA "light"	DNA "deuter"
References		24–26		10, 29–32	10, 29, 33, 34	14, 33, 35	10, 29, 31, 32	10, 31 32	10, 17–19, 23	
$-NH_2$ bound	ν_{as}	3350	s.	3367	—	—	3280	3310	3350	3103
	ν_s	3180		3155			3105	3077	3210	
—NH—bound	ν	3180—3000	m.	2778	3110 2924	3175	3000	2840	2950	
$-CH_3$	ν_{as}	2960	s.	—	—	3035	—	—	2950	
	ν_s	2880—2820				2900				
=CH	ν	3000—2750	m.	3081 2947	3000	2780	2780	2680	3090	
—C=O	ν	1690—1650	s.	1655	1724 1680	1735 1670	—	1700	1705	1685
$-NH_2$	δ	1680—1600	s-m	1667	—	—	1672	1681	1609	1557
—NH—	δ	1680—1560	s-m	1538	1666 1418	1570		1555	1528	
—C=C—	ν	1680—1620	m	1621	1623	1640	1578	1569	1575	1575
—C=N—	ν	1680—1630	m-w	1630	—	—	1605	1639	1655	1607
$-NH_2$	β	1450	s-m	1458	—	—	1451	1418	1444	
—NH—	β	1300—1200	m.		1388		1250	1263 1172	1296	
$-CH_3$	δ_{as}	1460±20	s.	—	—	1500	—	—	1450	1458
	δ_s	1380—1370	m.			1380			1375	1375
Ring	ν	1480—1200	s.	1527 1362 1236	1389 1238	1200	1418 1333	1477 1375	1503 1477	1516 1476
C—CH_3	ν	1250—1200	w.	—	—	1245	—	—	1292	1300
C—NH_2	ν	1300—1250	s.	1275	—	—	1206	1215	1331	1331
=C—H	δ	1460	w.		1451	1380		1464	1456	1453
=C—N—	ν	1200—1150	w.	1156			1124			
—C—N—	ν	1250—1100	w.	1011	1099	1200			1296	1300
$-NH_2$	β	900—600	m.		—	—	1022, 797	949	893	778
—NH	β	820—720	m.	823	822, 760	835	870	877, 776, 689	778	
—C—C	ν	1000—950	w.	995	994	1000	938		860	851
=C—H	β	860—700	w.	784	851	705		789, 703	795	794
Ring	γ	850—700	w.	794	780	740	722		727	715

In the range 1750–1550 cm^{-1}, where the in-plane vibrations of the rings of the bases are active, all the bands of Na- and Li-DNA are polarised at right angles to the direction of the orientation of the film. An analogous polarisation is observed also for the stretching and in-plane deformation vibrations of the NH_2, NH, and CH groups in the range 1600–1300 cm^{-1}.[18,19] It is interesting that the band at 1240 cm^{-1}, corresponding to the antisymmetric vibrations of the PO_2^- groups of Na-DNA,[10] does not exhibit dichroism at a relatively low moisture content, but, on increasing the latter, it is displaced from 1240 to 1220 cm^{-1} and is split into two components. Tsuboi believes[11] that this finding implies that the antisymmetric vibrations of each PO_2^- groups are not independent and that adjacent PO_2^- groups appreciably interact with one another, generating a series of vibrations which are propagated throughout the chain. The component with a lower wave-number (1215 cm^{-1}) and parallel dichroism may be assigned to the in-phase vibrations of the PO_2^- groups and the component with a higher wave-number (1225 cm^{-1}) and perpendicular dichroism may be assigned to the vibrations of the PO_2^- groups with a phase difference of $2\pi/n$, where n is the number of nucleotides corresponding to one turn of the DNA spiral. The wave-number difference between these components (~10 cm^{-1}) may be regarded as reflecting the strength of the interaction between the PO_2^- groups in the given crystalline Na-DNA specimen.

The band due to the symmetrical vibrations of the PO_2^- groups of DNA (1089 cm^{-1}) exhibits perpendicular dichroism. An analogous polarisation is observed also for the absorption bands in the range 1100–900 cm^{-1}, which are mainly due to the vibrations of the sugar and phosphate groups. The bands in the range 900 to 700 cm^{-1}, where the out-of-plane deformation vibrations at the N–H bond are active, also show parallel dichroism[17–19].

The effect of an increase of temperature from 22° to 90°C on the infrared spectra of DNA has been discussed by a number of investigators[10,20,38,39] and has been attributed to the breakdown of the secondary DNA structure (see Section V).

The infrared spectra of RNA have now been investigated in fair detail. All the general characteristics of the spectrum indicated for DNA hold also for RNA (Fig. 5). The vibrational spectrum of RNA has a set of intense absorption bands in the regions 3500–2000, 1700–1500, and 1250–1050 cm^{-1}. However, in the range 1100 to 800 cm^{-1}, where the sugar components of nucleic acids absorb, there is an appreciable difference between the DNA and RNA spectra[10,39,40]. The RNA spectra have bands at 1120 and 810 cm^{-1}, which are absent from the DNA spectra, and conversely the 1050 cm^{-1} band is characteristic only of polydeoxyribonucleotides. The spectroscopic characteristics of various types of RNA—ribosomal, transport, and viral—are in many ways similar, but the details of the spectra in the ranges 1750–1400 and 840 to 760 cm^{-1} are somewhat different, which is probably due to the different quantitative compositions of the bases and different percentage contents of the base pairs[27,41–43]. The infrared spectra of moist films of viral RNA show a weaker polarisation than DNA, which, however, may be due to the lower degree of orientation of the films. It is important to note that the symmetrical and antisymmetrical vibrations of the double helical RNA of the dwarf rice virus shows a dichroism which differs from that of DNA (Table 8). Quantitative data on the orientation of DNA and RNA films are normally quoted with the spectra, which greatly complicates their interpretation and comparison of spectra in polarised radiation. Oriented films of transfer RNA cannot be obtained owing to their low molecular weight.

The effects of changes in moisture content and temperature on the infrared spectra of RNA have been investigated to a lesser extent than for DNA. In contrast to DNA, the infrared spectrum of a solution of double stranded viral RNA is still lacking, but the spectra of transfer RNA have been recorded both for films and for D_2O solutions[11].

Synthetic polynucleotides exist either in a single-chain state or form double or triple helices, depending on a number of conditions (concentration, ionic strength, pH of the medium, etc.[6,44,45]). The infrared spectra of films comprising the double helices of polyadenylic acid (poly-A) and poly-(G/C) and the triple helix of poly-(A/2U) have been described[11,28] and the spectra of D_2O solutions of double-helical poly-(A/U), poly-(G/C), and poly-(I/C) have been measured by Miles and coworkers[46–52].

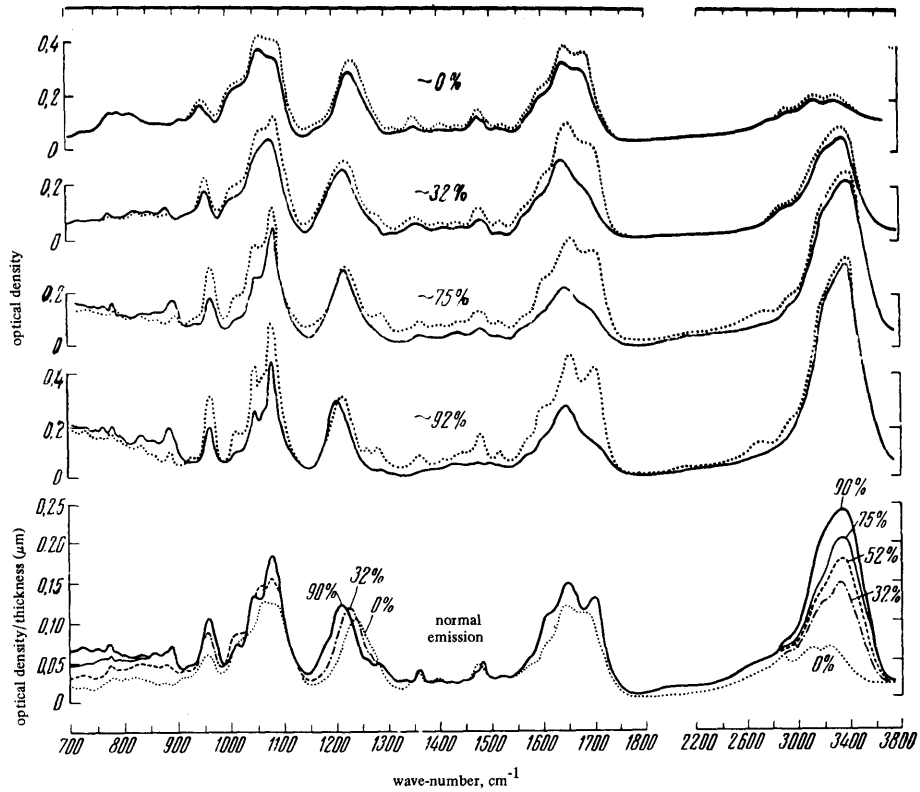


Figure 3. Polarised infrared spectra of oriented films of the sodium salt of DNA with different relative moisture contents[17]; dashed curves—emission vector perpendicular (⊥) to direction of specimen orientation; continuous curves—emission vector parallel (∥) to direction of specimen orientation.

The attempts to ob in the Raman spectra of aqueous DNA and RNA solutions remained unsuccessful for a long time. Only the Raman spectrum of polyadenylic acid in the single-chain state was known[53]. The laser Raman spectra of solutions of calf thymus DNA and the ribosomal RNA of *E. coli* were obtained by Tobin in 1969 [54] and Thomas in 1970 [55]. The positions of the bands in the Raman and infrared spectra of DNA largely coincide except for a discrepancy in the range 1700–1600 cm^{-1}, while the bands in the Raman spectrum of RNA from *E. coli* coincide satisfactorily with the bands in the corresponding region of the infrared spectrum[42].

III. VIBRATIONS OF THE MAIN VALENCE CHAIN OF NUCLEIC ACIDS

The theory of the normal vibrations of high-polymer molecules has recently developed considerably and, since nucleic acids are polymeric, it is quite reasonable to attempt a description of their vibrational spectra within the framework of the concepts formulated for polymeric systems[37,56].

A complete analysis of the vibrational spectrum of a polymer—a determination of the total number of its normal vibrations, their polarisation, and the selection rules for the infrared and Raman spectra and also the calculation of the frequencies and forms of the normal vibrations—is possible only for systems with a high degree of three-dimensional order. Despite their capacity for being packed in crystal lattices[57], neither DNA nor RNA possess such an order owing to the irregular sequence of bases. Only the molecules of synthetic polynucleotides such as poly-A and poly-C exhibit a rigorous chemical and steric (in the crystalline phase) periodicity and can be regarded as regular. Unfortunately the data for the vibrational spectra of these systems available in the literature are extremely limited[10,28], and yet they may prove to be indispensable in the interpretation of the vibrational spectra of nucleic acids. At the same time the main chains (skeleton) of the DNA and RNA molecules have an irregular chemical structure and under certain conditions also an irregular conformational structure[5,58–60], which allows an interpretation of the normal vibrations of the molecular skeleton using the periodic properties. Strictly speaking, the vibrational spectra of such helix complexes should be due to the vibrations of the atoms in both chains and to their interactions. However, one may suppose that the interaction of the chain vibrations in the double helix should be extremely insignificant, since the chains are separated by a considerable distance (the helix diameter is about 20 Å). The interactions between different double helices in the crystal phase can also be neglected. The most intense interaction between the main DNA and RNA chains occurs owing to the hydrogen bonds between the bases, but such interaction influences mainly the vibrations of the atoms in the bases, virtually without any perturbation of the atomic vibrations in the main chain.

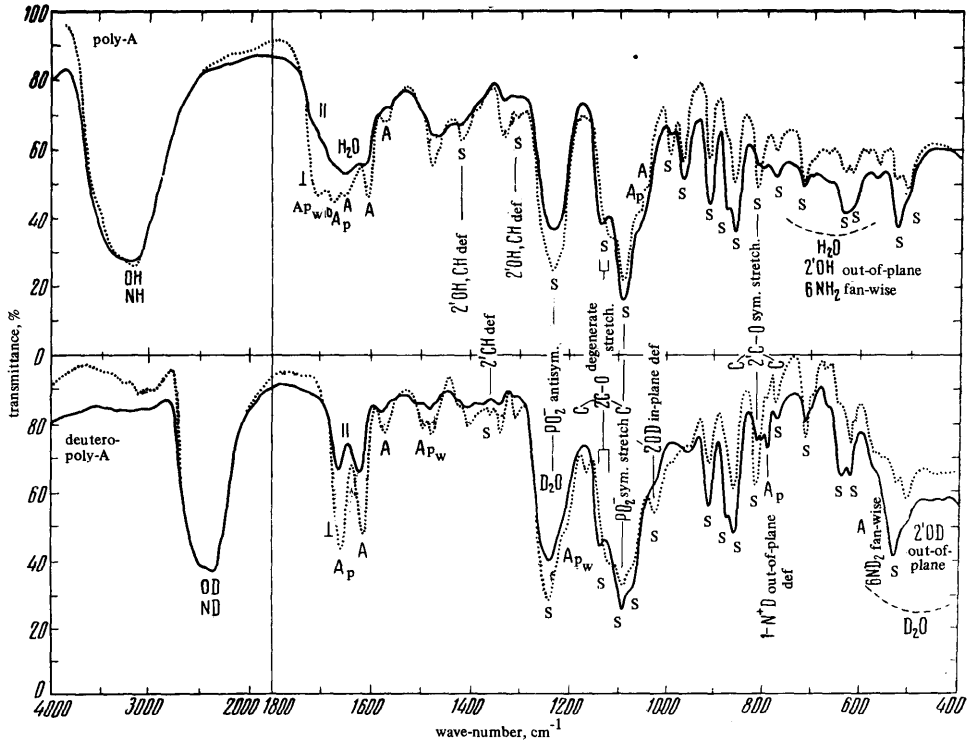


Figure 4. Polarised infrared spectrum of polyriboadenylic acid in the H- and D-forms with a 92% relative moisture content[28]; A—adenine absorption bands; A_p—bands of protonated adenine; A_{pw}—bands disappearing on drying; S—absorption bands due to the vibrations of the molecular skeleton.

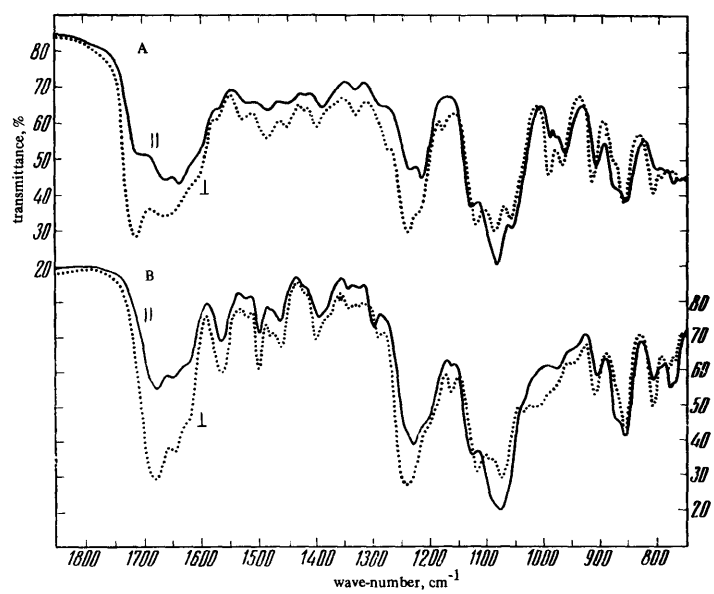


Figure 5. Polarised infrared spectrum of a film of the sodium salt of dwarf rice virus RNA in the H- and D-forms (A and B respectively) for a 75% relative moisture content[27].

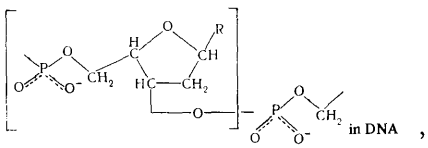
This suggests that both chains in the double helix have identical vibrational spectra and for the analysis of the latter it is sufficient to consider the vibrations of a single chain, formally assuming them to be doubly degenerate.

Summarising the foregoing, one may conclude that the expected vibration spectrum of nucleic acids as polymeric formations is obtained when a single chain of the double helix with a regular structure of the skeleton and a random sequence of the bases is considered.

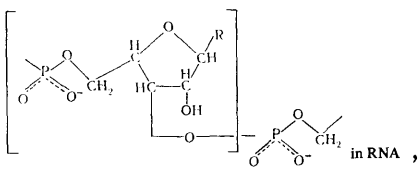
Let us consider the expected vibrational spectrum of the model

$$\underset{M}{\overset{\top}{R}\left[\overset{\top}{R}\right]\overset{\top}{R}},$$

where R is a point mass replacing any of the four bases and M is the monomeric unit which has the following structure:



M = 18 atoms (without R);



M = 19 atoms (without R).

Table 3. The characters, number of normal vibrations, and selection rules for the vibrations of the main DNA chain [rotational axis $C(\pi/5)$].

$C(\pi/5)$	E	C^1	C^2	$C^3 \ldots C^9$	N	Activity	
						i.r.	Raman
A	1	1	1	1...1	3·18—2=52 (T_π, R_π)	act. (∥)	forb.
B	1	—1	1	—1...—1	3·18=54	forb.	act.
E_1	2	$\varepsilon^{\pm1}$	$\varepsilon^{\pm2}$	$\varepsilon^{\pm3}\ldots\varepsilon^{\pm9}$	3·18—1=53 (T_σ)	act. (⊥)	»
E_2	2	$\varepsilon^{\pm2}$	$\varepsilon^{\pm4}$	$\varepsilon^{\pm6}\ldots\varepsilon^{\pm18}$	3·18=54	forb.	»
E_3	2	$\varepsilon^{\pm3}$	$\varepsilon^{\pm6}$	$\varepsilon^{\pm9}\ldots\varepsilon^{\pm27}$	54	»	forb.
E_4	2	$\varepsilon^{\pm4}$	$\varepsilon^{\pm8}$	$\varepsilon^{\pm12}\ldots\varepsilon^{\pm36}$	54	»	»

Note. i.r.—infrared spectrum; N—number of normal vibrations; act.—active vibrations; forb.—forbidden vibrations; T—pure translations of the entire chain parallel (π) and at right angles (σ) to its axis; R_π—rotation of the chain as a whole about the corresponding axis; C^K—rotation by an angle $K\omega$; $\omega = 2\pi/10$; $\epsilon = \exp[i(2\pi/10)]$.

This model probably constitutes a satisfactory first approximation, since here only those skeletal vibrations which are appreciably "mixed" with the vibrations of the bases are distorted.

Assuming the chains of the model to be infinitely long and regular macromolecules, the structure of which may be formulated as $-[M_i]_\infty-$, where M_i is a repeating chain unit, we can derive the general form of the vibrational spectra of such systems. The structure of model chains of this kind belongs to a one-dimensional space group with a $C(\pi/5)$ rotational axis, which is isomorphous with the C_5 point group [61,62]. Table 3 lists the characters, the number of normal vibrations, and the selection rules for the main DNA chain. For viral RNA containing 10 nucleotides per turn of the helix, the factor group remains the same and the characteristics of the spectra are as follows

M=20 (including R)
A=3·20—2=58 (∥) (i.r.)
B=60 (Raman)
E_1 = 59 (⊥) (i.r., Raman)
E_2=60 (Raman)
E_3 = 60, E_4 = 60 } forbidden (i.r., Raman)

The double helix of poly-A has a $C(\pi/2)$ rotational axis, M = 32 (chain unit together with adenine), and the following normal vibrations:

A=3·32—2=94
B=96
E_1=95
E_2=96

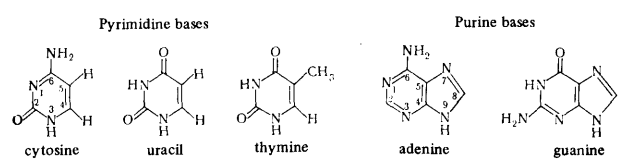
Examination of this model shows immediately that the total number of bands in the real infrared spectra of nucleic acids is less than expected. This finding may be due to several causes: (1) the low intensity of a number of bands; (2) the existence of numerous bands below 400 cm^{-1}; (3) the irregular structure of the molecules, which leads to a broadening of the bands and a pseudo-simplification of the overall pattern.

IV. VIBRATIONS OF NUCLEIC ACID BASES

As stated above, the theoretical calculation of the normal vibrations of nucleic acid bases is difficult owing to the complexity of their structures and very few studies have been made on this problem. Kanaskova [63] calculated the frequencies and the forms of the normal vibrations of free pyrimidine, imidazole, and purine on the basis of the valence force fields of these molecules.

1. Spectra of the Free Bases

The nucleic acid bases are aminoketo-derivatives of purine and pyrimidine—heterocycles containing ring nitrogen atoms.



The problem of the keto–enol and amine–imine tautomerism of the bases in the solid phase was already solved by infrared spectroscopy in the early investigations [29,64-73]. The molecules of the bases lack elements of symmetry and according to crystallographic data [74-81] have a planar configuration. The principal characteristics of the crystals are presented in Table 4.

According to the selection rules [62], all 3N-6 normal vibrations should be active in the infrared spectra of the free nucleic acid bases (30 for uracil, 33 for cytosine, 36 for adenine, 39 for thymine, and 42 for guanine).

The infrared spectra of nucleic acid bases, nucleosides, (base + sugar), and nucleotides (nucleoside phosphates), which are components of the DNA and RNA polynucleotide chains, have been quoted in a number of studies [24,30,32,33,70-72,82-96], where the absorption bands were also assigned.

In the majority of the investigations measurements were made of the spectra of these compounds in the solid phase (potassium bromide discs or mulls) in the light or deuterated forms in the range 4000–700 cm^{-1}, the spectra of the D_2O solutions having been obtained in only a few cases [14,31,35,97-101] over a narrow range (1700–1500 cm^{-1}). The spectra of the bases and nucleosides in the solid phase consist as a rule of narrow well resolved bands (Figs. 6 and 7).

Table 4. Crystallographic characteristics of the nucleic acid bases [74-77,81].

Base	C	U	T	A	G
Cell	orthorhombic	monoclinic	—	monoclinic	monoclinic
Space group	$P_{2_12_12_1}$	P_{2_1}	$P_{2_1/C}$	P_{2_1}	P_{2_1}
No. of molecules in cell	4	4	4	2	2

For the isolated nucleic acid bases, one may expect the occurrence of intense bands due to the stretching vibrations of NH, NH_2, and CH groups in the range 3500 to 2000 cm^{-1} and intense vibration bands of the carbonyl groups, moderately intense bands of the double bond vibrations in the rings of the bases, and deformation vibration bands of the NH and NH_2 group in the range 1800 to 1500 cm^{-1}; in the range 1500–1000 cm^{-1}, one should expect bands of moderate and low intensity associated with the vibrations of the single C–C and C–N bonds, the deformation vibrations of the C–H and N–H bonds, and the skeletal vibrations of the bases; in the range 1000 to 700 cm^{-1}, there should be weak bands due to the out-of-plane deformation vibrations of the NH and CH groups. The infrared spectra of nucleic acid bases are presented in Figs. 6–8; the positions and assignments of the fundamental absorption bands are given in Tables 2, 5, and 6.

The spectrum of cytosine (Fig. 7) shows intense stretching vibration bands of the amino-group at 3367 and 3155 cm^{-1}, an N–H stretching vibration band at 2778 cm^{-1}, which is displaced on deuteration towards lower frequencies, and moderately intense bands associated with the stretching vibrations of the C–H bonds at 3081 and 2948 cm^{-1}, the positions of which are unaffected by deuteration [29,30,32,104]. Indeed, the rate of isotope exchange involving the hydrogen atoms of the DNA bases has been investigated by infrared spectroscopy and other methods and it has been shown that the H atoms in the NH and NH_2 groups are exchanged almost instantaneously, while the exchange in the CH groups is very slow [17,18,103,105-116]. The stretching vibration frequencies of the amino- and imino-groups of the bases show that in both solutions and crystals there are hydrogen bonds between the bases [76,79-81].

The stretching vibration bands of the double bonds of the bases can be conveniently observed in the spectra of the deuterated forms (Fig. 8), since the NH_2 and NH deformation vibration bands, which overlap them, are then displaced towards longer wavelengths. At the same time there is also a bathochromic shift of the band due to the double bonds, which reflects the occurrence of an interaction between the deformation vibrations of the NH and NH_2 groups on the one hand and the vibrations of the rings double bonds and the C=O groups on the other [10,31]. This type of shift is observed, for example, in the spectrum of a D_2O solution of cytosine for the bands due to the $C_{(6)}$=N and C=C bonds adjoining the amino-group (Table 5). The C=C vibrations and the NH_2 deformation vibrations in the light form of cytosine in the solid phase give rise to two bands in the form of a doublet (1655 and 1667 cm^{-1} respectively). The wave-numbers corresponding to the double bond vibration frequencies of cytosine (1655 cm^{-1} for C=O, 1630 cm^{-1} for C=N, and 1621 cm^{-1} for C=C) are reduced, probably owing to conjugation.

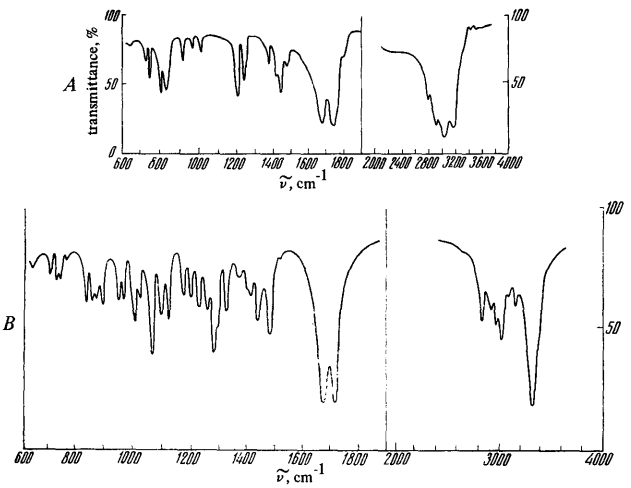


Figure 6. Infrared spectra of solid thymine (A) and thymidine (B) in a neutral medium.

The cytosine ring vibrations are reflected in the spectrum by bands at 1527 and 1365 cm^{-1}, close to the characteristic absorption bands of the pyrimidine ring (1565, 1462, and 1397 cm^{-1}) [89], which have not been assigned to the vibrations of the individual bonds in the ring. These bands and also those at 1236 and 794 cm^{-1} are active in the Raman spectra of cytosine [103].

Substituents in the N_3 position of pyrimidines and the $N_{(9)}$ position of purines in general influence the vibration frequencies of the bases. However, the addition of deoxyribose or ribose leads to only insignificant shifts in the bases. The spectra of nucleosides are complicated owing to the appearance of the sugar absorption bands: bands due to the stretching vibrations of the OH and CH bonds in the range 3700–2000 cm^{-1}, the deformation vibrations of the hydroxy-groups in the range 1350–1110 cm^{-1}, and the vibrations of the ribose ring in the range 1110–900 cm^{-1} (Fig. 6) [10,29,32]. The characteristic bands of the phosphate group (1220 and 1089 cm^{-1}) appear in the spectra of nucleotides and in the case of cytidylic and adenylic acids there are very significant displacements of the bands of the bases owing to the formation of zwitter-ions (a negative charge at the phosphate group and a positive charge at the base) [29,32].

Uracil and thymine, which have similar molecular structures, also have similar infrared spectra (Figs. 6 and 7). Each base has two carbonyl groups, the C_6=O group conjugated with the C=C bond and the $C_{(2)}$=O group

Table 5. Absorption bands of the free bases in infrared and Raman spectra.

Cytosine							Uracil							Thymine	
i.r.[10, 29–31, 33, 35, 82, 97, 98]			Raman [103]				i.r.[10, 29, 31, 33, 34]			Raman [103]				i.r.[14, 33]	
solid phase	solid phase after deuteration	D_2O* pD 7	solid phase	H_2O pH 7	D_2O pD 7	assignment	solid phase	solid phase after deuteration	D_2O* pD 7	solid phase	H_2O pH 7	D_2O pD 7	assignment	solid phase	assignment
3367 s.	3078 m.	—	—	—	—	$\nu_{as}\,NH_2$	3110 s.	3065 m.	—	—	—	—	$\nu\,N_3H$	3175 s.	ν NH
	2940 m.														
3115 s.	2525 s.	—	—	—	—	$\nu_s\,NH_2$	3100 s.	2400 w.					ν CH	3035 s.	$\nu_{as}\,CH_3$
3081 m.															
2948 m.	2320 s.					ν CH	2924 s.	2268 s.					$\nu\,N_1H$	2900 s.	$\nu_s\,CH_3$
2778 m.	2155 s.					ν NH		2135 s.		1710 w.				2780 m.	ν CH
							1724 s.	1712 s.	1690 s.	1662 m.	1680 m.	1690 m.	ν C=O	1735 s.	ν C=O
1667 s.	1680 w.					$\delta\,NH_2$	1680 m.	1690 s.	1655 s.	1655 m.	1640 m.	1650 m.	ν C=O	1670 s.	ν C=O
1655 m.		1652 s.	1660 m.	1660 w.	1650 w.	ν C=O	1666 s.	1640 s.					δ NH		
1630 m.	1637 s.	1615 m.	1635 w.		1610 m.	ν C=N	1623 w.	1630 w.	1620 w.	1620 w.		1633 w.	ν C=C	1640 m.	ν C=C
1621 w.	1605 s.	1582 w.				ν C=C									
								1565 w.	1582 w.	1580 w.				1570 m.	δ NH
1595 m.			1575 w.						1527 s.					1540 m.	
1538 m.	1548 w.					$\delta\,N_3H$	1508 m.	1475 s.	1504 s.			1500 w.		1500 m.	$\delta\,CH_3$
1527 w.		1527 w.	1540 w.	1530 w.	1510 w.	ring	1451 s.	1475 s.		1460 w.			ring	1380 w.	$\beta\,CH_3$
1506 w.	1502 s.	1504 s.	1500 w.			»									
1458 s.				1440 w.		$\beta\,NH_2$	1418 s.	1422 w.		1423 w.	1425 w.		β NH	1245 m.	ν C—CH_3
1362 s.	1374 s.	1365	1366 w.	1365 w.	1388 w.	ring	1389 s.	1390 w.			1390 w.		β NH	1200 m.	
1275 s.	1279 m.		1278 s.	1290 s.	1290 s.	ν C—NH_2	1238 s.	1230 w.		1237 s.	1235 s.	1270 s.	ring	1040 w.	ν C—C
1236 w.	1235 w.		1255 w.	1228 w.		ring	1099 w.	1140 s.		1105 w.		1158 w.	ν C—N	1000 w.	
1156 w.	1178 w.		1125 w.		1140 w.	ν C—N	1004 s.			1011 w.				945 w.	
							994 s.	980 s.		987 w.				900 w.	
1011 w.	1046 w.		1010 w.				851 m.	882 m.						835 m.	
995 w.	978 w.		965 w.	975 w.	980 w.	ν C—C	822 s.	820 s.				815 w.	β NH	800 m.	β NH
823 m.			820 w.			$\beta\,N_3H$	780 w.			781 s.		783 m.	ring	740 m.	
794 s.	787 s.		794 s.	787 s.	777 s.	ring	760 m.						β NH	705 w.	
784 w.	771 w.					β CH		733 w.		580 w.					

*Nucleoside.

Table 6. Absorption bands of the free bases in infrared and Raman spectra.

Adenine							Guanine					
i.r.[10, 29, 31, 32, 104]			Raman [103]				i.r.[10, 29, 31, 32]			Raman [103]		
solid phase	solid phase after deuteration	D_2O* pD 7	solid phase	H_2O pH 7	D_2O pD 7	assignment	solid phase	solid phase after deuteration	D_2O* pD 0,5	H_2O pH 0,5	D_2O pD 0,5	assignment
3280 m.						$\nu_{as}\,NH_2$	3310 s.	3300 s.				$\nu_{as}\,NH_2$
3105 s.	3096 w.					$\nu_s\,NH_2$	3077 s.	3086 s.				$\nu_s\,NH_2$
3000 w.	2463 m.					ν NH	2840 s.	2872 m.				ν NH
								2688 m.				
2780 w.	2288 s.					ν CH	2680 s.	2494 m.				ν CH
								2278 s.				
2680 w.	2155 m.						1701 s.	1695 s.	1690 s.	1685 w.	1680 w.	ν C=O
1672 s.	1675 w.					$\delta\,NH_2$	1681 s.	1678 w.				$\delta\,NH_2$
1605 m.	1610 s.	1627 s.	1600 w.		1613 w.	ν C=N	1639 w.	1616 s.	1609 m.			ν C=N
1578 m.	1575 s.	1578 m.		1585 m.	1563 m.	ν C=C	1569 m.	1565 m.	1578 s.			ν C=C
1510 w.	1510 s.		1530 w.	1512 m.	1512 m.	ring	1555 m.		1568 w.	1541 w.	1525 w.	δ NH
	1475 m.	1484 w.	1485 m.	1490 w.	1480		1477 m.	1475 m.		1489 s.	1480 s.	ring
1451 m.	1460 m.		1462 w.			$\beta\,NH_2$	1464 m.	1460 m.				δ CH
1418 m.	1420 m.			1425 w.	1435 s.	ring	1418 m.	1418 w.		1412 w.	1400 w.	$\beta\,NH_2$
1368 w.	1375 m.		1370 w.	1380 m.	1350 m.	»	1375 s.	1364 s.		1372 m.	1360 w.	ring
1333 m.	1335 s.		1332 s.	1340 s.	1328 s.	»	1263 s.	1261 w.		1240 w.		νC—NH_2
1305 m.	1310 s.		1312 w.	1310 m.			1215 w.	1215 w.				
1250 m.	1250 w.		1252 m.	1253 w.	1238 w.	β NH	1172 s.	1167 m.		1175 w.	1176 w.	β NH
1215 m.	1226 w.		1225 w.	1216 w.		ν C—NH_2	949 s.	948 w.		1080 w.		$\beta\,NH_2$
1124 m.	1130 w.		1130 w.			ν C—N	877 m.	876 w.		1025 w.		β NH
1022 m.	1010 w.		1025 w.	1010 w.		$\beta\,NH_2$	851 s.	850 m.				
							789 w.					β CH
938 m.	935 m.		945 m.			ν C—C	776 s.	776 m.				β NH
870 w.	855 w.		870 w.	870 w.		$\beta\,N_9H$	703 m.					β CH
847 m.							689 m.	687 w.				β NH
797 m.	796 w.			800 w.		$\beta\,NH_2$						
722 m.	720 w.		725 m.	733 m.	724 w.	ring						

*Nucleoside.

located between the imino-groups. The effect of the environment on the carbonyl groups in both positions should lead to a lowering of their vibration frequencies compared with the characteristic vibration frequencies of the carbonyl group in ketones (in the range 1725–1705 cm^{-1}). Indeed the vibration frequency of the C=O group in imidazolone corresponds to 1684 cm^{-1}.[108] However, two bands at 1735 and 1670 cm^{-1} appear in the spectrum of crystalline uracil[29,32,33], the wave-number of the first being higher than expected. The 1670 cm^{-1} band has been assigned to the vibrations of the $C_{(6)}$=O group conjugated with the C=C bond and the 1730 cm^{-1} band has been assigned to the vibrations of the $C_{(2)}$=O group[29,31–33]. Probably there is an interaction between the carbonyl groups in the uracil and thymine molecules of the type known for dicarbonyl compounds, which leads to a displacement of the vibration frequency of one of the groups towards higher values[109]. It is also possible that the increase of the vibration frequency of the $C_{(2)}$=O group is due to its combination with the N_1H bond vibrations.

Sukhorukov et al.[33] determined the multiplicity n and the length r of the bonds of the carbonyl groups of uracil from

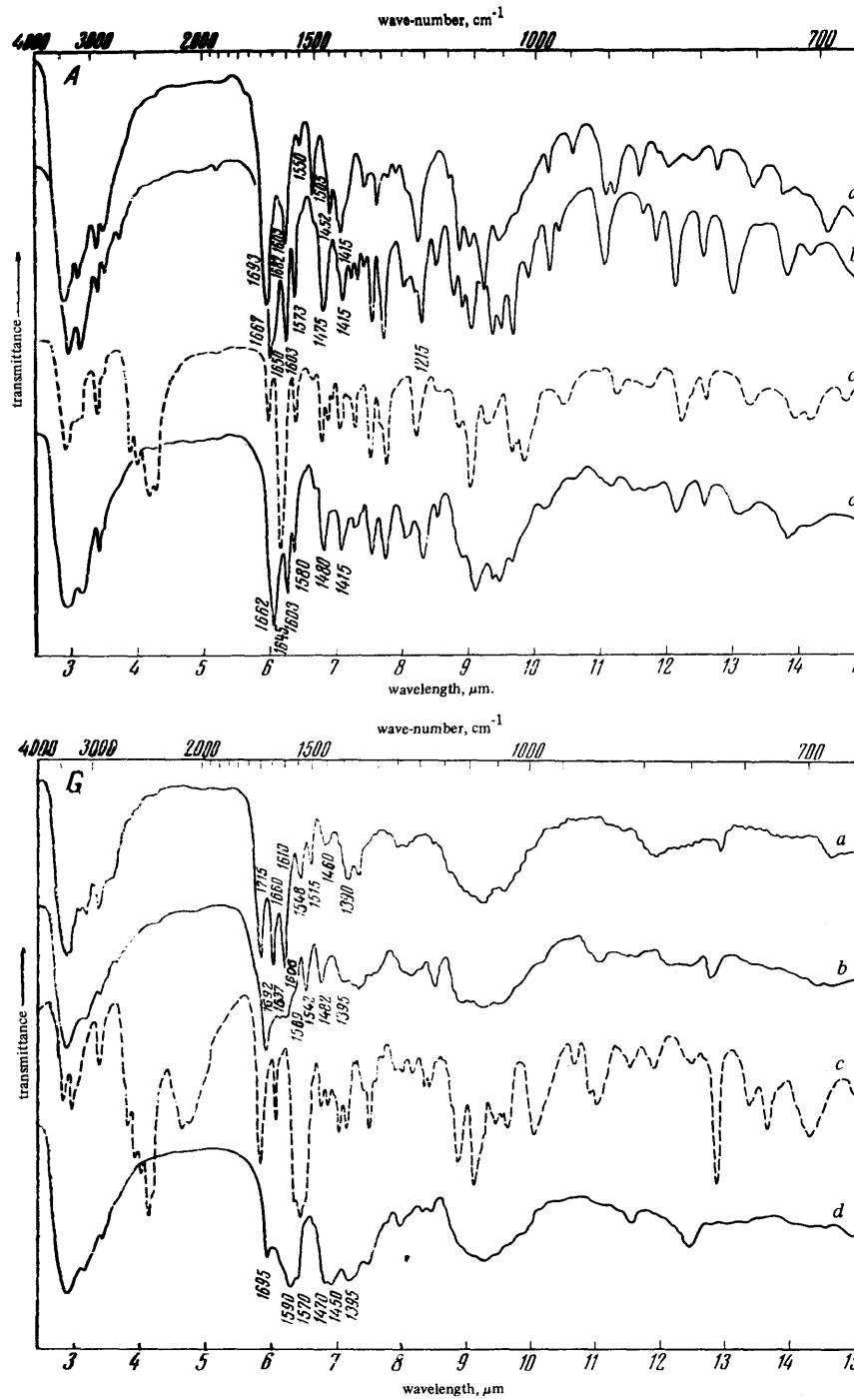


Figure 7. Infrared spectra of solid nucleosides[31]:
a) from an acid solution in H_2O; *b*) from a neutral solution in H_2O;

their vibration frequencies in the infrared spectrum and the empirical relations between these quantities quoted in the literature[110,111]. The vibration frequency of the $C_{(2)}$=O group (wave-number 1735 cm^{-1}) corresponds to $n = 2.07$ and $r = 1.225$ Å, while that of the $C_{(6)}$=O group (1670 cm^{-1}) corresponds to $n = 1.85$ and $r = 1.241$ Å; the values of r obtained agree satisfactorily with the X-ray diffraction data[80]. The intense 1451 and 1238 cm^{-1} bands and the weak 780 cm^{-1} bands have been assigned to the vibrations of the uracil rings coupled with deformation vibrations of the NH bonds.

The spectrum of thymine differs from that of uracil mainly by the presence of bands corresponding to the stretching and deformation vibrations of the methyl group.

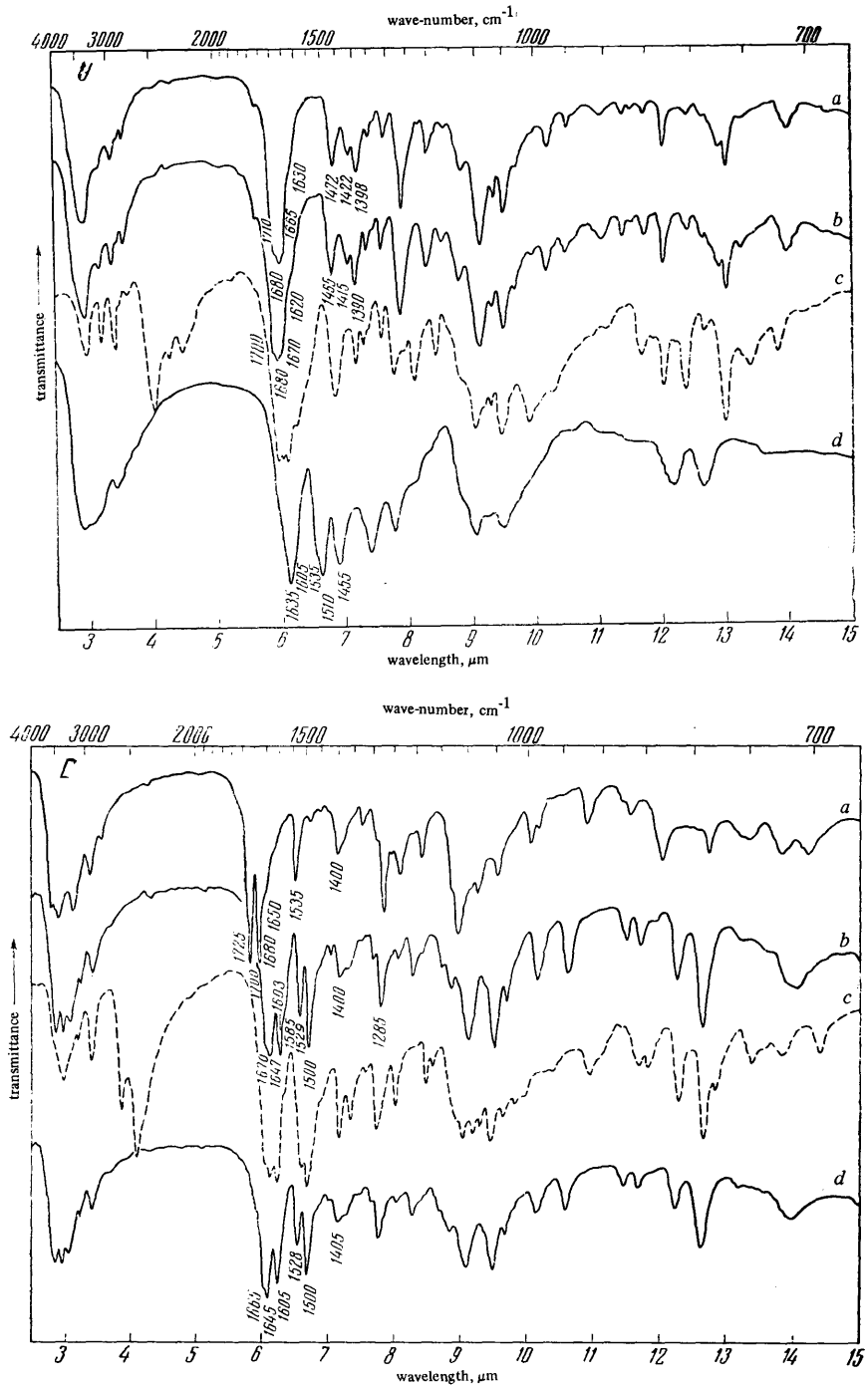


Figure 7 continued. Infrared spectra of solid nucleosides[31]:
c) from a neutral solution in D_2O; *d*) from an alkaline solution in H_2O.

In the low-frequency part of the spectrum (700 to 200 cm^{-1}), polysubstituted pyrimidines have two intense absorption bands at 525 ± 25 and 450 ± 25 cm^{-1}, corresponding to the out-of-plane and in-plane deformation vibrations of the pyrimidine ring[111-115]. The 450 cm^{-1} band can serve for identification, since its position is not affected by substituents. The position of the band due to the out-of-plane vibrations of the pyrimidine ring (525 ± 25 cm^{-1}) depends on the mass of the substituent (NH_2, OH, SH, and $S-CH_3$ groups), the relation being linear[116].

Guanine has a structure similar to that of cytosine. However, the vibration frequency of its carbonyl group

(wave-number 1700 cm^{-1}) is much higher than in cytosine (1655 cm^{-1}) and higher than the expected vibration frequency of the C=O group conjugated with the C=C double bond. Intense bands characteristic of the purine ring have been observed in the guanine spectrum[88]: 1639 (C=N), 1567 (C=C), 1518, 1477, and 1375 cm^{-1}.[29,31,32] The deuteration of guanine is accompanied by a slight decrease of the C=O and C=N bond frequencies, which may be evidence of a slight interaction of their vibrations with those of the NH and NH_2 groups.

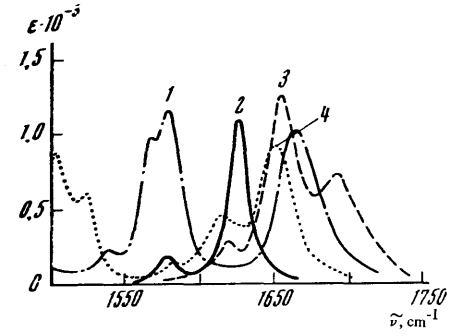


Figure 8. Infrared spectra of D_2O solutions of nucleotides: 1) guanine; 2) adenine; 3) uracil; 4) cytosine; pD 7 (Thomas[102]); ε—molar extinction coefficient.

Adenine is the only base without a carbonyl group. Its amino-group gives rise to intense bands at 3280 and 3105 cm^{-1} (ν) and at 1672, 1451, 1022, and 797 cm^{-1} ($\beta + \delta$).[29,32,65] The vibrations of the amino-group interact strongly with those of the adjacent C=N bonds, as a result of which the wave-number of the latter increases on deuteration of adenine from 1605 to 1627 cm^{-1}.[59] Since the structure of adenine differs from that of purine only by the presence of a single substituent, its spectrum shows six characteristic bands due to the skeletal vibrations of purine: at 1605 (C=N), 1575 (C=C), 1510, 1458, 1418, and 1368 cm^{-1}.[10,29,32,97] The C=C bond stretching vibration band usually has a low intensity in infrared spectra, but in the adenine spectrum it is fairly intense, possibly owing to the aromatic nature of the ring of this base.

In a study of the effect of temperature on the infrared spectra of the crystalline bases, Sukhorukov, Kanaskova, Pentin, and coworkers[33,63,117,118] observed that, in the spectra of imidazole, purine, and a number of their derivatives in the range between −160° and 100°C, the bands due to the out-of-plane NH and NH_2 deformation vibrations are the most sensitive to changes in temperature. It was shown that the temperature variation of the frequencies of the out-of-plane vibrations is in all cases linear and may be described by the equation $\nu_{o.o.p.} = A - BT$, where A and B are constants characteristic of each compound. In this connection a method was proposed for the identification of the out-of-plane deformation vibration frequencies of the NH and NH_2 groups of nitrogeneous bases, called the temperature shift method[63,117]. The author used this method to identify a number of bands in the infrared spectra of adenine and its N-methyl derivatives. On the other hand, it was shown that the frequency shift of the proton-donating NH and NH_2 groups depends on the length of the hydrogen bonds (r) formed by them: $B = 0.93 - 0.29r$ (for NH) and $B = 0.83 - 0.27r$ (for NH_2). The temperature shift method proposed makes it possible to distinguish the NH and NH_2 deformation vibration bands and, when combined with other methods, allows a more reliable determination of the structure of the bases in the crystalline state.

The Raman spectra of the free bases and nucleosides in the solid phase and in solution were measured by Lord and Thomas[103]. The frequencies in this spectra are listed in Tables 5 and 6.

The NH and NH_2 deformation vibration bands in the Raman spectra are very weak or altogether absent, but the double bond and ring vibrations give rise to more intense bands than in the infrared spectra. Ribose and phosphate give rise to very weak Raman bands. In the Raman spectra the bands due to the carbonyl groups and those in the range 800 to 750 cm^{-1} in the spectra of pyrimidines and in the range 730–680 cm^{-1} in the spectra of purines are highly polarised. Bands polarised to a moderate extent are observed in the range 1500–1200 cm^{-1}. The depolarisation ratio is determined by the local planar symmetry of the ring of the base, the in-plane deformation vibrations being polarised and the out-of-plane vibrations depolarised.

2. The Spectra of the Nitrogeneous Bases in Polynucleotides

The main problem in the study of the infrared spectra of polynucleotides is the determination of the specific spectroscopic characteristic of the interaction of the bases forming part of nucleic acids, in contrast to those of the free bases.

When the vibration bands of the bases in polynucleotides and nucleic acids are considered, one should expect shifts of certain frequencies owing to the enhancement of the interaction between the complementary bases, since it is known that the specific interaction of such bases via hydrogen bonds is much stronger than their self-association (see Section VI). Moreover, the dispersion interaction between the π electrons of the bases in the vertical "piles" within the polynucleotide chain may make a definite contribution to the change in the vibration frequencies of the bases.

Assignments of the absorption bands due to the vibrations of specific groups in the bases within nucleic acids are available in the literature only for the stretching vibrations of the NH_2 (3350 and 3210 cm^{-1}), NH (2950 cm^{-1}), and CH (3090 cm^{-1}) groups[10,17-19]. The 1705 cm^{-1} band, characteristic of the spectra of native DNA and RNA preparations, which on deuteration shift towards lower frequencies down to 1685 cm^{-1}, has also been discussed. According to Shimanouchi and coworkers[10,38,39] and also Fritzsche[20], the 1705 cm^{-1} band is associated with the stretching vibrations of the carbonyl groups of the bases interacting with the deformation vibrations of the amino-groups. The frequency of this band is higher than those associated with the vibrations of the carbonyl groups of the free bases (with the exception of one of the groups in thymine and uracil). The increase of the C=O vibration frequency of the bases forming part of nucleic acids is probably due to their involvement in hydrogen bonds between the complementary bases.

There are virtually no assignments in the literature for the remaining absorption bands of the bases in nucleic acids. On the basis of published experimental data, we attempted to make a more detailed assignment of the bands

of the bases in DNA. However, for the majority of the bands in the range 1400–600 cm^{-1} such refinement can be regarded as merely conventional. The results are presented in Table 2. Analysis of the data in Table 2 reveals certain regularities. Thus the position of the C=N band in the DNA spectrum is very close to the positions in the corresponding spectra of the individual bases.

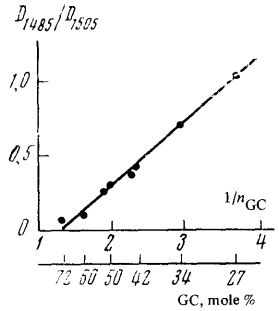


Figure 9. Variation of the ratio of the optical densities of the 1485 and 1505 cm^{-1} bands of deuterated DNA films with $1/n_{GC}$ (n_{GC} = mole fraction of G-C pairs in DNA) [22].

The vibration frequencies of the C=C bonds in the DNA spectrum and in the spectra of free guanine and adenine are almost identical, while in the spectra of free pyrimidines they are somewhat higher. However, the reasons for this effect are so far obscure. The bands due to the in-plane deformation vibrations of the NH_2 and NH groups of the bases are displaced in the DNA spectrum towards lower frequencies compared with the corresponding bands in the spectra of the free bases, which may be caused, as for the C=O groups, by the involvement of the hydrogen atoms of the NH_2 and NH groups in hydrogen bonds. In the remaining parts of the spectrum the vibration frequencies of the bases in nucleic acids are the same as those of the free bases, within the expected limits.

Fritzsche [21,22], who studied the infrared spectra of DNA specimens with different base compositions in the range 1800–1200 cm^{-1}, observed a quantitative linear relation between the intensity ratio of the 1505 and 1485 cm^{-1} bands, which are characteristic of the absorption by guanine and adenine respectively, and the percentage content of the G-C pairs (Fig. 9). He suggested that the infrared spectra of DNA be used for analytical purposes—in order to determine the content of the G-C pairs. In a further development of studies on these lines, Tsuboi et al. [23] measured the infrared spectra of DNA from different species of bacteria with different ratios of the G-C (guanine–cytosine) and A-T (adenine-thymine) base pairs and observed a correlation between the contents of the G-C and A-T pairs and the intensity of the majority of bands in the spectrum. On the basis of these data, they found spectroscopic features characteristic of the presence of the AT and GC base pairs in DNA (listed in Table 7).

Thus the infrared spectrum of DNA does indeed show shifts of certain absorption bands compared with the corresponding bands in the spectra of the free bases and also there are a number of bands characteristic of the AT and GC base pairs.

3. Effect of pH on the Spectra of the Bases

The nucleic acid bases can exist in different ionic forms, since in their molecules there are several sites for proton addition. However, in practice relatively few tautomeric forms are observed, because in many cases protonation is unfavourable on energy grounds. One of the methods for the determination of the site of addition or abstraction of a proton is infrared spectroscopy of the ionic forms of the bases.

Table 7. Absorption bands of DNA bases (92% relative moisture content).

G-C pairs	Deuterated G-C pairs	A-T pairs	Deuterated A-T pairs
1705 s.	1676 s.	1705 s.	1687 s.
			1659 s.
	1648 s.	1636 m.	1638 m.
1609 m.	1623 m.	1605 m.	1618 s.
1576 w.	1576 s.	1574 w.	1571 m.
	1557 m.		
	1537 w.		
1528 m.	1523 w.		
1493 m.	1501 m.	1503 w.	1516 w.
		1477 m.	1476 m.
1456 w.	1453 w.	1450 m.	1458 w.
1444 w.	1439 w.		
1414 w.			
1380 m.	1377 w.	1375 w.	1375 w.
1331 w.	1350 w.	1331 w.	1334 w.
1296 m.	1302 w.	1292 w.	1300 w.
		1276 w.	1153 w.
		932 m.	
893 m.		888 m.	
860 w.	851 w.		
	831 m.	831 m.	834 m.
	797 w.	795 w.	794 w.
778 m.	778 s.	763 w.	773 m.
	727 w.	722 w.	715 w.
	698 w.		

The studies by Sukhorukov [30,32,33,119] and Angell [29] (solid phase), Tsuboi and Shimanouchi [10,31] (solid phase and D_2O solutions), and Sinsheimer et al. [35] (D_2O solutions) were devoted to the elucidation of this problem. The studies showed that, for all the nucleic acid bases, the formation of cations involves a shift of the double bond vibration frequencies towards higher values and the formation of an anion causes a shift towards lower frequencies in both infrared and Raman spectra [31–33,53].

The infrared spectrum of cytidine ($pK = 4.5$) [120] in an acid medium differs considerably from its spectra in neutral and alkaline media (Fig. 10).

The spectrum of protonated cytosine is characterised by an increase of the wave-numbers associated with the C=O bond vibrations (from 1655 to 1680 cm^{-1}) and the vibrations of the NH_2 group (from 1667 to 1725 cm^{-1}). Cytosine may be protonated in two ways: at the amino-group and at the N_1 ring atom. The shift of the absorption bands due to the multiple bonds towards higher frequencies indicates an increase of the multiplicity of the C=O and C=N bonds which is more likely to occur as a result of loss of conjugation following the addition of a proton to the N_1 atom rather than to the amino-group. An analogous shift of the absorption frequencies of the ring double bonds is observed on protonation of pyridine ($C_5H_5NH^+$) but not aniline ($C_6H_5-NH_3^+$). [10,31,32]

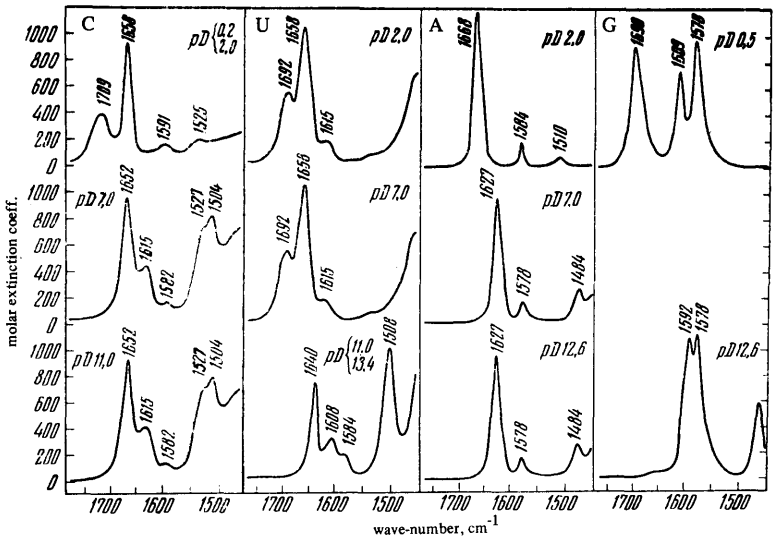


Figure 10. Infrared spectra of D_2O solutions of nucleosides at different pD. [31,100]

A decrease of the intensity of the NH stretching vibration band and a decrease of the frequency of the C=O stretching vibrations (the wave-number decreases from 1680 to 1638 cm^{-1}) are observed in the infrared spectrum of uracil in an alkaline medium ($pK = 9.5$), which is due to the abstraction of a proton from the $N_{(1)}$ or $N_{(3)}$ ring atom and the delocalisation of the electron over the system of conjugated double bonds [31,32]. An empirical relation between the frequency of the stretching vibrations of the carbonyl group and the ionisation potential I, [116]

$$\nu_{C=O} = 29.2\,I + 1409,$$

yields ionisation potentials of 9 and 11 eV for frequencies corresponding to wave-numbers of 1670 and 1735 cm^{-1} respectively; the ionisation potential of the ionic form of uracil is reduced to 7.8 eV; [33] however, all these data require confirmation by independent methods.

In highly alkaline solutions of thymine ($pK = 9.8$), one of the carbonyl groups is enolised and the corresponding band disappears from its infrared spectrum. The remaining bands are displaced towards lower wave-numbers (1735, 1670, 1640, and 1570 cm^{-1} bands in a neutral medium and 1650, 1600, and 1580 cm^{-1} bands in an alkaline medium) [14,98].

The formation of the adenine anion in an alkaline medium ($pK_2 = 9.8$) is accompanied by the disappearance from its infrared spectrum of the band associated with the $N_{(9)}H$ bond, which indicates unambiguously the site of abstraction of the proton from the imidazole ring of adenine [29,32]. In infrared spectra of protonated adenine ($pK_1 = 4.1$), in both the solid phase and in solution, the frequencies of the ring vibrations are enhanced, including the vibrations of the $N_{(1)}=C_{(6)}$ bond (the wave-number increases from 1626 to 1668 cm^{-1} in D_2O solution) [32]. This is most likely to occur as a result of the addition of a proton to the ring $N_{(1)}$ atom rather than to the amino-group. Indeed, it has been shown by X-ray diffraction that in crystalline adenine hydrochloride the proton is located at the ring $N_{(1)}$ atom [121].

As for the remaining bases, the protonation of guanine ($pK_1 = 1.6$) is accompanied by a general shift of the absorption bands in the range 1700–1400 cm^{-1} towards higher frequencies, including the NH_2 deformation vibration band (from 1681 to 1718 cm^{-1}) and resembles the frequency shift on protonation of pyridine (Fig. 10). [12,13,31,32,101] According to crystallographic [75] and NMR [122] data and Pullman's calculations [123], guanine is protonated at the ring $N_{(7)}$ atom and infrared spectroscopic data [31,101,124] are consistent with this postulate. A shift of pH to the alkaline region lowers the intensity of the absorption band due to the guanine carbonyl group ($pK_2 = 9.4$) and gives rise to new absorption bands at 1638 and 1413 cm^{-1}. [31,101] The spectrum of an alkaline solution of guanine resembles that of 2-amino-6-methoxypurine. Probably these changes in the infrared spectrum of guanine are caused by the abstraction of a proton and a redistribution of the charge, resulting in a decrease of the multiplicity of the C=O bond and in increase of electron density at the guanine oxygen atom [31].

The purine and pyrimidine bases may exist in solution in various tautomeric forms, and a different form may predominate than in the solid phase. Miles and coworkers [31,97–101,109] solved this problem by comparing the infrared spectra of D_2O solutions of the bases with those of solutions of model compounds, in which a particular structural element is fixed. For example, *N*-dimethylcytosine and 1-methyl-2-oxopyrimidine served as model compounds for cytosine and 1,9-dimethylguanine and 2-amino-6-methoxypurine were used for guanine. Thus it was shown that the aminoketo-form predominates in cytosine and guanine solutions, the amino-form in adenine solutions, and the diketo-form in uracil and thymine solutions, this being confirmed by NMR data [125].

Thus the study of the spectroscopic changes in the infrared region as the pH of the medium is varied makes it possible to determine the site of abstraction or addition of the proton in purine and pyrimidine bases. Measurements of the infrared spectra of solutions of the bases also make it possible to establish the dominant tautomeric form of the base.

V. INFRARED SPECTROSCOPIC STUDY OF THE SECONDARY STRUCTURE OF NUCLEIC ACIDS

According to the model of Watson and Crick[4,5], the secondary DNA structure consists of a double helix with antiparallel chains (stable in both the crystalline state and in solution[126,127]) stabilised by hydrogen bonds as well as van der Waals forces. The disruption of the DNA helix and the separation of its chains (denaturation) occur both on heating and under the action of acids and alkalies.

The study of the secondary structures of DNA and RNA is one of the most important tasks in molecular biology. In the study of the secondary structure of nucleic acids, X-ray diffraction has hitherto played the main role and infrared spectroscopy an auxiliary role. However, in the study of DNA and RNA structures in solutions, the infrared spectroscopic method has many advantages and yields important information when combined with other methods—hydrodynamic and optical methods and low-angle X-ray scattering[126-129].

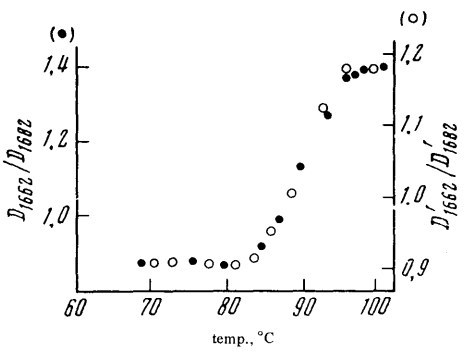


Figure 11. Temperature variation of the ratio of the optical densities of the 1662 and 1682 cm^{-1} bands of D_2O solutions of DNA; 10 mg ml^{-1} of DNA in 0.15 M KCl.[20]

In the infrared spectra of native DNA (in solution or in a film), an intense absorption band, characteristic of its secondary structure, was found; it is located at 1705 cm^{-1} for the light form and at 1685 cm^{-1} for the deuterated form of DNA.[15,20,23,38,37,130] On denaturation, the band is displaced towards lower wave-numbers, for example, from 1685 to 1660 cm^{-1}. The fact that the 1705 (1685) cm^{-1} band is characteristic of the secondary DNA structure has been confirmed by a study of the effect of temperature on its intensity. The curve relating the relative intensities of the 1662 and 1682 cm^{-1} bands to temperature (Fig. 11) resembles the melting curve for DNA in measurements of ultraviolet absorption in the region of 260 nm.[20,39] It has been shown[131] that the temperature variation of the intensity of the maxima in the difference spectra of D_2O solutions of DNA, corresponding to the DNA absorption bands in the region 1700–1550 cm^{-1}, also agrees with the melting curve. This makes it possible to follow the "helix–coil" thermal transition on the basis of the vibrational spectra of DNA solutions and to determine fairly accurately the melting point of the DNA solution (T_{fu}) and the width of the transition (ΔT_{fu}). In contrast to measurements of T_{fu}, ultraviolet spectroscopy, or measurements of the viscosity of DNA solutions, the infrared spectroscopic method makes it possible to determine the melting points of concentrated and gel-like DNA solutions.

At present it is not yet clear why the above bands are sensitive to changes in the secondary DNA structure: whether they are due to changes in the interaction between the two chains or arise in consequence of a breakdown of regularity. However, there is no doubt about the practical usefulness of such data.

Classical X-ray diffraction studies on crystalline DNA specimens[58,59,132] showed that the DNA helix can have different conformations depending on the degree of hydration. The sodium salt of DNA can exist in the B-form, which is stable when the relative moisture content is in excess of 92%, and the A-form is stable for a 75% relative moisture content[58,59,132]. The lithium salt of DNA also has two conformations: the B-form for a relative moisture content in excess of 66% and the C-form for a relative moisture content in the range 44–66%.[139] Further decrease of the water content leads to a gradual disordering of the DNA structure. These conformations of the DNA helix differ from one another in their parameters and the orientation of the bases.

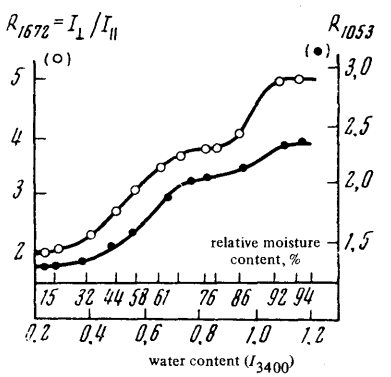


Figure 12. Variation of the dichroic ratios R_{1672} and R_{1053} with the water content in oriented DNA films[18].

The study of the infrared spectra of DNA confirmed and extended the X-ray diffraction data for the conformational transitions in DNA. Bradbury et al.[18] investigated the dependence of the polarisation of a number of absorption bands on the relative moisture content of oriented specimens of the sodium and lithium salts of DNA. A constant dichroic ratio R for the 1672 and 1053 cm^{-1} bands in the relative moisture content ranges corresponding to the stability of the B- and A-forms of DNA, namely above 90% and between 80 and 70%, has been observed for the sodium salt of DNA (Fig. 12). For the lithium salt of DNA, a plateau of this kind was observed on the curve relating R_{1670} to the relative moisture content in other ranges: above 66% and between 56 and 44% for the B- and C-forms respectively. It has been shown[18,134] that, for each conformation of the sodium salt of DNA, there is a characteristic frequency of the antisymmetric vibrations of the phosphate group (two plateaus on the frequency–moisture content curves for this band).

Sutherland and Tsuboi[17] and Falk et al.[19], who carried out similar investigations, also observed an increase of the dichroic ratio of the absorption bands due to the rings of the bases in the sodium salt of DNA with increasing water content in the specimen, but the curves are of a different type, which does not yield a clear proof of the interconversion of the A- and B-forms of DNA. Nevertheless these results show that an ordered helical DNA structure depends on the amount of adsorbed water and its partial dehydration leads to a considerable disorganisation of the molecular structure.

Quite recently Webb and Buther[135] succeeded in finding by the infrared spectroscopic method the structural characteristics of tumour DNA isolated from the tissue of Rous sarcoma and the mammary gland carcinoma in mice[135]. They observed that the tumour DNA is less hydrated for higher values of the relative moisture content and more hydrated for low values than DNA from normal tissues and that the dichroic ratio for tumour DNA is smaller than for normal DNA, remaining constant for relative moisture contents in the range 92–45%. They interpret the infrared spectroscopic data as evidence that the structure of the tumour DNA is intermediate between the B- and A-forms and does not alter for moderate degrees of dehydration.

The study of the vibrational structure of DNA spectra using polarised radiation yielded information about the orientation of its structural elements. Thus the knowledge of the dichroic ratio for the 1670 cm^{-1} band for relative moisture contents of 92 and 75% makes it possible to determine the orientation of the planes of the bases in the A-form of DNA on the hypothesis that in the B-form they are perpendicular to the axis of the helix. The results of such calculations show that in the A-form the planes of the bases deviate from the vertical orientation by 13–15°.[17,18] Measurement of the dichroism of the 1220 and 1089 cm^{-1} bands also permits the calculation of the orientation of the phosphate groups, since it is known that the transition moment of their antisymmetrical vibrations is directed along the O...O line and that of the symmetrical vibrations lies along the bisector of the OPO angle. It has been shown[17,18] that in both the A- and B-forms of DNA the O...O line is inclined to the axis of the spiral by 50–60° and the bisector of the OPO angle is perpendicular to the molecular axis. However, this conclusion is valid only when the form of the vibrations is highly characteristic. But, since the vibrations of the phosphate group are undoubtedly appreciably mixed with other skeletal vibrations, the angles of the orientation of this group in DNA must be assumed to be only approximate. The experimentally observed orientation of the PO_2^- groups in DNA contradicts the Watson–Crick model[4,5], according to which in the B-form of DNA the O...O line is perpendicular to the axis of the helix and the bisector of the OPO angle is parallel to it.

In order to investigate the hydration processes of DNA macromolecules, it is important to elucidate the sequence of the hydration of the structural elements of DNA (bases, deoxyribose, and phosphate groups), which can be achieved with the aid of infrared spectra, since changes in the relative moisture content involve shifts of the absorption bands associated with these structural elements. Thus an increase of the relative moisture content from 0 to 92% causes a shift of the carbonyl band of the DNA bases from 1705 to 1715 cm^{-1}, of the PO_2^- band from 1240 to 1220 cm^{-1}, and of the C–O band of deoxyribose from 1066 to 1053 cm^{-1}.[17,19] By studying the variation of the spectroscopic shifts with the moisture content of the DNA specimens, Falk et al.[19] established that the phosphate groups of DNA are hydrated when the relative moisture content is in the range 0–66% (six water molecules per phosphate group for a 66% relative moisture content), while above 66% the hydration of the bases begins. It has not yet been possible to elucidate the relation between the transition from the A-form to the B-form and the characteristics of the adsorption of water. The positions of the water bands in the infrared absorption spectrum of DNA show that all the adsorbed water layers except the first have a structure similar to that of liquid water[16,137]. Therefore the amount of water adsorbed by the DNA film may be calculated from the intensity of the 3400 cm^{-1} band, assuming that its molar extinction coefficient ϵ is the same as that for liquid water.

The secondary structure of RNA has been investigated much less than that of DNA, because RNA crystallises with difficulty and yields low-quality X-ray diffraction patterns. Nevertheless, it has been established by X-ray diffraction and other methods that RNA molecules consist of single coiled chains with an alternation of helical and non-helical sections[129,137]. The fraction of the A–U and G–C base pairs is different for different types of RNA. The infrared spectra of RNA films, like those of DNA, show a band at 1705 cm^{-1} (1680 cm^{-1} in D_2O), indicating the presence of paired bases in the RNA chain[38]. The variation of the intensity of this band as the temperature is raised from 22° to 90°C is represented by a gently sloping curve, resembling the melting curve of RNA in the ultraviolet region[39]. Infrared spectroscopy has been successfully employed to determine the secondary structure of RNA. The relative amounts of the A–U and G–C pairs have now been found by comparing the observed and calculated spectra for five varieties of transfer RNA: alanine, valine, methionine, formylmethionine, and tyrosine RNA[41,138,139] by the Thomas method[102] and for the ribosomal RNA of *E. coli* by the method of Cotter and Gratzer[42,43]. Both methods of calculation are based on the fact that the absorption by hydrogen-bonded bases differs from that of the free bases and on the hypothesis that the dispersion interaction between the bases in the vertical stacks does not affect the spectrum, although the latter postulate contradicts the data of Maleev and coworkers[140]. The Thomas method consists in the calculation of the RNA spectrum on the hypothesis that the RNA absorption is made up additively from the absorption by the A–U and G–C pairs and the four unpaired bases. The overall RNA spectrum is calculated from the absorption spectra of the four nucleotides and two helical polynucleotides: poly-(A/U) and poly-(G/C). The method of Cotter and Gratzer consists in the calculation of the difference spectrum of RNA (relative to the dialysate) with the aid of the analogous spectra of poly-(A/U) and poly-(G/C), which take into account only the contribution by the paired bases. An advantage of this method over the Thomas method is that of a greater simplicity of the calculation of the spectra, since it involves the analysis of a two-component and not a six-component system.

The data for the secondary structure of RNA obtained from infrared spectra are consistent with the results of other methods, for example the method of optical rotatory dispersion, ultraviolet, spectroscopy, acid–base titration, and the "clover leaf" model of transfer RNA proposed by Dube[141].

It has been shown by X-ray diffraction that the RNA of dwarf rice virus has a secondary structure resembling that of DNA. However, the infrared spectrum of the RNA exhibits a weaker polarisation than the DNA spectrum

(Fig. 5).[27] The bands of the in-plane vibrations of the bases are polarised at right angles to the direction of orientation, as in the DNA spectrum, but the polarisation of the absorption bands of the RNA and DNA phosphate groups is different and hence there is a difference between the orientations of the PO_2^- groups. In the dwarf rice virus RNA helix, the O...O line makes an angle of 70° with the axis and the bisector of the OPO angle makes an angle of 40° (Table 8).

Table 8.

Double helix	1220 cm^{-1} band		1085 cm^{-1} band	
	dichroism	θ, deg*	dichroism	θ, deg*
DNA	nil	55	$\perp$	65
RNA	$\perp$	70	$\parallel$	40
DNA-RNA hybrid	$\perp$	68—78	nil	53—57

*θ—angle between the axis of the helix and the O...O line for the 1220 cm^{-1} band or the angle between the axis of the spiral and the bisector of the OPO angle for the 1085 cm^{-1} band.

The infrared spectrum of the DNA–RNA hybrid contains intense absorption bands characteristic of both DNA and RNA.[142] The dichroism of the absorption bands of the phosphate groups is evidence that the orientation of these groups relative to the axis of the helix of the hybrid is not completely identical with their orientation either in the double-helical DNA or in the double-helical RNA. It has been suggested[142] that the observed dichroism can be explained by the fact that in the hybrid molecule the PO_2^- groups of the DNA chain retain the same orientation as in the double-helical DNA, while in the RNA chain the orientation is the same as in the double-helical RNA.

DNA molecules are known to form nucleoprotein complexes with histones and with polypeptides, for example with poly-L-lysine. Information about the structures of DNA and the histone in deoxynucleoprotein (DNP) is important for the determination of the structure of chromosomes. The spectrum of the DNP film in the range 3500–1400 cm^{-1} resembles more closely the spectrum of the histone than that of DNA, since the bands of the protein are more intense than those of DNA. Below 1400 cm^{-1}, the spectrum of the nucleoprotein is identical with that of DNA[143]. The histone in DNP has an intense band at 3300 cm^{-1} (stretching vibrations of the NH bonds), an Amide I band at 1660 cm^{-1} (stretching vibrations of C=O groups), an Amide II band at 1545 cm^{-1} (deformation vibrations of the NH group), and also weak bands at 1450, 1400, and 1320 cm^{-1}.[144] The absorption bands of the histone are weakly polarised even for high moisture contents. The study of the infrared spectrum and also of the optical rotatory dispersion of DNP in the normal and deuterated states showed that in DNP part of the protein (50%) is in the α-helical form, the conformation of the protein varying with time. Measurement of the dichroism of the absorption bands of DNA for high relative moisture contents of DNP films showed that DNA in the nucleohistone is in the crystalline B-form, in agreement with X-ray diffraction data[134].

The stoichiometric complex of DNA with poly-L-lysine consists of fibres giving rise to distinct X-ray diffraction patterns, resembling that of the B-form of DNA when the relative moisture content is 75 and 66%.[145] The infrared spectrum of this complex is similar in broad outline to that of DNP, the band due to the phosphate groups undergoing only an insignificant shift (from 1224 to 1233 cm^{-1}) as the relative moisture content is reduced to zero, compared with the shift for DNA (from 1225 to 1240 cm^{-1}). In the spectrum of the DNA–histone complex, this shift is somewhat greater than for the DNA–poly-L-lysine complex.

The authors regard the shift of this band on dehydration of DNA as evidence of the liberation of phosphate groups from hydrogen bonding. From this point of view, the slight shift of the band due to the asymmetric PO_2^- vibrations on dehydration of the DNA–poly-L-lysine complex may imply that in this complex there are hydrogen bands between the PO_2^- groups of DNA and the NH_3^+ groups of the poly-L-lysine side chains. However, the details of the molecular environment of the phosphate groups have not been elucidated and therefore such interpretation cannot be regarded as unambiguous.

VI. INFRARED SPECTROSCOPIC STUDY OF THE INTERACTION OF NUCLEIC ACID COMPONENTS WITH ONE ANOTHER AND WITH OTHER SUBSTANCES

The interaction of the complementary bases of nucleic acids via hydrogen bonding, postulated by Watson and Crick in 1953,[5] is fundamental in biological systems. The linear sequence of nucleotides in DNA molecules stores the genetic information about the cell (the triplet code). An important process in the reading and transmission of this information is the formation of complementary structures with the aid of specific hydrogen bonds. It has been suggested that this type of interaction occurs when DNA controls the synthesis of RNA and also in the interaction between nucleic acids during the synthesis of protein. Therefore it is necessary to find physical and chemical criteria of the specificity and stability of the pairing of the bases in helix nucleic acids, a problem which can be successfully solved by infrared spectroscopy.

The formation of association complexes in aqueous purine and pyrimidine solutions has been observed by measuring the concentration variation of their water vapour pressure[146,147] and also by a chromatographic method in which one of the bases is attached covalently to a column and then eluted by a solution of the other base[148,149]. However, it has been shown by NMR that in aqueous solutions association complexes of the bases can be formed both via hydrogen bonding and via π-electron interaction between the heterocyclic rings and the formation of vertical stacks of the bases[150,151]. On the other hand, Raman spectroscopy failed to show the formation of hydrogen bonds between the complementary bases in aqueous solutions[152]. In water the hydration effect is too large, i.e. the degree of hydrogen bonding between water and the solutes is too high for the interaction between the solutes to be investigated.

It proved possible to demonstrate by infrared spectroscopy the formation of hydrogen bonds between the complementary bases of nucleic acids, initially in the solid phase for mixed crystals of the bases. A new absorption band at 1710 cm^{-1} was observed in the infrared spectrum of a mixed crystal of adenosine and uridine and a 1720 cm^{-1} band was found in the spectrum of a mixed crystal of guanosine and cytidine, both being absent from the spectra of the components[41,153]. Miles[154] failed to reproduce these results, but X-ray diffraction confirmed the presence of hydrogen bonds in mixed A–U and G–C crystals[155–170]. These observations are of fundamental

importance, because they revealed the possibility of determining the ratio of the specific base pairs from infrared spectra.

The study of the hydrogen bonding of nucleic acid bases in a pure form in solution can be conveniently carried out in non-polar solvents such as carbon tetrachloride or weakly polar solvents of the type of chloroform, which form weak hydrogen bonds with the solutes and rule out hydrophobic and electrostatic interactions between the bases and hence the formation of vertical stacks[161-165]. The study of the interaction of the bases in non-aqueous solvents is also important because it may resemble the interaction between the bases within the DNA double helix, where the bases are hardly in contact with water molecules. Such investigations became possible owing to the synthesis of *N*-derivatives of the bases and derivatives substituted in the nucleoside sugar residues, which are soluble in organic media.

Table 9. Vibration frequencies (wave-numbers) of the free NH groups of the bases and the bound NH groups of the homo- and hetero-association complexes.

Compound	$\tilde{\nu}_{NH}$(free), cm^{-1}	$\tilde{\nu}_{NH}$(self-assoc.), cm^{-1}	$\tilde{\nu}_{NH}$(hetero-assoc.), cm^{-1}
Adenine	3530—3527 3415	3485, 3250 3312, 3200	3490 3330
Uracil	3400—3395	3210—3185 3110, 3050	3260 2800
Guanine	3515—3510 3408	3480, 3305 3355	 3490
Cytosine	3531, 3418	3485 3320	3472

The interaction of the bases in solution may be studied on the basis of the infrared spectra in the range 3500 to 2800 cm^{-1}, since the stretching vibration frequencies of the NH_2 and NH groups decrease on formation of hydrogen bonds. The formation of association complexes of the bases is accompanied by a decrease of the intensity of the bands due to the free bases and the appearance of a series of new bands due to the bound NH and NH_2 groups (Table 9). Self-association of the bases in fairly concentrated (10^{-2} M) solutions and association in mixed dilute (10^{-4} M) solutions of the complementary bases of nucleic acids was observed from these spectroscopic changes[161-166] (Fig. 13). Infrared spectroscopy has provided direct proof of homo- and hetero-association of purines and pyrimidines via hydrogen bonding. It also revealed the specificity of this interaction, since, among all possible combinations of the four bases, the G–C and A–U (A–T) combinations proved to be the most stable, the G–C complex being more stable than the A–U complex, probably owing to the formation of three hydrogen bonds. These results have been fully confirmed by studies on the association of the bases and nucleosides by the NMR method[168,169].

In a number of studies[163,170-173] on the concentration variation of the intensity of the NH bands of the monomers, self-association and heteroassociation complexes were obtained for different bases (Table 10). The results of different workers for association in chloroform are satisfactorily consistent with one another and the high values of the constants obtained by Küchler and Derkosch[163] are probably due to the use of carbon tetrachloride as a solvent (see also Drozdova et al.[172]). The values of the constants confirm that the association of adenine with uracil and particularly of guanine with cytosine is much stronger than the self-association of these bases.

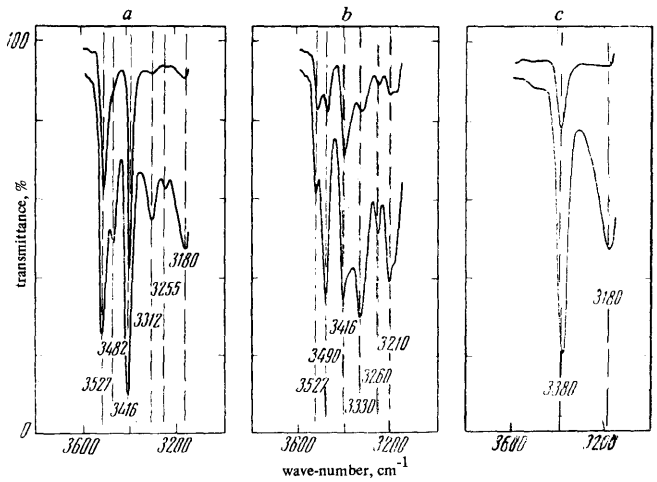


Figure 13. Infrared spectra of solutions in $CDCl_3$: *a*) 9-ethyladenine; *b*) 5-bromouracil; *c*) 1 : 1 mixture of 9-ethyladenine and 5-bromouracil; upper curves—0.019 M; lower curves—0.077 M.

The thermodynamic parameters of the association of the bases in different solvents were calculated from the temperature variation of the association constants. These data are presented in Table 10, which shows that the heats of formation of the association complexes are higher by a factor of 2–3 than the heat of formation of a hydrogen bond of the type H...O–C,[174] which may be due to the cyclic structure of these complexes.

The calculations of the association constants in all the studies mentioned above were made on the hypothesis of dimeric association of the bases, which is supported by the finding that the intensity of the absorption at all the bands of the heteroassociation complexes for a constant overall concentration of the components but with a variable ratio of the latter has a maximum corresponding to a 1 : 1 concentration ratio[161-164,167,170] (Fig. 14). This has been demonstrated[163] by determining the degree of association *n* from the variation of the concentration of the association complex with that of the monomer. For the association of adenine with uracil in their equimolar mixture and for the self-association of adenine and uracil, $n = 2$ was obtained in all cases. The infrared spectroscopic data have also been confirmed by the cryoscopic method.

Another argument in favour of the dimerisation of the bases is the constancy of the ratio of the intensities corresponding to the free NH and NH_2 groups of uracil and adenine in their mixture with variable concentrations of the components[164]. The heats of formation of the dimers, which are 4–6 kcal $mole^{-1}$, indicate the possibility of a cyclic structure maintained by two hydrogen bonds. X-Ray diffraction showed that in the crystalline state the A–U and G–C dimers have a cyclic structure[155,158].

The majority of the investigators of the specific pairing of nucleic acid bases suggest that one of the several

possible cyclic structures of the dimers predominates in solution, although so far no-one has succeeded in establishing the structure which actually exists. However, the formation of dimers of only one kind has been questioned[172] on the basis of the following facts. Firstly, on dimerisation of the bases a larger number of new bands appear in the infrared spectra than might have been expected for dimers of only one type. Secondly, calculation of the association constants based on the bands of the monomers and dimers leads to different results. The authors of this study believe that the results can be accounted for either by the formation of dimers of different kinds or of trimers of the type A + 2U. The possibility of the formation of trimers in solutions of adenine and a mixture of adenine and uracil is also indicated by NMR data[168,176].

Table 10. Association constants of different bases.

Association complex	Solvent	Association constant, litre mole^{-1}	Temp., °C	ΔH, kcal mole^{-1}	Ref.
A-A	$CHCl_3$	13±2	25	1.3±0.1	173
	$CDCl_3$	3.1±0.3	25	4.0±0.8	170
	CCl_4	83±7	20		163
U-U	$CHCl_3$	11.6±2.0	25		172
	$CHCl_3$	19±4	25	2.0	173
	$CDCl_3$	6.1±0.6	25	4.3±0.4	170
	$CDCl_3$	10±1	25	4.9±0.2	171
	CCl_4	115±8	20		163
A-U	$CHCl_3$	$1\cdot10^2$	25	6.2±0.3	173
	$CDCl_3$	$1\cdot10^2$	25		175
	$CDCl_3$	$1.4\cdot10^2$	25	6.2±0.1	170
	$CDCl_3$	$1.5\cdot10^2$	25		167
	CCl_4	$6\cdot10^2$	20		163
G-C	$CHCl_3$	10^5	30		164

The study of the effect of various substituents (CH_3, SH, Br, and I) on the degree of association of uracil with adenine reveals that substituents which decrease pK_{ass} for uracil or increase electron density in the N(7)-position of adenine also increase their capacity for association. Thus, complexes of 2,6-diaminopurine with uracil and of 5-bromouracil with adenine are the most stable. On the other hand, substitution of the hydrogen atoms in the amino-group of adenine lowers its association constant, for example 6-dimethylaminopurine is completely incapable of association[175].

Miles and coworkers[47-49,52,99] used the infrared spectroscopic method to investigate various structural complexes of synthetic polynucleotides in solution. Polycytidylic (or poly-5-bromocytidylic) and polyinosinic acids are known to interact in solution, forming helices with a structure resembling that of DNA, and polyuridylic and polyadenylic acids form a double or triple helix depending on the experimental conditions[6,45,177-181]. The formation of helical complexes in the interaction between polynucleotides is accompanied by considerable and characteristic changes in the infrared spectra owing to the formation of hydrogen bonds and the change in the chemical environment of the bases (Fig. 15). The bands due to the vibrations of the carbonyl groups are then displaced towards higher frequencies, as for DNA. When the double helix of poly-(A/U) is formed, the infrared spectrum of the complex reveals a shift of the carbonyl band from 1660 to 1672 cm^{-1}.[49,99,154] The spectrum of a solution of the helical poly-(I/2C) complex reveals a shift of the absorption band of polyinosinic acid from 1678 to 1697 cm^{-1} and a decrease of the intensity of the 1651 cm^{-1} band of polycytidylic acid[47,49,50,154]. The 1710 cm^{-1} band, which is characteristic of the secondary structure of double helices, appears in the spectrum of the double-helical polyadenylic acid. A similar increase of the vibration frequency of the carbonyl group of guanine (the wave-number increases from 1666 to 1680 cm^{-1}) occurs on formation of the spirals of 3'- and 5'-guanylic acids.

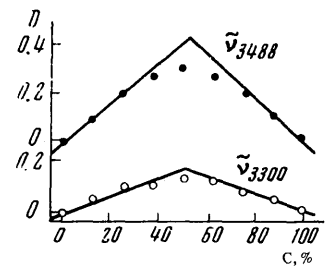


Figure 14. Variation of the optical densities of the 3300 and 3488 cm^{-1} bands of the association complexes with the percentage content of cytosine in a mixture of guanine and cytosine derivatives (overall concentration 1.6×10^{-3} M)[162].

Guanylic acid is known to be capable of forming helical macromolecular complexes which are stable at reduced temperatures[182]. The melting of these helical aggregates has been investigated[48] in the temperature range 10 to 60°C by measuring the intensities of the carbonyl bands.

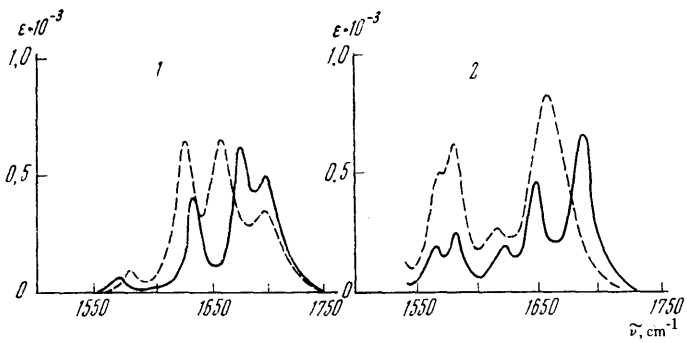


Figure 15. Infrared spectra of D_2O solutions (pD 7.0) of complexes: 1) poly-(A/U); 2) poly(G/C); dashed curves—sum of the spectra of the corresponding mononucleotides[102].

The formation of a helical secondary structure has been observed on the basis of infrared spectra not only in the interaction between complementary polynucleotides but also in the interaction of mono- and oligo-nucleotides with a polynucleotide, for example of guanosine 5'-phosphate or the trimer of guanosine phosphate with polycytidylic acid, of adenosine with poly-(U/C), etc.[51,52] The infrared spectra of these complexes also differ from the sum of the

spectra of the components. However, the complexes are stable only below 40°C (m.p. about 40°C). The parallel variation of the melting curves for the characteristic frequencies of the purine and pyrimidine bases is evidence of the specificity of the pairing of the bases in the complexes of polynucleotides with mono- and oligo-nucleotides.

A number of studies on complexes of nucleic acids and their components with metal ions by different procedures, including the infrared spectroscopic method, have been published recently [183-192]. The physicochemical properties of nucleic acids (intrinsic viscosity, sedimentation rate, and melting point) are known to alter under the influence of metal ions or the acids undergo degradation.

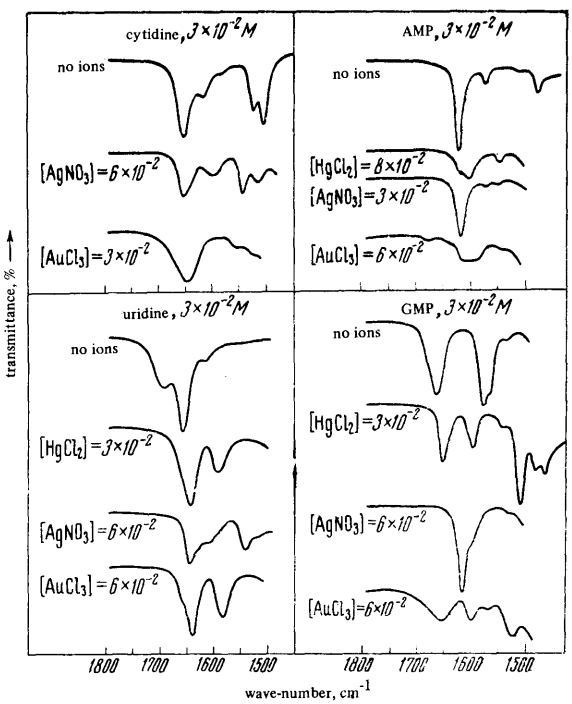


Figure 16. Infrared spectra of D_2O solutions of cytidine, uridine, GMP, and AMP (3×10^{-2} M) in the absence and presence of metal ions [198].

For example, alkali metal, alkaline earth metal, and transition metal ions increase the melting point of DNA and Cu^{2+}, Cd^{2+}, Ag^{2+}, and Fe^{3+} ions reduce it [193,194].

Metal ions can interact with the phosphate groups of nucleic acids (an ion–ion type of interaction) or with the dipoles of the rings of the bases (ion–dipole type of interaction). Therefore in a study of metal complexes of nucleic acids it is important to discover the site of binding of the ion. It has been shown by conductimetric titration that metal ions stabilising the DNA structure combine with its phosphate groups [195,196], while ESR, [197] NMR, [198] and spectrophotometric measurements [193,199-201] showed that destabilising ions (Cu^{2+}, Cd^{2+}, Pb^{2+}, Ag^{+}, and Hg^{2+}) are bound to the DNA bases at the sites of formation of hydrogen bonds. In agreement with these data, it has been observed that Na^{+}, Ca^{2+}, Mg^{2+}, Zn^{2+}, Fe^{2+}, Co^{2+}, and Ni^{2+} do not cause a displacement of the bands in the infrared absorption spectra of nucleic acid bases, while Ag^{+}, Hg^{2+}, and Au^{3+} ions do give rise to a displacement of this kind [202-204]. Shifts of the phosphate bands but not of the bands due to the bases have been observed in the infrared spectrum of a DNA–Fe^{2+} complex [203,204]. Hg^{2+} and Ag^{+} ions lead to considerable shifts of the bands in the region 1800–1500 cm^{-1} in the infrared spectra of all the nucleic acid bases for a metal : base ratio of 2 : 1 (Fig. 16). [202] In the region of the double bond vibrations of the bases, the spectrum of the DNA–Hg^{2+} complex is also appreciably different from that of DNA, which is evidence of the addition of mercury ions to the bases in the macromolecules [202,205,206].

The infrared spectroscopic data concerning the interaction of copper ions with nucleic acid bases are extremely contradictory: some investigators [207] have observed band shifts in the spectra of certain bases in the presence of Cu^{2+} ions, while others [202] failed to observe such shifts. Indeed, Drozdova-Tikhomirova and Kikoina showed [208] that, in the absorption spectrum of solid guanosine and its solution in dimethyl sulphoxide (DMSO) with added copper, the positions of the maxima in the region 1700–1600 cm^{-1} remain unchanged. Changes in the intensities of the carbonyl, amino-group, and double bond bands have been observed in the spectrum of solid guanosine in the presence of Cu^{2+} ions, the changes reaching a maximum for an equimolar ratio of the Cu^{2+} and guanosine concentrations, which is evidence of the formation of a 1 : 1 complex. The existence of a complex in a guanosine solution in DMSO was demonstrated with the aid of a differential spectrum in which analogous changes were observed. The authors postulate that the formation of the G.Cu^{2+} complex is associated with the shift of the tautomeric equilibrium of guanine towards its enolic form, and that this shift may be the reason for the lowering of the melting point of DNA. Uranyl ions form an insoluble complex with DNA, the stoichiometry of which depends on the pH of the medium and the concentration of the ions. Uranyl ions combine with the phosphate groups of DNA, since the spectrum of its complex shows a displacement of the phosphate absorption bands [107]. Thus infrared spectroscopy may be useful for the determination of the location of metal ions in their complexes with nucleic acids.

The interaction of DNA with various compounds, which are of interest from the standpoint of biochemistry or the protection of DNA molecules from various effects, can also be investigated by infrared spectroscopy. One of such compounds is myoinositol, which prevents the destruction of bacterial cells on dehydration and protects them when they are irradiated with ultraviolet light. A considerable increase of the sensitivity of micro-organisms to irradiation and dehydration occurs in the range of relative moisture content between 75 and 50%, i.e. in the region where the packing of the bases in the DNA helix becomes disorganised [209-213]. Preliminary physicochemical studies led to the hypothesis that compounds similar to inositol play the role of combined water on partial dehydration or irradiation of the cells and their components [214,215]. A study of the variation of the polarisation of the infrared spectrum of DNA yielded a direct proof of this hypothesis [206]. As stated above, a decrease of the relative moisture content of DNA films from 75 to 30% is accompanied by a considerable decrease of the dichroic ratio for the 1670 cm^{-1} band. Inositol keeps R_{1670} constant when the DNA film is dehydrated in the relative moisture content range 84–10%. These results may mean that myoinositol replaces the water molecules in the DNA

structure when it is dehydrated and thus stabilises its helical configuration[216]. Unfortunately so far this is the only study of this kind. Nevertheless infrared spectroscopy may prove very promising in the study of the interaction of nucleic acids with agents protecting against radiation, mutagenic and carcinogenic agents, and other biologically active substances.

Measurement of the intensity of the infrared bands of DNA and its components is extremely important in the study of the damage of DNA and various interactions, which has been convincingly demonstrated in the investigation of the specific interactions of DNA bases in solution, discussed in this Section.

In addition, using the area of the absorption bands as a measure of intensity (after Ramsay)[218], Miles[217] showed that the integral intensity of the bands in the range 1700 to 1600 cm^{-1} in the spectra of D_2O solutions of certain nucleotides and polynucleotides is proportional to their concentration. Thus Miles succeeded in demonstrating quantitatively that, when solutions of polyadenylic and polyuridylic acids are mixed, an appreciable deviation from the additivity of the band intensities is observed in the above range as a result of the formation of hydrogen bonds, while for a mixture of mononucleotides additivity is found to hold.

Measurements of the intensity of the absorption bands for DNA solutions and nucleotides apparently make it possible to follow the changes in the structure of the bases in shifts of the tautomeric equilibrium or under the influence of various factors.

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Spin-Spin Coupling between Geminal and Vicinal Protons

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The geminal (HCH) and vicinal (HCCH) proton spin-spin coupling constants are of fundamental importance in the applications of nuclear magnetic resonance (NMR) spectroscopy in structural and conformational analysis, since they are extremely sensitive to fine details of steric and electronic molecular structure. The nature of the dependence of the constants on individual structural factors (bond length, valence and dihedral angles, electronic structure of the substituents and their orientation, etc.) has been examined in detail. At present *a priori* theoretical calculations do not allow an exact description of these relations and therefore a semiempirical approach, based on general qualitative relations found by quantum-mechanical calculations, is very promising.
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I. INTRODUCTION

Spin–spin coupling between protons observed in the NMR spectra of liquids and gases has been attracting attention for many reasons. From the theoretical standpoint, this is one of the simplest cases of the transfer of nuclear spin polarisation via the electron cloud, which depends in the most critical way on the electronic structure of the molecule. From the practical standpoint, the H–H constants in fact constitute the basis of the study of molecular structure, conformation, and configuration—one of the most important applications of NMR spectroscopy in chemistry. Moreover, H–H constants (J_{HH}) are important for structural analysis and the study of the electronic structure of molecules and kinetic processes, such as internal rotation, inversion transitions, and hydrogen exchange [1].

In the present review attention has been concentrated on the relation between the H–H constants and the steric and electronic structures of molecules. On the basis of the extensive data which have accumulated, a number of correlations have been obtained, in particular with the relative steric positions of hydrogen atoms. Some of these relations have found wide application in the solution of chemical structural problems, while others are not so well known. Many of the correlations have a firm theoretical basis. In order to employ such correlations, it is important to bear in mind the limits of their applicability and also the deviations caused by certain structural factors. One must also emphasise that the ranges of the possible values of the H–H constants for the fundamental structural fragments overlap significantly:

		+280 HZ
^1J	H—H	(Carr and Purcell) (Ref.2)*
^2J	H—C—H	from −22 to +40 Hz
^3J	H—C—C—H	from 0 to +19 Hz
^4J	H—C—C—C—H	from −2 to +18 Hz

* The sign of the constant was established for HD molecules by the molecular beam method [3].

This makes it necessary to analyse thoroughly the causes of the variation of the constants by both theoretical and empirical procedures.

Spin–spin coupling in molecules with saturated valences is due to slight unpairing of the electron pair spins (i.e. a contribution by excited electronic structures), induced by the magnetic moment of the nucleus. It has been reliably established [4-6] that the principal mechanism (which can actually be said to be dominant) of the transfer of interaction between protons is Fermi contact interaction. The extent of this interaction is proportional, to a first approximation, to the probability $S(0)$ that the orbital electrons are located at the sites of the protons A and B (Fig. 1):

$$J \propto S_A^2(0) S_B^2(0).$$

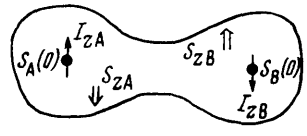


Figure 1. Schematic representation of the electronic properties of the spin–spin contact interaction between protons. I_{zA} and I_{zB} are the spin moments of electrons.

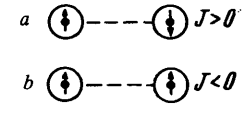


Figure 2. Illustration of the physical significance of the sign of the spin–spin coupling constant.

The sign of the coupling constant, which characterises the relative distribution of the spin energy levels of the nuclear system, is a characteristic no less important than J itself. If the lowest level corresponds to a state with an antiparallel arrangement of nuclear spins (Fig. 2*a*), a positive sign is attributed to the constant, a negative sign corresponding to a parallel arrangement (Fig. 2*b*).

The signs of the coupling constants are established by special methods. The absolute signs are determined from spectra in nematic solvents [7,8], from the changes in splitting in a strong electrostatic field [8], and from the relaxation parameters of multispin systems [9]. The relative signs of the constants are determined by double resonance methods [10], by analysing spectra with strong interaction [11], and from the positions of the signals due to two-quantum transitions [12].

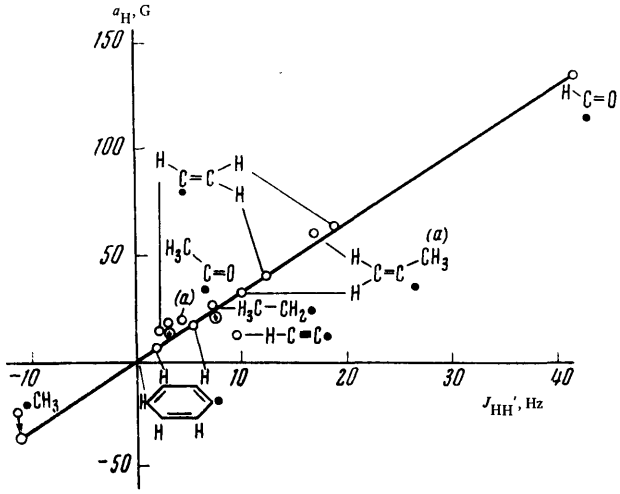
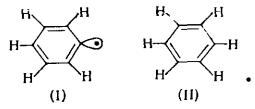


Figure 3. Relation between the spin–spin proton coupling constant $J_{HH'}$ (NMR) and hyperfine coupling constant a_H (ESR). The values of a_H for the radicals $\dot{C}H_3$, $\dot{C}H_2CH_3$, and $\dot{C}OCH_3$ have been corrected for the structure factor; the corrected values are designated by an arrow [15].

The problem of the relations governing the transfer of unpaired-electron density is of considerable interest for theoretical chemistry. Together with the widely familiar delocalisation over a system of conjugated bonds, the methods of magnetic microwave spectroscopy made it possible to investigate finer details of the perturbing influence of the unpaired electron, largely localised at a single atom. The delocalisation of spin density caused by such perturbation may be reflected in various molecular parameters—such as the spin–spin coupling constant J in molecules with saturated valences and the contact chemical shift in the NMR spectra of paramagnetic complexes as well as the isotropic hyperfine coupling constant (a) in electron spin resonance spectra. The most typical example demonstrating the general properties of delocalisation is provided by a comparison of the constants a for free radicals with a localised valence [for example the phenyl radical (I)] and the constants J_{HH} of the corresponding molecules [benzene (II)] in which the free valence is saturated by a hydrogen atom (H) [13–17].



(I) (II)

The linear relation obtained (Fig. 3) [15],

$$J_{HH'} \simeq 0{,}3\,a_H,$$

where J_{HH} and a_H are expressed in Hertz and Oersted units respectively, shows that the non-compensated electron density at the σ orbital of the carbon atom, induced by the magnetic moment of the H′ proton, plays a fundamental role in the spin–spin interaction. Therefore the perturbing effects in the molecule and the free radical obey the same relation. Recent theoretical calculations [17] by the valence bond method confirmed the existence of a linear relation:

$$J_{HH'} = 4.1\,a_H/\Delta E,$$

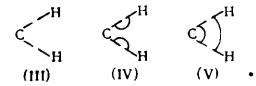
where ΔE is the average energy of the perturbed state in electron-volts. With the usually adopted value ΔE = 10 eV, the proportionality coefficient (0.41) agrees satisfactorily with the empirical value. A linear relation has also been found between the J_{HH} constants and contact chemical shifts [15]. Thus the data obtained by different methods for similar systems with identical structures can significantly complement one another. For example, the sign of a_H may be established from that of J_{HH} or from the sign of the contact chemical shift.

We shall now pass to a discussion of the dependence of the H–H interaction constants for HCH and HCCH structural fragments in organic compounds on various factors associated with steric and electronic structures.

II. THE GEMINAL CONSTANT $^2J_{HH}$

The simplest fragment (apart from the hydrogen molecule) is H–C–H, where the hydrogen atoms occupy *gem*-positions (with the geminal constant $^2J_{HH}$). As already mentioned, the values of ^2J are in the range between −22 and +40 Hz, i.e. not only their magnitude but also their sign can vary.

In the calculation of ^2J by the valence bond method, the geminal fragment is regarded as a four-electron system (III), consisting of two 1s orbitals of the hydrogen atoms and two hybridised sp orbitals of carbon [18,19]. The ground electronic state (IV) corresponds to complete pairing of bond electrons. Since there is then no interaction between the electron pairs, no spin–spin coupling between protons is shown. For H–H interactions to occur, it is necessary to mix the ground state (IV) with an excited state (V).



(III) (IV) (V)

The degree of such mixing is determined by the energy difference between the ground and excited states, which is as a rule estimated very approximately. In terms of the mean excitation energy approximation, it has been found [18,19] that

$$^2J \propto \frac{K(HH') + K(\sigma\sigma') - 2K(\sigma H')}{K(\sigma H)}, \qquad (1)$$

where K are exchange integrals between the corresponding atomic orbitals (Fig. 4). The values of these integrals are difficult to estimate quantitatively. One can only assume with a degree of certainty [20] that $K(\sigma H) < 0$, $K(HH'') < 0$, and $K(\sigma\sigma') > 0$. It then follows from Eqn. (1) that the contribution by the $K(HH')$ integral to ^2J is positive and that of $K(\sigma\sigma')$ is negative. However, calculations show that the absolute values of $K(HH')$ and $K(\sigma\sigma')$ are approximately the same and cancel out. $K(\sigma H')$ is even more

difficult to calculate. Its sign may be both positive or negative. In the first case $^2J < 0$ and in the second $^2J > 0$. The error in the estimation of the integrals (about ±10%) can lead to discrepancies between the values of $^2J_{HH}$ up to ±6 Hz.[6]

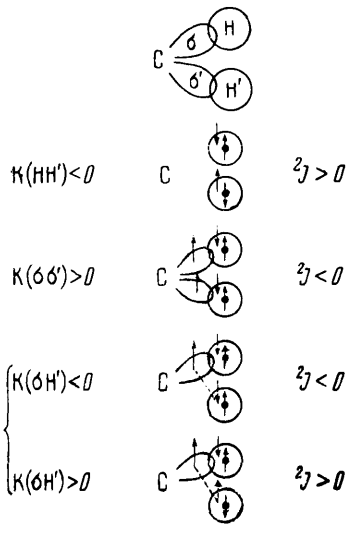


Figure 4. The H–H geminal constant within the framework of the valence bond method and a schematic representation of exchange integrals. In this and other figures the arrows denote energetically favourable relative orientations of the spin moments of protons and orbital electrons.

Numerical calculations by both the valence bond method[20-23] and by the molecular orbital method[24-36] in different modifications show significant discrepancies with experimental data (Table 1)†. This applies not only to the absolute values but even to the sign. Therefore analysis of the empirical relations becomes important. The theoretical justification and prediction of the relation between ^2J and molecular structure probably should not be based on the calculation of the overall values of the constants but should consist in isolating the additional contributions due to specific structural factors.

Significant advances on these lines have been achieved by the molecular orbital method taking into account the excitation energies of the triplet states[20,36,39,40]. For a qualitative examination[39] of an isolated four-electron CH_2 fragment, one may restrict the treatment to four molecular orbitals ψ_i (Fig. 5) constructed by a linear combination of the atomic orbitals φ_k:

$$\psi_i = \sum_k c_{ik}\varphi_k.$$

Table 1. Theoretical calculations of the $^2J_{HH}$ geminal constant (Hz) by the valence bond method (VB), the molecular orbital method without allowance for overlapping (MO), with allowance for overlapping (MO–O), with allowance for delocalisation (MO–D), by the self-consistent field method with complete and partial neglect of differential overlapping (CNDO and INDO), and the complete self-consistent field method (SCF).

Compound	Experiment	VB (Ref.20)	MO (Ref.25)	MO–O (Ref.26)	MO–D (Ref.27)	CNDO (Ref.27)	INDO (Refs.28 & 36)	SCF (Ref.32)
CH_4	−12.4[37]	+12.5	+20.7	−16.5	−2.1	+1.17	−6.13	−7.0
$CH_2=CH_2$	+2.5[38]	+3.05	+32.5	−15.2	+1.5	+8.48	+3.24	+9.6

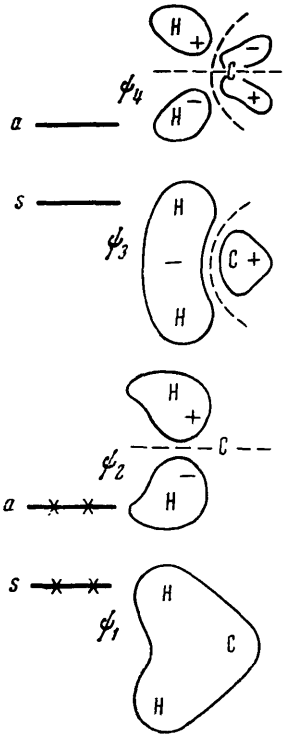


Figure 5. Molecular orbitals of the CH_2 fragment.

Two of the molecular orbitals are bonding and populated (ψ_1 and ψ_2) and two are non-bonding and unpopulated (ψ_3 and ψ_4). These orbitals are delocalised over both C–H bonds and can be divided into symmetrical (s) and antisymmetric (a) orbitals in relation to the plane bisecting

†The geminal constant $^2J_{HH}$ for the magnetically equivalent CH_3 protons is found from the $^2J_{HD}$ constant for the CHD fragment in the spectra of the corresponding deuterated compounds[37]: $^2J_{HH} = (\gamma_H/\gamma_D)\ ^2J_{HD} = 6.5144\ ^2J_{HD}$, where γ_H and γ_D are the gyromagnetic ratios for the proton and deuteron respectively. $^2J_{HH}$ for CH_2CH fragments with magnetically equivalent CH_2 protons may be determined from the satellite spectra due to ^{13}C.[38]

the H–C–H angle. The symmetrical bonding orbital ψ_1 includes the 2*s* orbital of the carbon atom and therefore has a lower energy than ψ_2 which includes the 2*p* carbon orbital. The proton spin–spin interaction constant is expressed as follows in perturbation theory:

$$^2J_{HH'} \propto S_H^2(0)\, S_{H'}^2(0)\, \pi_{HH'}, \quad (2)$$

$$\pi_{HH'} = -4 \sum_k \sum_l (E_l - E_k)^{-1} c_{kH} c_{kH'} c_{lH} c_{lH'}, \quad (3)$$

where $S_H(0)$ and $S'_H(0)$ are the densities of the 1*s* atomic orbitals at the H and H′ protons, $\pi_{HH'}$ is the mutual polarisibility coefficient of the hydrogen 1*s* orbitals of H and H′, the index *k* corresponds to populated states and *l* to unpopulated states.

Table 2.

Transition	Sign of contribution to $^2J_{HH}$
$\psi_1 \rightarrow \psi$	−
$\psi_1 \rightarrow \psi$	+
$\psi_2 \rightarrow \psi_3$	+
$\psi_2 \rightarrow \psi_4$	−

The $\psi_k \rightarrow \psi_l$ electronic transitions make contributions of different signs (Table 2), which are determined by the coefficients c_{kH}, $c_{kH'}$, c_{lH}, and $c_{lH'}$. The effect of different factors on $^2J_{HH}$ is treated as a change in the relative contribution caused by a given electronic transition, taking into account the energy difference of the transition $(E_l - E_k)^{-1}$. A number of qualitative conclusions based on this theory[39] and the results of calculations by the INDO method[36] will be discussed below.

One can regard it as established that the H–H geminal constant for the H_2C–X–Y system depends on the following fundamental factors[6,41–45]: (1) hybridisation of the carbon atom; (2) electronegativity of the substituent X; (3) the presence of a π-electron system at the atom X; (4) the presence of a lone electron pair at the atom X; (5) the nature of the β-substituent Y; (6) the nature of the solvent‡. These factors will be considered separately.

1. Hybridisation of the Carbon Atom

Experimental data for hydrocarbons show that, as the contribution by the *p* orbital of the carbon atom diminishes, $^2J_{HH}$ increases (Table 3).

A more detailed relation can be more conveniently derived[43] on the basis of the valence angle α as the parameter determining the hybridisation of carbon (Fig. 6). The relation is of course significant only for systems where the effect of the other factors mentioned above is fairly weak§. However, as a rule such "pure" systems are encountered rarely and therefore in the general case the determination of valence angles from the constant $^2J_{HH}$ is invalid. It is remarkable that the first calculation of $^2J_{HH}$ by the valence bond method[18,19] predicted an approximately the same relation but with the opposite sign of the constant (Table 1). Recent calculations by the molecular orbital method[26,36] yielded the correct sign of $^2J_{HH}$ and the correct overall relation with the valence angle, but for specific molecules (ethylene, cyclopropane, cyclohexane, and methane) there was no agreement with experiment (Table 1).

Table 3.

Molecule	CH_4		$H_2C{=}CH_2$
Hybridisation	sp^3	$sp^{2,3}$	sp^2
HCH angle	109°	116°	120°
^2J, Hz	−12.4[37]	−4.31[55]	+2.5[38]

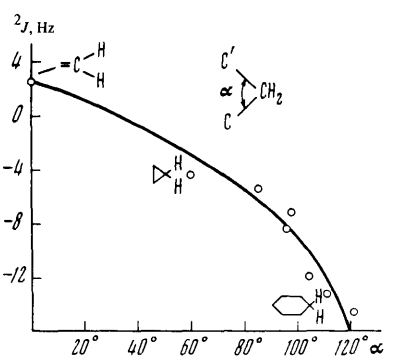
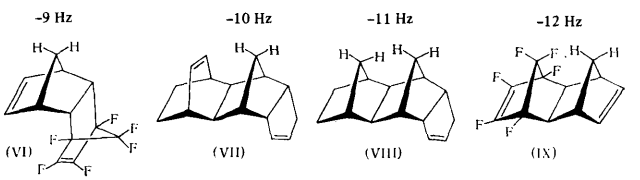


Figure 6. Variation of the H–H geminal constants with the C–CH_2–C valence angle for hydrocarbons[43].

One of the features of the relation between $^2J_{HH}$ and the H–C–H angle is the effect of the steric factor. For example, the constant for the bridge protons in the bicyclo[2,2,1]heptane system decreases with increasing degree of steric hindrance in the series (VI)–(IX).[57–59] We may suppose that the H–C–H angle decreases in the same series.



‡A change in temperature is reflected in a redistribution of the populations of the torsional vibrational levels of the HCH fragment, which should lead to a change of the H–H geminal constant. Experimental data[46–54] and theoretical calculations[46,47,49,50] show that, with increase of temperature, the absolute value of $^2J_{HH}$ increases only slightly (the relative change is about 3×10^{-4} per degree).

§The lack of the $^2J_{HH}$ constants for cyclobutane makes it difficult to decide whether four-membered rings obey this relation. For cyclobutane derivatives, values of ^2J ranging from −11.0 to −14.0 Hz have been observed[43,45,56].

2. Effect of the α-Substituent

In the presence of a substituent X at the carbon atom ($X-CH_2$), one can postulate intuitively that, since the electron-accepting inductive effect of X leads to a decrease of electron density at H atoms, the absolute value of $^2J_{HH}$ should diminish. Such a relation is in fact observed experimentally (Table 4).

Table 4. Variation of $^2J_{HH}$ with the electronegativity of the α-substituent.

Compound	$^2J_{HH}$, Hz	X	$^2J_{HH}$, Hz
$(CH_3)_4C$	−14.1[60]	CH_2	−4.31[55]
CH_4	−12.4[37]	S	−1.4[62]
$(CH_3)_3N$	−11.7[44]	NCH_3	+1.0[63, 64]
CH_3OH	−10.8[61]	O	+5.4[65]
CH_3F	−9.6[61]	N^+	+5[66]

A qualitative explanation of the effects of electronegative α-substituents on $^2J_{HH}$, based on the molecular orbital method[39], involves an inductive withdrawal of electrons from the symmetrical orbital ψ_1 (Fig. 5). As a result, the orbital becomes less "hydrogen-like" and the coefficients c_1H and c_1H' in Eqn. (3) diminish. Since the molecular orbitals are made up of a complete orthogonal set of atomic orbitals, the other symmetrical orbital ψ_3 becomes more "hydrogen-like" and the coefficients c_3H and c_3H' increase. In view of the fact that the antisymmetric orbitals do not change under the influence of the inductive effect of the substituent, the product of the coefficients in Eqn. (3) for the $\psi_1 \rightarrow \psi_4$ transition will be more negative and for the $\psi_2 \rightarrow \psi_3$ transition less negative. Since a lower excitation energy $E_3 - E_2$ corresponds to the latter transition than to the $\psi_1 \rightarrow \psi_4$ transition (Fig. 5), the overall contribution to the change in $^2J_{HH}$ is positive. Thus theoretical considerations are consistent with experimental data (Table 4): electronegative substituents (for example F) in the CH_3X series leads to an increase of $^2J_{HH}$ and electropositive substituents (for example Si) lead to a decrease of the geminal constant relative to methane. Theoretical calculation by the MO–INDO method[36] indicated an increase of $^2J_{HH}$ for CH_3F by 4.28 Hz compared with methane (Table 1).

In the valence bond method, the inductive effect of the substituent on $^2J_{HH}$ is taken into account by including polar structures reflecting the ionic character of the C–X bond[21,22]. These calculations yield an incorrect sign of the geminal H–H constant, but correctly predict a decrease of $|^2J_{HH}|$ with increasing amount of ionic character of the C–X bond.

However, the electronic properties of the substituent X are not restricted to electronegativity. For example, a relation has been derived between $^2J_{HH}$ for compounds of the type $(CH_3)nX$ and the number of the Period of the atom X (Fig. 7), which makes it possible to predict the constant for compounds not hitherto investigated[67].

3. Effect of the π-Electron System of the Substituent X

If the electronic system of X includes a π orbital, an additional contribution to the constant $^2J_{HH}$ for the $X-CH_2$ fragment is generated. In the valence bond method this contribution is proportional to the product of the overlap integrals of the C–H orbitals and the π orbital of the atom X:[19,68]

$$\Delta^2 J^\pi \sim -K(\sigma\pi)\, K(\sigma'\pi).$$

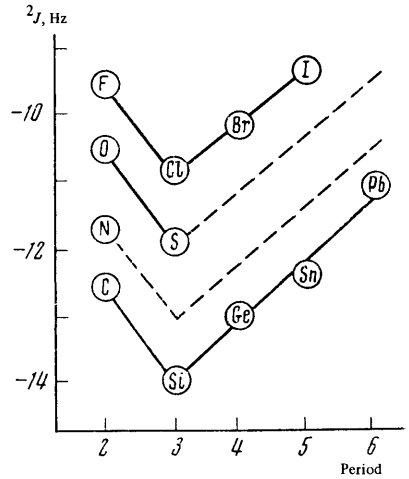
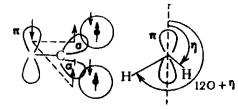


Figure 7. Variation of the H–H geminal constants for compounds of the type $(CH_3)_nX$ with the number of the Period of the atom X.[67]

Its negative sign is due to the preferential antiparallel orientation of proton spins when the interaction is transmitted via the π orbital of the atom X (X). Indeed the $^2J_{HH}$ constant for the methyl group decreases in the series CH_4 (−12.4 Hz)[37] > CH_3Ph (−14.6 Hz)[19] > $CH_3C{\equiv}N$ (−16.9 Hz)[19]. In acetonitrile the first atom of the substituent has two π orbitals, which results in a doubling of the contribution $\Delta^2 J^\pi$.



Since the integral $K(\sigma\pi)$ is proportional to $\cos^2\eta$, where η is the dihedral angle between the C–H bond at the direction of the π orbital (XI), it follows that, for molecules with fixed positions of the C–H bonds, the contribution by the π-electron system depends on the angle η:[68]

$$\Delta^2 J^\pi \propto \cos^2\eta \cos^2(120 + \eta).$$

This theoretical relation (Fig. 8) is satisfactorily confirmed by experiment[43,68] (almost quantitatively), which makes it possible to employ it for the determination of molecular structures and conformations.

Qualitative[39] and quantitative[36] treatment by the molecular orbital method leads to similar conclusions concerning the sign of the contribution of the π orbital or the α-substituent to the geminal H–H constant and its dependence on

stereochemical factors. The effect of the π orbital is treated as involving a withdrawal of electron density from the antisymmetric populated orbital ψ_2 of the CH_2 fragment (Fig. 5).

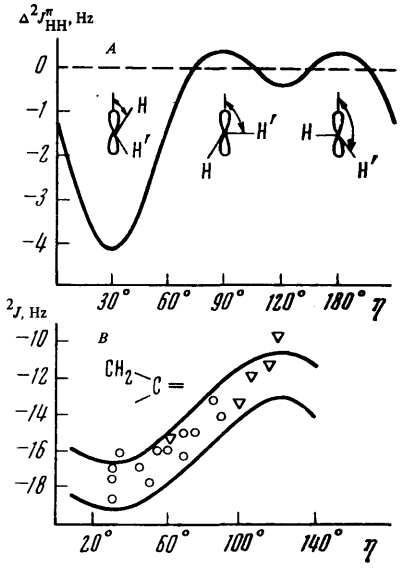
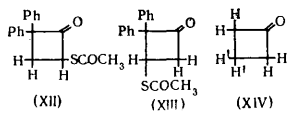
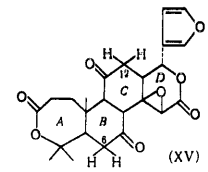


Figure 8. Theoretical [68] (*A*) and experimental (*B*) [43] dependence of the contribution by the π-electron system to the constant $^2J_{HH}$ on the projection angle η.

As an example of structural studies, one may quote the determination of the position of the acetylthio-group in a derivative of cyclobutane [69]. For structure (XII), $^2J_{HH}$ should not differ markedly from the usual value for cyclobutanes, i.e. −(12–15) Hz. [42,56] On the basis of the theoretical relation (Fig. 8), −4.2 Hz (η ≃ 30°) should be added for structure (XIII) because of the neighbouring π-electron system of the carbonyl carbon atom: $^2J \simeq -(16–19)$ Hz. Experiment yielded −18.4 Hz, which proved structure (XIII). For unsubstituted cyclobutanone (XIV), it has been found that $^2J_{HH} = -17.5$ Hz and $^2J_{H'H'} = 11.1$ Hz. [70]

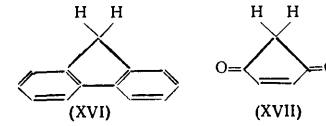


The angular variation of the contribution by the π orbital may be used, for example, to determine the conformation of the cyclohexane ring. In the chain conformation (η ≃ 86°) the geminal constant has the normal value for cyclohexanones (−13 Hz). In the boat conformation (η ≃ 30°), a decrease of the constant by 4–5 Hz is to be expected. For zapoternone (XV) [71], $^2J_{HH} = -13$ Hz for the $C_{(6)}H_2$ methylene group, which indicates a chair conformation of the *B* ring, while −19 Hz was found for the $C_{(12)}H_2$ group, which corresponds to a boat conformation of the *D* ring:



(XV)

The effect of the π-electron system leads to values of $^2J_{HH}$ which constitute the lower limit of the known geminal constants. For fluorene (XVI) [72] and cyclopenta-3,5-dione (XVII) [68], in the molecules of which the methylene group is linked to two carbon atoms involved in a double bond, $^2J_{HH} = -22.3$ and −21.5 Hz were found respectively.



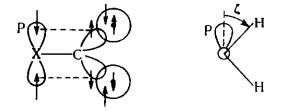
(XVI) (XVII)

These values agree well with $^2J_{HH} \simeq -12.5-4.2-4.2 = -20.9$ Hz calculated for η = 30°.

The lower value of $^2J_{HH}$ for 1,1-dimethylallene (−9.0 Hz) [73] compared with ethylene (+2.5 Hz) [38] can also be attributed to the effect of the additional π orbital of the atom X. For keten $H_2C=C=O$ ($^2J_{HH} = -15.8$ Hz) [73], the effect of the electronegativity of the β-substituent is also important (see Section II, 5).

Effect of the Lane Electron Pair of the Substituent

According to theoretical considerations based on the valence bond [6] and molecular orbital [36,39] methods, the contribution by the lone pair to the geminal constant should be positive [formula (XVIII)] and should depend on the dihedral angle ζ [formula (XIX)] between the C–H bond and the axis of the lone pair. In the qualitative molecular orbital theory [39], this effect is regarded as due to the supply of electron density to the antisymmetric populated orbital ψ_2 (Fig. 5). The effect is opposite in sign to that of the π orbital of the α-substituent.

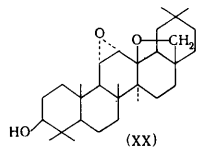


(XVIII) (XIX)

A confirmation of the effect of the lone pair can be found by comparing the $^2J_{HH}$ constants in the series of six- and five-membered heterocyclic compounds (Table 5). Two factors are noteworthy. Firstly, the monotonic increase of $^2J_{HH}$ with increasing electronegativity breaks down at the piperidinium and pyrrolidinium cations. Although the electronegativity of N^+ is higher than that of N, the latter has a lone electron pair, the positive contribution $\Delta^2 J^P$ of which increases $^2J_{HH}$, which leads to the breakdown of the sequence. Secondly, the introduction of the heteroatom has a much greater effect on $^2J_{HH}$ in five-membered rings than in six-membered rings. One must assume that this is due to the difference between the angles ζ in the two types of rings.

Theoretical calculation by the MO–INDO method showed [36] that the geminal constant for methanol depends on the orientation of the O–H bond. However, the numerical result, in particular −2.12 Hz for the average value of

$^2J_{HH}$, differs significantly from the experimental constant (Table 4). The actual variation of the geminal constant for the CH_2 group with the orientation of the lone pairs of α-oxygen can be found from the experimental data taking into account the form of the theoretical curve. Tetrahydropyran ($\zeta \simeq 180°$ and 300°), tetrahydrofuran ($\zeta \simeq 210°$ and 270°), oxetane (−6.02 Hz, [182] $\zeta \simeq 240°$) and a steroid (XX) [45] (−6.0 Hz, [83] $\zeta \simeq 240°$) were chosen (Table 5) as the reference points in the above relation (Fig. 9).



(XX)

Table 5. Values of $^2J_{HH}$ (Hz) for five- and six-membered heterocyclic compounds [43,44,74,75].

X	Y		
CH_2	CH_2	−13.05 [76]	−13
S	CH_2	−13	−10
S+	CH_2	−15 [77]	—
N	CH_2	−12.0 [78]	−9.5
N+	CH_2	−13	−13
O	CH_2	−11.5	−8
S	S	−14	−9.7
N	S	—	−9.4
N	N	−8.5	−3.5
O	N	−8	−2.5
O	S	−11.1	−5.2
O	O	−6.18 [79,80]	+0.8 [81]

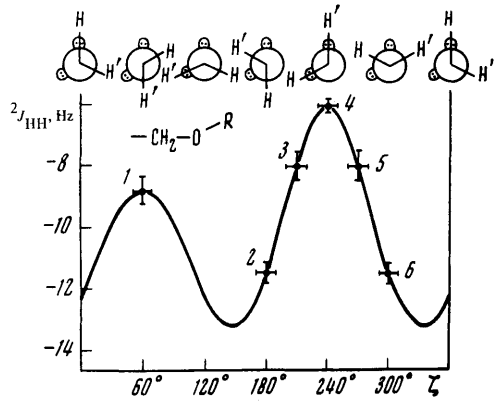


Figure 9. Variation of the H_2C-O geminal constant with the orientation of the orbitals of the lone electron pairs of oxygen: 1) calculated from the average $^2J_{HH}$ for $(CH_3)_2O$ (see text); 2) and 6) tetrahydropyran; 3) and 5) tetrahydrofuran; 4) steroid (XX) and oxetane.

The value for $\zeta \simeq 60°$ was calculated from $^2J_{HH} = -10.6$ Hz for $(CH_3)_2O$, [44] assuming rotational averaging:

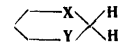
$$\langle {}^2J_{HH} \rangle = \frac{1}{3}(J_{60°} + J_{180°} + J_{300°}),$$

where $J_{180°} = J_{300°} = -11.5$ Hz, as for tetrahydropyran.

Fig. 9 shows that the maximum contribution by the lone pair orbitals of α-oxygen is +7.8 Hz when both C−H bonds are eclipsed¶. The minimum value in Fig. 9 (−13.3 Hz) is confirmed indirectly by the minimum recorded value $^2J_{HH} = -14$ Hz for the CH_2-O fragment [45,84].

An empirical analysis of the effect of the orientation of the lone pair on the geminal constant has been carried out for nitrogen-containing cyclic compounds with a fixed conformation [86]. Table 6 lists the values of $^2J_{HH}$ for six-membered rings. Comparison of the geminal constants for five- and six-membered nitrogen-containing rings with known steric structures made it possible to derive a relation between $^2J_{HH}$ and the dihedral angle ζ (Fig. 10).

Table 6. Effect of the orientation of the lone electron pair of nitrogen (indicated in brackets) on the geminal constants of the six-membered rings [86]



X	Y	$^2J_{HH}$, Hz	Refs.
N (e)	CH_2	−13.6	87
N (a)	CH_2	−11.5	88
N (e)	O	−10.5	88
N (a)	O	−7.5	89
N (e)	N (e)	−13.0	90
N (e)	N (a)	−11.3	86
N (a)	N (a)	−8.5	91

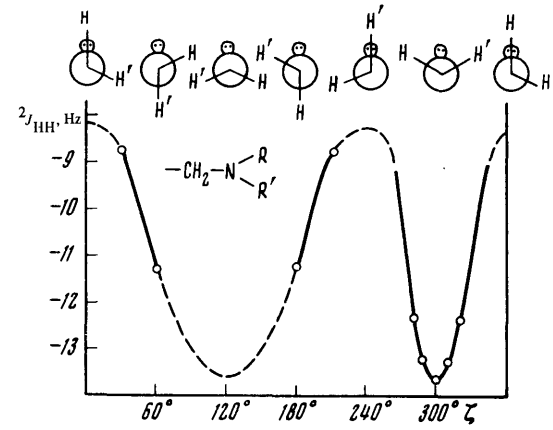
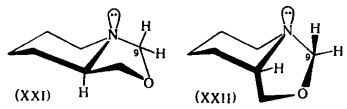


Figure 10. Variation of the H_2C-N geminal constant with the orientation of the lone electron pair of nitrogen in cyclic systems with a fixed conformation [86].

¶Empirical analysis of data for oxygen-containing ring systems showed [84,85] that, when one of the C−H bonds is eclipsed by the lone pair of the α-substituent X, the geminal constant for the H_2C-X fragment increases by 1.8 Hz. Theoretical calculation [40] by the molecular orbital method gave a maximum contribution of +12.6 Hz by the p^π orbital of the lone pair, +5.3 Hz by the sp^2 orbital, and a negative contribution by the σ orbital.

As an example of the use of the lone pair effect in conformational analysis, one may quote the determination of the configuration of the isomers of 1-aza-8-oxabicyclo-[4,3,0]nonane with *trans*- (XXI) and *cis*-junctions (XXII) between the six- and five-membered rings [92]. In the *trans*-isomer the C_9–H bond is virtually eclipsed by the lone pair of electrons of nitrogen ($\zeta \simeq 210°$) and oxygen, while in the *cis*-isomer the projection of the axis of the nitrogen lone pair bisects the H–C_9–H′ angle ($\zeta \simeq 300°$). In the first case there is a possibility of a considerable positive contribution to the H–C_9–H′ geminal constant (Fig. 10). In fact the constant for isomer (XXI) is less negative (−0.8 Hz) than for isomer (XXII): −5.0 Hz.



The effect of the lone pair together with that of the electronegativity of the α-atom explains [36,39] the very high positive values of the H–H geminal constants for formaldehyde O=CH_2 (+42.4 Hz) [93] and *N*-alkylmethyleneimines RN=CH_2 [up to +16.5 Hz, R=$C(CH_3)_3$]. [94,95] The formaldehyde value is the upper limit of the known range of $^2J_{HH}$ constants.

A non-linear relation between $^2J_{HH}$ and the electronegativities of the substituents (E_X and E_Y) was found [103] for compounds of the type H_2C=CXY:

$$^2J_{HH} = \frac{61.6}{E_X + E_Y} - 12.9 . \quad (4)$$

The form of this relation differs significantly from the linear relation proposed previously [99] on the basis of limited data:

$$^2J_{HH} = 8.7 - 2.9(E_X + E_Y). \quad (5)$$

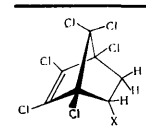
In order to refine the relation between $^2J_{HH}$ and electronegativity, theoretical calculations are probably necessary. Nevertheless, the available data [39,43,44,99,103,104] make it possible to employ the value of $^2J_{HH}$ in order to obtain information about the structure of olefins.

The effect of the β-substituent in saturated fragments depends on its orientation relative to the geminal protons. Theoretical considerations [39] lead to the qualitative conclusion that, when the β-substituent X is within the H–C–H′ geminal angle on the Newman projection (XXIII), the contribution to the $^2J_{HH'}$ constant is positive, but, if the β-substituent is outside this angle, the contribution is negative, i.e. $^2J_{HH'} > {}^2J_{H'H''}$. In contrast to ethylenes, the H–H geminal constants for *endo*-substituted hexachlorobicyclo[2,2,1]heptenes are seen to decrease (Table 8).

Table 7. Effect of the β-substituent on the geminal constant.

H_2C=CHY	$^2J_{HH'}$, Hz	Refs.	H_2C=CHY	$^2J_{HH'}$, Hz	Refs.
Li	+7.1	96	I	−1.5	53
$Si(CH_3)_3$	+3.6	97	Cl	−1.5	53
H	+2.5	38	Br	−1.7	53
CH_3	+2.1	98	OCH_3	−2.0	100
$N(CH_3)_2$	0.0	99	F	−3.2	53
SCH_3	−0.3	100, 101	$N^+(CH_3)_3$	−4.1	102

Table 8.

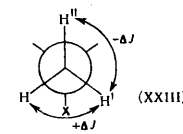
	$^2J_{HH'}$, Hz	Refs.
H	−12.62	105
SCH_3	−13.00	106
$SCOCH_3$	−13.10	10
Br	−13.30	107,108
Cl	−13.32	109
$OCOCH_3$	−13.3	109
F	−13.53	110

5. Effect of the β-Substituent

The H–H geminal constant is influenced not only by the α-substituent but also by the more remote β-substituent. The general tendency, observed for substituted ethylenes, indicates a decrease of $^2J_{HH}$ with increasing electronegativity of the β-substituent (Table 7). The tendency is opposed to that observed for the effect of the α-substituent, which is consistent with the intuitive hypothesis concerning the influence of the inductive effect. This example clearly illustrates the limitations of such intuitive considerations concerning the influence of the inductive effect in NMR.

In the molecular orbital method [39] the effect of the electronegative β-substituent is treated as a result of the withdrawal of electron density from the antisymmetric bonding orbital ψ_2 of the CH_2 fragment (Fig. 5). In contrast to the effect of the α-substituent, in this case theory predicts a negative contribution to $^2J_{HH}$ with increasing electronegativity.

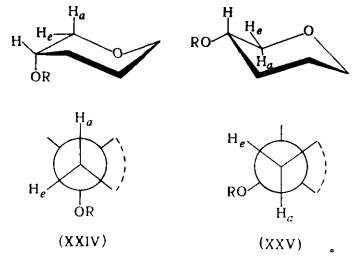
In this case the substituent is at the limit of the H–C–H geminal angle.



(XXIII)

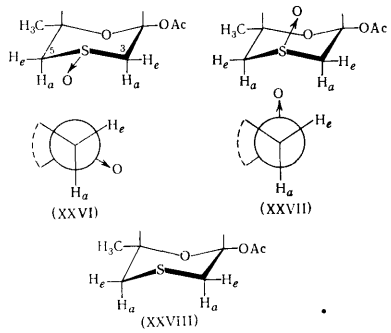
The geminal H–H constants for the inversion conformations of a number of heterocyclic compounds provide an experimental confirmation of the theoretically predicted orientation effect of the substituent. For example, among pentopyranose derivatives [111,112] a lower constant $^2J_{5e,5a}$ = −13.3 Hz is observed for the axial orientation of the substituent C_4OR (XXIV) (the electronegative β-oxygen atom is outside the $H_eC_5H_a$ geminal angle) than for the equatorial orientation (XXV): $^2J_{5e,5a}$ = −11.2 Hz (the oxygen atom is

within the $H_eC_5H_a$ angle). Similarly among 2-deoxy-D-arabohexapyranose derivatives[112], $^2J_{2e,2a} = -13.8$ Hz for the axial C_1–OR orientation is lower than for the equatorial orientation: $^2J_{2e,2a} = -12.4$ Hz.



(XXIV) (XXV)

The orientation effect of the β-atom has been used in the determination of the absolute configuration of the sulphoxide group in derivatives of 1,4-oxathian *s*-oxide[113]. For the equatorial orientation of the oxygen atom in the S → O group (XXVI), the $^2J_{5e,5a}$ and $^2J_{3e,3a}$ constants should be higher than for the axial orientation (XXVII), since in the first case the β-atom is within the H_eCH_a geminal angle. Therefore the isomer with constants of −12.0 and −11.3 Hz can be regarded as having an equatorial S → O bond, while the isomer with constants of −14.2 and −13.8 Hz should have an axial S → O bond. For comparison, we may point out that the corresponding sulphide (XXVIII) has $^2J_{5e,5a} = -13.1$ Hz and $^2J_{3e,3a} = -13.5$ Hz.



(XXVI) (XXVII)

(XXVIII)

After a suitable detailed development, the orientation effect of the β-substituent may find large-scale application in conformational analysis.

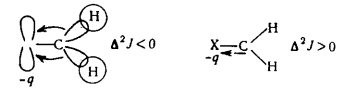
The γ-substituent (the substituent in the 4-position) has been found to influence the coupling constant of the $O-CH_2-O$ *gem*-protons in 1,3-dioxans, the effect depending on the electronic nature and orientation of the substituent[114].

6. Effect of the Medium

Careful investigations[50,51,81,93–95,115–122] showed that the H–H geminal constant clearly depends on the dielectric constant of the medium ϵ (Fig. 11). With increase of the polarity of the medium, the negative contribution to $^2J_{HH}$ also increases, the direction of the effect having an equal influence on positive (formaldehyde[93]) and negative (phenylthi-iran[81]) H–H constants (Fig. 11). The experimental data show that the effect may be used to determine the sign of ^2J: if $^2J > 0$, an increase of ϵ should entail a decrease of the absolute value of the H–H constant; if $^2J < 0$, the constant should increase.

The reason for the variation of $^2J_{HH}$ under the influence of the medium is the effect of the reaction field, induced by the solvent molecules, on the molecular dipole of the test compound[81]. Under the influence of this field, the local dipole moment of the molecule increases in two possible ways.

a. By pseudoconjugation [formula (XXIX)] in which the effect of the lone electron pair of the α-atom diminishes (see Section II, 4), resulting in a positive contribution to $^2J_{HH}$. Consequently when this effect is weakened under the influence of the medium, $^2J_{HH}$ decreases owing to the withdrawal of electrons from the antisymmetric orbital ψ_2 (Fig. 5).



(XXIX) (XXX)

b. By an inductive effect [formula (XXX)] involving the C–X σ bond, which is equivalent to an increase of the electronegativity of X. This should entail a positive contribution to $^2J_{HH}$ in consequence of the withdrawal of electrons from the symmetrical orbital ψ_1 (Fig. 5).

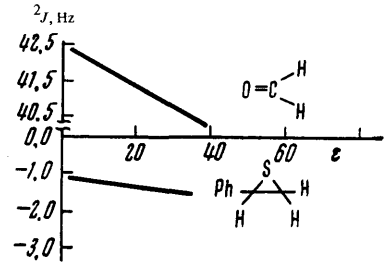


Figure 11. Effects of the polarity of the medium on the H–H geminal constants of formaldehyde[93] and phenylthi-iran[81].

Experimental data have shown that the main contribution comes from pseudoconjugation. Evidently the higher the dipole moment of the molecule, the greater the influence of the solvent. This has been confirmed experimentally: the slope of the plot of $^2J_{HH}$ against ϵ is higher for formaldehyde than for phenylthi-iran (Fig. 11).

7. H–X–H Heteroatomic Fragments

H–H geminal coupling is transmitted not only via the carbon atom but also via any other atom X of the H–X–H fragment (Table 9).

Certain evident analogies with the $^2J_{HCH}$ constant (for example the identity of the sign and the similarity of the magnitudes of the $^2J_{HH}$ constants for CH_4, NH_3, N^+H_4, PH_3, $RCONH_2$, and $CH_2{=}CH_2$) suggest that many relations found for the H–C–H fragment are valid also for H–X–H. The increase of $^2J_{HH}$ in the series $CH_4 < SiH_4 < GeH_4 < SnH_4$ can be explained qualitatively by an increase in the difference between the energies of the bonding and antibonding orbitals of the H–X–H fragment (Fig. 5), as a result of which the positive contribution by the $\psi_2 \rightarrow \psi_3$ transition becomes dominant[134]. The relatively high value of $^3J_{HH}$ for interaction between the bridge and "window" hydrogen

atoms in diborane indicates the presence of a stable three-electron bond[134]. Unfortunately the sign of this constant has not been determined, which makes comparison with theoretical calculations difficult[33].

Table 9. Geminal interactions between the protons of the H–X–H heteroatomic fragments.

Fragment	Compound	$^2J_{HH'}$, Hz	Refs.
H–B–H	B^-H_4	10.7	123
H···B–H	B_2H_6	7.0	124
H–C–H	CH_4	−12.4	37
H–N–H	NH_3	−10.35	125
	N^+H_4	−11.6	126
H–O–H	H_2O	7.2	127
H–P–H	PH_3	−13.2	128,129
H–S–H	H_2S	13.7	130
H–Si–H	SiH_4	+2.75	131,132
H–Ge–H	GeH_4	+7.69	133
H–Sn–H	SnH_4	+15.3	134
H–C–H ‖ H–N–H	$CH_2{=}CH_2$ $RCONH_2$	+2.5 +2.8	38 135

There is no doubt that more extensive studies and theoretical calculations of $^2J_{HXH}$ are of considerable importance for the understanding of the nature of geminal coupling.

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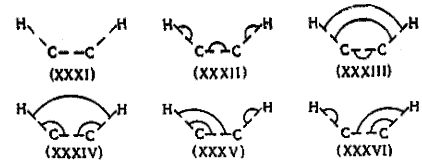
In conclusion of the discussion of the H–H geminal constant, we may note that the constant contains information not only about the electronic structure of the molecule but also about the conformation of adjacent atomic fragments. Although the use of $^2J_{HH}$ for conformational analysis is at present limited by the inadequate knowledge of the orientation effect and the insufficiently clear separation of the contributions by different factors, one can reasonably suppose that these limitations will be overcome by systematic accumulation of experimental data and theoretical calculations. Then NMR spectroscopy will acquire a new parameter for the conformational analysis of molecules.

III. THE VICINAL CONSTANT $^3J_{HH}$

One can claim without exaggeration that spin–spin interaction between the vicinal protons of the H–C–C–H fragment deservedly attracted most attention. The $^3J_{HH}$ constants are widely and very successfully employed in structural analysis (in the determination of the number of adjacent protons and the nature of substitution in molecules), in the study of exchange processes (based on the "obliteration" of the multiplet structure of the spectra), and particularly in configurational and conformational analysis.

Calculation by the valence bond method of the constant for the interaction between vicinal protons in the six-electron system (XXXI) takes into account the mixing with the ground state (XXXII), in which electron pairing is complete, of the four excited states (XXXIII)–(XXXVI).

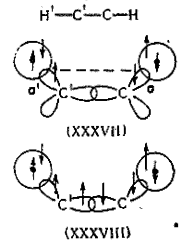


(XXXI) (XXXII) (XXXIII) (XXXIV) (XXXV) (XXXVI)

The electronic mechanism of the vicinal interaction is determined mainly by the polarisation of the "quasi-π" orbitals of the C–H and C–H bonds [(XXXIII) and (XXXVII)], which makes a positive contribution[136]:

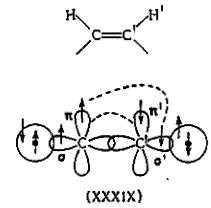
$$^3J \propto 3K(\sigma\sigma')/K(\sigma H)\,, \qquad (6)$$

where $K(\sigma H)$ is an integral with a constant value and $K(\sigma\sigma')$ depends on the relative positions of the σ and σ' orbitals. The mechanism of the consecutive transmission of spin–spin polarisation via the chain of atoms—Hund's mechanism[137] [formula (XXXVIII)]—also makes a positive, but probably very small, contribution.



(XXXVII) (XXXVIII)

Therefore, in contrast to the geminal constant, in the case of the H–H vicinal constant there is no competition between mechanisms with different signs. All the experimental $^3J_{HH}$ values available are positive.



(XXXIX)

If the carbon atoms of the vicinal fragments are separated by a double (or triple) π bond, additional contributions[138] [formula (XXXIX)] to the $^3J_{HH}$ constant are produced and are transmitted via a σ–π interaction mechanism—from the hydrogen atom to the carbon π orbital:

$$\Delta^3J(\sigma\pi) \propto K(\sigma\pi')K(\sigma'\pi)[K(\sigma H) + K(\pi\pi')]\,.$$

This contribution depends on the relative orientations of the C–H bond and the π orbital and is independent of the configurational orientation of the C–H bonds (*cis*- or *trans*-). Comparison of the theoretical relations for the contribution by the σ–π interaction to the vicinal coupling constant and for the hyperfine structure constant in the ESR spectra shows that the contribution by π electrons may be expressed in terms of experimental parameters[138]:

$$\Delta^3J_{HH'}(\sigma\pi) = h a_H(T) a_{H'}(T)/2\Delta E\,,$$

where $a_H(T)$ and $a_{H'}(T)$ are hyperfine coupling constants for the radical fragment H–Ċ=C and ΔE is the average singlet–triplet excitation energy. With $a_H(H{-}C_{sp^2}) = -65 \times 10^6$ Hz and $\Delta E = 6$ eV, +1.5 Hz was found for ethylene, and with $a_H(H{-}C_{sp}) = 95 \times 10^6$ Hz and $\Delta E = 8$ eV, +4.6 Hz was found for acetylene[138].

1. Dependence of $^3J_{HH}$ on the Stereochemical Factor

The $K(\sigma\sigma')$ exchange integral in Eqn. (6) depends on the dihedral angle θ between the H–C–C and C–C–H planes [139]. Hence follows the familiar Karplus relation [136] (Fig. 12), which constitutes the basis of the configurational and conformational analysis in NMR spectroscopy. Since the function $K(\sigma\sigma') = f(\theta)$ does not have an [exact] analytical expression, several versions of an analytical equation have been proposed to describe the variation of $^3J_{HH}$ with the stereochemical factor:

$$^3J_{HH} = k_i \cos^2\theta + C \begin{cases} k_1 & \text{for } 0° < \theta < 90° \\ k_2 & \text{for } 90° < \theta < 180°; \end{cases} \quad (7)\ [136]$$

$$^3J_{HH} = A\cos^2\theta - B\cos\theta + C; \quad (8)\ [6]$$

$$^3J_{HH} = \alpha\cos 2\theta - \beta\cos\theta + \gamma. \quad (9)\ [141]$$

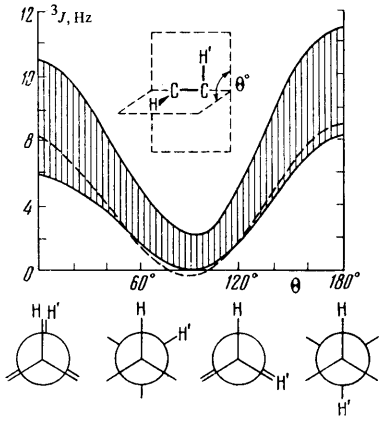


Figure 12. Variation of the vicinal constant $^3J_{HH}$ with the dihedral angle θ for the HC–CH saturated fragment. The dashed curve represents Karplus's theoretical calculation [138,141]. The shaded band corresponds to the most probable values of $^3J_{HH}$. Its upper limit is the curve for ethane [140].

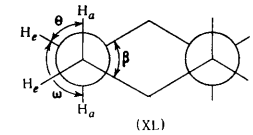
With appropriate values of the constant coefficients (all positive), these equations yield virtually coincident curves, so there is no fundamental difference between them. The choice of the equation is dictated by the suitability of its formulation. Eqns. (7) and (8) are usually employed.

The coefficients of Eqns. (6)–(8) have been evaluated theoretically [6,136,141], but these differ significantly from the experimental values (see Section III, 4). Therefore in the analysis of the conformational states of a particular series of compounds, it is recommended that these coefficients be determined empirically on the basis of models for the given series.

As an example, one may quote the determination of the HCCH dihedral angle in cyclohexane. At –100°C the rate of the "chair–chair" inversion is retarded so much that the individual signals due to the axial and equatorial protons are observed in the NMR spectrum of cyclohexane (5% solution in CS_2). The vicinal constants of these protons have been measured for 1,1′,2,2′,3,3′,4,4′-octadeuterocyclohexane: $^3J_{aa}$ = 13.12 Hz, $^3J_{ae}$ = 3.65 Hz, and $^3J_{ee}$ = 2.96 Hz [formula (XL)]. [76] These data made it possible to determine by Eqn. (8) with $C = 0$ the $H_aC–CH_e$ dihedral angle ($\theta = 57°$) for $\omega = 118°$. The stereochemical relation for cyclohexane then becomes:

$$^3J_{HH} = 12.95\cos^2\theta - 0{,}26\cos\theta.$$

The value of θ obtained agrees extremely well with electron diffraction data for cyclohexane in the gas phase (CC–CC dihedral angle $\beta = 55.9°$). [142]

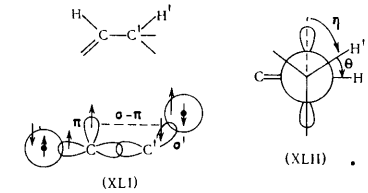


(XL)

When the values of $^3J_{HH}$ and the corresponding angles θ are plotted for compounds of different classes, a fairly broad band is obtained (Fig. 12). The scatter is due to the effect of a number of electronic and geometrical structural properties of the molecules, which are discussed below.

When vicinal protons interact in a system with an allylic double bond =CH–CH, an additional contribution by the interaction of the σ and π orbitals appears together with the interaction between σ orbitals (which depends on the orientation of the C–H bonds) [138,143,144] [formula (XLI)]:

$$\Delta^3J^{\sigma\pi}_{HH} \sim K(\sigma'\pi),$$



(XLI) (XLII)

The contribution is positive and depends on the projection angle η between the direction of the π orbital and the C–H bond [formula (XLII)]:

$$\Delta^3J^{\sigma\pi}_{HH} \propto \cos^2\eta \equiv \sin^2\theta.$$

The overall stereochemical relation for the vicinal interaction constant $^3J_{HH}$ for the =CH–CH fragment is (Fig. 13)

$$^3J_{HH} = {}^3J^{\sigma\sigma}_{HH} + {}^3J^{\sigma\pi}_{HH} = A\cos^2\theta - B\cos\theta + D\sin^2\theta. \quad (10)$$

The coefficients were determined empirically from data for a set of compounds with a fixed geometry: A = 9.1 Hz, B = 2.5 Hz, and D = 2.6 Hz. [145] D = 3.4 Hz was calculated theoretically [138]. Owing to the contribution by $^3J^{\sigma\pi}_{HH}$, the above stereochemical relation is smoother than the analogous relation for the saturated HC–CH fragment.

The coefficients in the stereochemical relations [Eqns. (7)–(9) and (10)] depend significantly on the nature of the compound containing the given CH–CH fragment. The most important factors are the geometry of the fragment (the H–C–C valence angle and the C–C bond length and also the nature and orientation of the X–CH–CH substituent.

2. Effects of the H–C–C Valence Angle and the C–C Bond Length

An increase of $^3J_{HH}$ for the CH=CH fragment of cycloolefins with increasing ring size has been observed experimentally [148,149] (Table 10). The H–C–C valence angle decreases in the same sequence, from about 150° for cyclopropene and about 135° for cyclobutene to the

normal value of about 120°. A similar tendency has been noted for $^3J_{HH}$ in aromatic systems. For example, the constant is ≤ 0.25 Hz for the three-membered cyclopropenium ring[152], 4.0 Hz for the five-membered azulene ring[153], 7.54 Hz for benzene[154], and 9.5 and 10.3 for the seven-membered azulene ring[153]. Possibly the reason for the variation of the vicinal constant with ring size arises from a number of factors, including the hybridisation of the carbon atoms, the degree of strain in the ring, and geometrical parameters of the CH=CH fragment. The above tendency may be represented[155] by a relation between $^3J_{HH}$ and the C–CH=CH valence angle (Fig. 14), which has been determined for many compounds by X-ray diffraction analysis.

Table 10. The $^3J_{HH}$ constants in the series of cycloolefins

n	1	2	3	4	5	6	7	8	9
$^3J_{HH}$, Hz	1.3 [149]	2.87 [150]	5.57 [151]	10.11 [151]	10.8 [146]	10.3 [146]	10.7 [146]	10.8 [146]	10.7 [146]

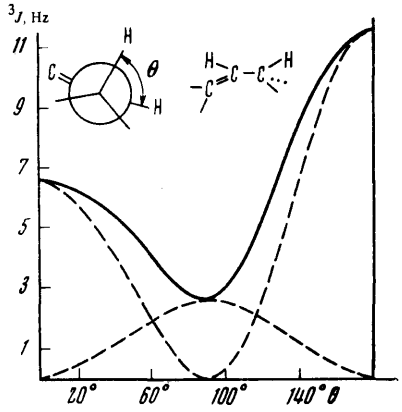


Figure 13. Variation of $^3J_{HH}$ for a vicinal fragment having an allylic double bond with the stereochemical factor[145]. The dashed curves represent the contributions by $^3J(\sigma\sigma)$ and $^3J(\sigma\pi)$.

The observed variation of $^3J_{HH}$ with the valence angle has been given a theoretical basis[27,141,161]. With increasing ring size, the distance between the hydrogen atoms diminishes and consequently the contribution by the canonical structures (XXXIII) and (XXXIV) increases, which leads to a higher vicinal constant. However, the theoretical values[141], 2.1 Hz for an H–C–C angle of 130°, 6.1 Hz for 120°, and 16.0 Hz for 110°, agree with the experimental data only qualitatively. The molecular orbital method gives a less critical sequence, namely 2.4, 5.7, and 10.1 Hz respectively[27] (see the dashed curves in Fig. 14).

It has also been shown theoretically[141] that the vicinal constant for the ethylene fragment *cis*-CH=CH decreases with the length R (Å) of the C=C bond:

$$^3J_{cisHH} = J_0[1 - 2.9(R - 1.35)], \quad (11)$$

where J_0 is the interaction constant for R = 1.35 Å.

The experimental data for carbocyclic compounds (cyclohexene, cyclohexa-1,3-diene, 1,2-dihydronaphthalene, benzene, and condensed aromatic compounds) also yield a linear relation[151]:

$$^3J_{cis} = -36.40R + 58.46,$$

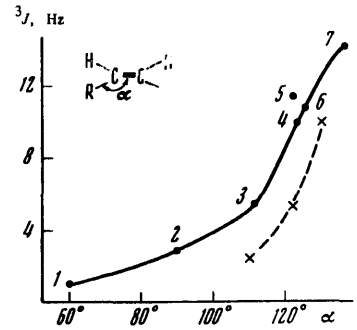


Figure 14, Variation of the vicinal constant $^3J_{cis}$ for an olefinic fragment with the valence angle α.[155] Experimental points: 1) cyclopropene[149]; 2) cyclobutene[150]; 3) cyclopentene[151]; 4) cyclohexene[151]; 5) ethylene[19]; 6) *cis*-but-2-ene[156]; 7) *cis*-di-t-butylethylene[155]. The X-ray diffraction data for compounds *3–7* were taken from Refs. 157–160. The dashed curve represents the theoretical calculation[27].

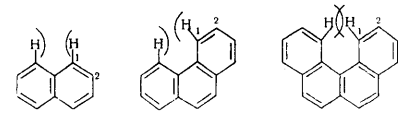
which agrees fairly well with the theoretical Eqn. (11): the ratio of the constants for bond lengths of 1.35 and 1.45 Å is 1.63, whereas Eqn. (11) predicts 1.41. For compounds of the type $R(CH{=}CH)_nCH{=}R'$ with a *trans*-configuration of the double bonds, it has been found that[162]

$$^3J_{transHH} = -81.85R + 127.86,$$

which yields the ratio $^3J_{1.35Å}/^3J_{1.45Å} = 18.4$, also in satisfactory agreement with theory.

It is noteworthy that the constants $^3J_{HH}$ for the above series of compounds[151,161] and also for a series of aromatic compounds[163,164], including charged five-membered rings[165], are linearly correlated with the C=C bond order calculated by the simple Hückel method.

When the vicinal protons come closer together in space in a series of condensed aromatic molecules, $^3J_{HH}$ deviates from the linear relation with the length and order of the bond[151].



The steric contraction effect leads to an increase of the $^3J_{1,2}$ constants by 0.08 Hz for naphthalene (XLIII), 0.30 Hz for phenanthrene (XLIV), and 0.50 Hz for benzo[*c*]phenanthrene (XLV). It has been suggested that the reason for the deviations is distortion of molecular geometry, and in the first place a decrease of the $H-C_1=C_2$ valence angle [151].

3. Effect of the Electronegativity of the Substituents

Many experimental data show that the constant $^2J_{HH}$ for the X–CH=CH fragment as a rule decreases with increasing electronegativity of the substituent **X** (Tables 11 and 12).

Table 11. Effect of the α-substituent **X** on the vicinal constant $^3J_{HH}$ (Hz).

X	CH_3CH_2X	refs.	CH_2=CHX			
			trans-H–H	refs.	*cis*-H–H	refs.
Li	8.90	167	23.9	96	19.3	96
$Si(CH_3)_3$	8.0	168	20.2	97	14.6	97
$H(^3J_0)$	8.0	38	19.1	38	11.5	38
CH_2R	7.53*	169	16.8**	98	10.0**	98
SCH_3	7.42	170	16.4	100,101	10.3	100,101
I	7.45	169	15.9	53	8.0	53
Br	7.33	169	15.0	53	7.2	53
$N(C_2H_5)_2$	7.13	169	16.1	99	9.4	99
Cl	7.23	169	14.8	53	6.9	53
OC_2H_5	6.97	169	14.5	100	7.0	100
F	6.9	171	12.6	53	4.6	53
$C^+(CH_3)_2$	5.2	172	—		—	
$N^+(CH_2R)_3$	7.4**	173	15.0*	102	8.5*	102
$O^+(C_2H_5)_2$	4.7	174	—		—	
k experiment	−0.09	41	−0.17	41,99	−0.34	41,99
k calculation (Ref.141)	−0.07		−0.25		−0.60	

*R=CH_3;
**R=H.

It has been established [41,42,99,166] that the relation is as a rule described by the additive equation

$$^3J_{HH} = {}^3J_0\left(1 + k\sum_i \Delta E_{X_i}\right), \qquad (12)$$

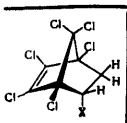
where $^3J_0$ is the interaction constant for the unsubstituted fragment (X=H), k a coefficient which depends on the class of compound (usually $k < 0$), and $E_X = E_X - E_H$ the difference between the electronegativities of the first atom of the substituent and hydrogen. The coefficients k found experimentally for substituted ethanes and ethylenes† (Table 11) agree satisfactorily with the values calculated theoretically [141] by the valence bond method taking into account ionic structures [175,176]. The dependence of $^3J_{HH}$ on the substituent is used to determine the mutual influence of the electronegativities of the groups of disubstituted ethylenes [177].

†On the basis of a set of disubstituted ethylenes XCH=CHY with a wider range of electronegativities of the substituents, non-linear relations of the type of Eqn. (4) have been found [71]:

$$^3J_{cis} = 91.2/(E_X+E_Y)-9.7,$$
$$^3J_{trans} = 75.0/(E_X+E_Y)+0.3.$$

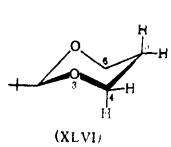
It is striking that the electronegativity of the substituent in the ethylene fragment affects the constant $^3J_{HH}$ for *cis*-protons much more than for *trans*-protons. The influence of the orientation of the substituent **X** must also be taken into account for the saturated fragments X–CH–CH, [178] otherwise erroneous conclusions concerning the conformation of the compound may be arrived at.

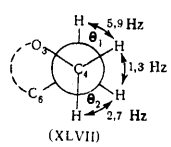
Table 12.

	Refs.	$^3J_{cis}$	$^3J_{trans}$
H	105	9.63*	3.67
C_6H_5	121	9.16	4.27
$SCOCH_3$	10	8.85	3.88
Br	107,108	8.4	3.5
Cl	121	8.20	3.16
OH	121	7.70	2.51
$OCOCH_3$	121	7.58	2.47
F	110	7.19	1.81
k	109	−0.14	−0.33

*$^3J_{endo\text{-}endo}$ = 9.17 Hz. [105]

We shall now consider an example of such influence. For 2-t-butyl-1,3-dioxan (XLVI), the dihedral angles θ_1 and θ_2 in the C_5–C_6 fragments (XLVII) should be identical (regardless of the distortion of the ring conformation) in consequence of their symmetrical disposition relative to the symmetry plane of the ring. The different values of $^3J_{HH}$ corresponding to these dihedral angles (5.9 and 2.7 Hz) [85] are due to the orienting influence of the electronegativities of the O_3 and C_6 atoms. Protons with θ_1 and $^3J_{HH}$ = 5.9 Hz have hydrogen and carbon atoms in the *trans*-position (the oxygen atom is in the *gauche*-position), while protons with θ_2 and $^3J_{HH}$ = 2.7 Hz have a hydrogen atom and an oxygen atom (which is more electronegative than the carbon atom) in the *trans*-position (the carbon atom is in the *gauche*-position). An even lower value $^3J_{HH}$ = 1.3 Hz corresponds to protons with carbon and oxygen atoms in the *trans*-position.

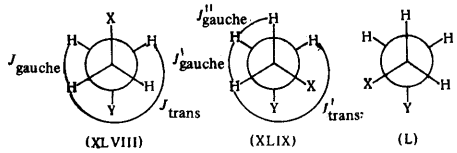

(XLVI)



(XLVII)

A systematic study of the orienting effect of substituents on the vicinal constants has been made for 1,2-disubstituted ethanes XCH_2CH_2Y. [179–186] A special technique for the interpretation of the variation of the observed constants, which have been averaged over the rotational states [formula (XLVIII)–(L)], with the polarity of the medium makes it possible to determine the constants J_{trans} and J_{gauche} for the *trans*-isomer (XLVIII) and the

constants J'_{gauche} and J''_{gauche} + J'_{trans} for the *gauche*-isomers (XLIX) and (L).[181,185]



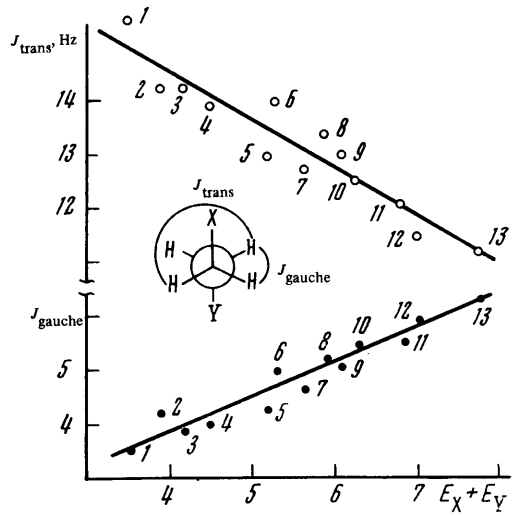


Figure 15. Variation of the vicinal constants for the *trans*-isomers of 1,2-disubstituted ethanes with the electronegativity of the substituents[185]. Substituents X and Y: 1) $C(CH_3)_3$, Li; 2) $C(CH_3)_3$, MgR_2; 3) $C(CH_3)_3$, AlR_3; 4) $C(CH_3)_3$, $Si(CH_3)_3$, 5) $C(CH_3)_3$, $C(CH_3)_3$; 6) I, I; 7) $C(CH_3)_3$, $N^+(CH_3)_3$; 8) Br, Br; 9) Cl, Br; 10) Cl, Cl; 11) F, Br; 12) F, Cl; 13) F, F. The data were taken from Ref. 1.79 for points *1*, *3*, and *4*, from Ref. 180 for point *2*, and from Ref. 185 for points *5–13*.

Fig. 15 shows the variation of J_{trans} and J_{gauche} for the *trans*-isomers with the sum of the electronegativities of the substituents X and Y. In agreement with the theoretical calculations[141], the J_{trans} constant decreases with increasing E_X and E_Y:[185]

$$J_{trans} = 14.28\,[1 - 0.062\,(\Delta E_X + \Delta E_Y)]\,. \qquad (13)$$

However, J_{gauche} increases with the electronegativity ($k > 0$):

$$J_{gauche} = 3.99\,[1 + 0.16\,(\Delta E_X + \Delta E_Y)], \qquad (14)$$

which is inconsistent with the theoretical prediction. The constant J_{ee} for *trans*-1,2-disubstituted 4-t-butylcyclohexanes[187], which corresponds to the same orientation relative to the substituents as J_{gauche} in 1,2-disubstituted ethanes, behaves in the same manner.

The coefficients J_0 in Eqns. (13) and (14) may be assumed to be identical with J_{trans} and J_{gauche} for unsubstituted ethane, if one postulates that in the *trans*-isomer the H–C–C–H dihedral angles are not distorted by substituents. In agreement with theory, the constants for the *gauche*-isomers are found to decrease as $E_X + E_Y$ increases[185]:

$$J'_{gauche} = 4.99\,[1 - 0.24\,(\Delta E_X + \Delta E_Y)], \qquad (15)$$

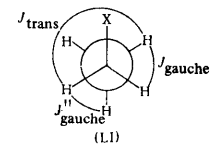
$$J''_{gauche} = 4.45\,[1 - 0.32\,(\Delta E_X + \Delta E_Y)], \qquad (16)$$

$$J'_{trans} = 13.95\,[1 - 0.043\,(\Delta E_X + \Delta E_Y)]. \qquad (17)$$

It is quite likely that the inconsistency between the coefficients J_0 for the *trans*- and *gauche*-oriented protons in the relations for the *trans*- and *gauche*-isomers [Eqns. (13)–(17)] indicates different dihedral angles, which may be due, in particular, to steric and electrostatic interactions between the substituents in the *gauche*-isomer. Moreover, the changes in the C–H and C–C bond lengths and in the H–C–C valence angles under the influence of substituents may play a definite role.

Nevertheless the coefficients $J_0 = 7.9$ Hz and $k = -0.074$ for the averaged vicinal constant $\langle J \rangle$ for monosubstituted ethanes (LI), calculated by the equation

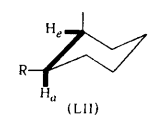
$$\langle J \rangle = (1/3)(J_{trans} + J_{gauche} + J''_{gauche}),$$

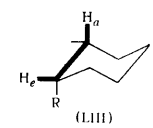


(LI)

and Eqns. (13), (14), and (16), agree satisfactorily with the experimental data (Table 11).

One must assume that the orienting effect of the substituent is in fact responsible for the observed inequality $^3J_{ae} > {}^3J_{ea}$ of the vicinal constants for six-membered rings (cyclohexanes[178,187], steroids[188]), while the dihedral angle is the same ($\theta \simeq 60°$). For example, in the series of 5β-steroids with a 3α-hydroxy- or acetate group (occupying an equatorial position), $J_{ae} \simeq 5.5$ Hz is observed [compound (LII)] and in the series of 5α-steroids with 3β-substituents (in the axial position), $J_{ae} \simeq 2.5$–3.2 Hz has been found [compound (LIII)].[189] In the first case the electronegative substituent has the *gauche*-orientation relative to the vicinal proton H_e and has virtually no effect on $^3J_{HH}$. In the second case the substituent occupies the *trans*-position relative to the proton H_a and therefore a significant effect of its electronegativity appears.


(LII)


(LIII)

The angular variation of $^3J_{HH}$ with the orientation of the substituent can be conveniently represented by a schematic relation between the coefficient k in Eqn. (12) and the dihedral angle ξ between the substituent X and one of the protons (Fig. 16). The greatest effect of the substituent is to be expected with the C–X and C–H bonds in the eclipsed and *trans*-positions.

Another type of orientation relation has been proposed[193] on the basis of an empirical treatment of a large number of experimental data for fragments of the type $X_1X_2CH–CHX_3X_4$:

$$^3J_{HH} = 11.3\cos^2\theta - 2.5\cos\theta + 1.8 - \left(0.4 + 1.2\cos^2\frac{3}{2}\theta\right) \cdot \sum_{i=1}^{4} \frac{1}{i}\,\Delta E_{X_i}.$$

Appropriate recalculation shows that this equation yields a result which differs significantly from the $k-\xi$ plot in Fig. 16. There is no doubt that the orientation effect of the substituent on the H–H vicinal constant requires further detailed experimental and theoretical study.

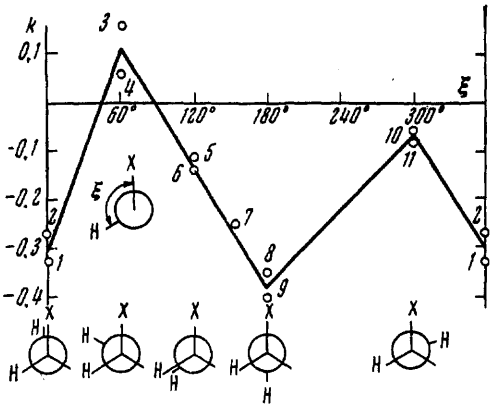
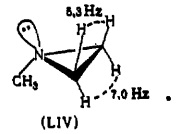


Figure 16. Variation of the effect of the electronegativity (k) of the substituent X on the $^3J_{HH}$ constant with the orientation of X relative to the interacting protons of the X–CH–CH fragment: 1) and 6) hexachlorobicyclo[2,2,1]-heptenes[109] ($\theta \simeq 120°$ and 0°); 2) and 7) cyclopropanes[190] ($\theta \simeq 147°$ and 0°); 3) and 10) *trans*-isomers of 1,2-disubstituted ethanes[185] ($\theta \simeq 60°$ and 180°); 4) and 8) *trans*- and *cis*-isomers of 1,2-disubstituted 4-t-butylcyclohexanes[187] ($\theta \simeq 60°$ and 180°); 5) bicyclo[2,2,1]heptenes[191] ($\theta \simeq 120°$); 9) and 11) 6β- and 6α-substituted 5α-cholestan-7-ones[192] ($\theta \simeq 60°$ and 180°).

An additional complication in the analysis of the effect of the electronegativity of the substituent on the vicinal constant arises from the fact that substituents do not have axial symmetry as a rule. The orientation of the C–X bond is especially significant for substituents having a lone electron pair. In particular, $^3J_{HH}$ in the series of five-membered heterocycles with X = S and O and also $^3J_{trans}$ in the series of four-membered ring compounds have high values, contrary to the expected low values (Table 13), while for three-membered heterocycles the usual tendency towards a decrease of $^3J_{HH}$ with increasing electronegativity of the atom X is observed. It has been suggested[86,198] that the lone electron pair of the heteroatom makes a positive contribution to the constant $^3J_{HH}$, which reaches 2.3 Hz[88] for the transoid orientation of the C–H bond relative to the axis of the lone pair atomic orbital. The higher value of the constant $^3J_{cis}$ for protons with *cis*-orientation relative to the substituent in *N*-methylaziridine (LIV) compared with $^3J_{cis}$ for protons with *trans*-orientation relative to N–CH_3 serves as a clear illustration[94]. In the first case the lone electron pair of the nitrogen atom occupies the transoid position relative to the C–H bonds of the interacting protons.



(LIV)

The orientation effect of the substituent gives rise to significant difficulties in the employment of H–H vicinal constants for the investigation of conformational equilibrium processes[200]‡. Even when a Karplus curve is plotted for the given class of compounds, the required accuracy in the determination of the statistical weight of the conformers from the average constant ^3J is not secured under conditions of a rapidly attained equilibrium[204].

Table 13.

X		CH_2	References	C=O	References	S	References	NH	References	O	References
	J_{cis}	8.98	55	—		7.15	63	6.3	63	4.45	63
	J_{trans}	5.57	55	—		5.65	63	3.8	63	3.08	63
	J_{cis}	10.4	194	10.4	70	8.93	195	—		8.65	196
	J_{trans}	4.9	194	6.4	70	6.27	195	—		6.87	196
	J_{cis}	7.4	197,198	7.2	197,198	10.0	199	8.83	199	10.7	197,198
	J_{trans}	4.6	197,198	2.2	197,198	7.5	199	8.85	199	8.3	197,198

There are certain data showing that the sign of the effect of electronegativity alternates with increase of the number of chemical bonds between the substituent and the fragment with vicinal protons[205]. The $^3J_{12}$ vicinal constant for the $XC_1H-C_2H-C_3H-C_4H$ chain decreases with the electronegativity of the substituent X ($k < 0$, see above), the constant $^3J_{23}$ increases ($k > 0$), and $^3J_{34}$ again decreases. A number of examples are presented in Table 14. It is noteworthy that the magnitude of the effect decays rapidly as the substituent becomes more remote. For example, the following formula has been found to represent the constant for the interaction of *ortho*-protons of monosubstituted benzenes[212]:

$$^3J_{23} \equiv {}^3J_{ortho} = 7.56(1+0.065\ \Delta E_X),$$

where k is smaller by a factor of 5 than for the *cis*-protons of monosubstituted ethylenes (Table 11). In order to observe the expected changes in $^3J_{34}$, a very high experimental accuracy is required.

4. Theroetical Calculations of $^3J_{HH}$

A complete *a priori* calculation[6] of vicinal constants has been made both by the valence bond[136,138,141,175,176,218] and molecular orbital[25–27,29–33,35,219,220] methods. However, the calculated values agree with experiment only qualitatively (Table 15). The difficulties encountered in the calculations apply generally to the quantum-chemical theory of complex chemical compounds. This is primarily

‡In the absence of conformational transitions or when the energy parameters of the conformations with respect to which $^3J_{HH}$ is averaged are equal, temperature has a very weak effect on the vicinal constant[46,48,52–54]. The solvent may be responsible for changes in $^3J_{HH}$ for polar molecules[201–203], but as a rule this effect is much weaker than the effect on the H–H geminal constant[121].

due to the approximate nature of the mathematical expressions for the physical quantities and the low accuracy of the estimates of the parameters entering into the equations.

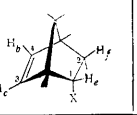
Table 14. Effect of substituents on the vicinal constants in the $XC_1H-C_2H-C_3H$ chain.

$XC_{(1)}=C_{(2)}-C_{(3)}H_3$		J_{12}^{trans}	J_{23}
Li	206	22.2	4.2
$Ge(CH_3)_3$	207	19.2	4.8
$Si(CH_3)_3$	207	18.6	5.4
H	98	16.81	6.4
Br	208	13.5	6.8
Cl	208	13.2	6.9
F	208	11.1	7.0

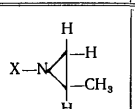
$XC_{(1)}H_2C_{(2)}H_2C_{(3)}H_3$		J_{12}	J_{23}
H	209	7.35	7.35
Cl	210	6.3	7.4
NO_2	210	6.8	7.5
NO_3	210	6.5	7.6

X-(1,2,3)		J_{23}	J_{34}
H	154	7.54	7.54
CH_3	211	7.68	7.48
Cl	212	8.05	7.46
Br	212	8.01	7.42
OCH_3	212	8.33	7.37

$XC_{(1)}H_2C_{(2)}H=C_{(3)}H_2$		J_{12}	J_{23}^{cis}	J_{23}^{trans}
H	98	6.4	10.02	16.81
CH_3	98	6.22	10.32	17.23
Cl	213	6.46	10.11	16.92
F	214	5.31	10.64	17.21



		$J_{12(ef)}$	$J_{34(bc)}$
H	191	(9.2)	5.8
COOH	191	8.5	5.7
Cl	191	8.2	5.6
$OCOCH_3$	191	7.9	5.4



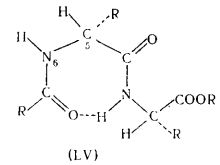
		$J_{22'}^{cis}$	$J_{22'}^{trans}$	J_{33}
$Si(C_2H_5)_3$	215	4.2	2.2	5.0
H	216	5.6	3.2	5.2
$SO_2C_6H_5$	217	7.2	4.5	5.5
Br	215	7.4	5.5	6.0

Therefore a semiempirical approach is promising. When an equation giving a correct description of the qualitative aspect of the spin–spin interaction (for example, the stereochemical relation) is available, it is possible to determine from the experimental data a number of parameters (for example, the overlap integrals, the exchange integrals, and the average excitation energies) of the theoretical equations. The values may be used to calculate other interaction constants or may be employed in other types of quantum-chemical calculations. In particular, the spin–spin interaction constants may serve as a basis for the calculation of the contribution by the spin–polarisation mechanism to the hyperfine structure constant of ESR spectra [13–17] and also the reactivities of compounds in scission [221] and bimolecular nucleophilic [222] reactions.

5. Vicinal Interaction in Heteroatomic Fragments

Experimental data show that, when the vicinal interaction is transmitted via the heteroatom (H–X–C–H), the sign of the $^3J_{HH}$ constant persists (Tables 16 and 17). It is quite likely that the properties of the vicinal interaction examined above for the HC–CH fragment hold also (at least qualitatively) for the HX–CH heteroatomic fragment. In particular, the higher value for the H–H *trans*-configuration relative to the *cis*-configuration is maintained (Table 16).

The variation of the HX–CH vicinal constant with the dihedral angle is particularly important for conformational analysis. For the $CONH-C^{\alpha}HRR'$ peptide fragment, a relation of this kind has been derived by analysing data for dipeptides with *trans*-amide bonds [240–244]. Since the N–CO bond has partial double bond character, a contribution to $^3J_{NHCH}$ by the π orbital of the nitrogen atom should be expected. Therefore the analysis was based on Eqn. (10). Positive values of its coefficients were chosen, since it is known that $^3J_{NHCH}$ for amide fragments is positive [135]. Since it has been pointed out that $^3J_{NHCH}$ for substituted N-methylanilines decreases with the electronegativity of the ring substituent [245], the effect of the substituent at C^{α} was taken into account by means of Eqn. (12). The coefficient $k = -0.1$ was chosen on the basis of experimental data for ethanes (Table 11 and Ref. 246).



(LV)

Table 15. Comparison of the experimental constants $^3J_{HH}$ (Hz) for the interaction of vicinal protons and the values calculated by the valence bond method (VB), the molecular orbital method without allowing for overlapping (MO) with allowance for overlapping (MO–O), with allowance for delocalisation (MO–D), and by the self-consistent field method with complete and partial neglect of differential overlapping (CNDO and INDO).

Compound	$^3J_{HH}$	Experiment	VB[136, 141]	MO[25]	MO–O[128]	MO–D[27]	CNDO[28]	INDO[28]
Ethane	$\langle J \rangle$	8.0±0.2[38]	4.3	5.5	5.2	5.8	6.76	8.38
	$J_{180°}/J_{60°}$	3.3	5.4	2.9	6.6	6.0	6.35	5.73
	$J_{cis\ 0°}$	13.0[a]	8.2	11.7	7.8	10.3	11.61	14.89
	$J_{trans\ 180°}$	15.0[a]	9.2	9.8	11.9	13.1	15.43	18.63
	$J_{gauche\ 60°}$	4.5[a]	1.7	3.4	1.8	2.2	2.43	3.25
	A[b]	12.0	9.0	10.8	9.6	11.7	13.52	16.76
	B[b]	1.0	0.5	−1.0	2.1	1.4	1.91	1.87
	C[b]	2.0	−0.3	~0.0	0.2	0.0	~0.0	~0.0[d]
Ethylene	J_{cis}	11.6±0.1[38]	7.6[c]	8.2[c]	7.4[c]	7.2[c]	8.04	9.31[d]
	J_{trans}	19.1±0.1[38]	13.4[c]	11.8[c]	18.3[c]	17.9[c]	19.50	25.15[d]
	J_{trans}/J_{cis}	1.65±0.02	1.77	1.44	2.48	2.49	2.40	2.70
Acetylene	$^3J_{HH}$	9.5±0.1[38]	11.6	6.5[c]	13.1[c]	8.9[c]	6.55	10.99
Benzene	$^3J_{HH}$	7.54±0.04[154]	—	—	7.24	7.6	7.55	8.15

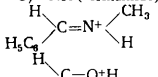
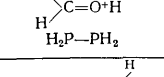
a. Found for 1,2-disubstituted ethanes taking into account the effect of electronegativity of the substituents [140].
b. The coefficients in Eqn. (8).
c. Taking into account the contributions of the π-electron systems for ethane (1.5 Hz) and acetylene (4.6 Hz) [138].
d. Application of the complete self-consistent field method showed that $J_{cis} = 9.6$ Hz and $J_{trans} = 20.1$ Hz. [32]

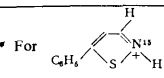
In view of the planarity of the group $\backslash N-C^{O}/$, there is no reason to expect in this case an orientation effect of the substituents R and R′ (see Section III, 3). Infrared spectroscopic data show that in a non-polar medium dipeptide molecules exist predominantly in the coiled form (LV) [246, 248], which limits significantly the range of permissible dihedral angles for the N_6H-C_5H fragment. The rotational states of this bond have been examined for two models

using the constants averaged with respect to the dihedral angles (*N*-methylformamide, Table 17). The model with the discrete angles $\theta = 0°$, 60°, 120°, 240°, and 300° led to the following ranges of allowed values (in Hz) of the coefficients of Eqn. (8):

$$8.0 \leqslant A \leqslant 9.8;\ 0.0 \leqslant B \leqslant (A - 8.0) \text{ and } C = 9.8 - A.$$

Table 16. The vicinal constants $^3J_{HH}$ for the *trans*- and *cis*-configurations in heteroatomic fragments.

Fragment	References	$^3J_{trans}$	$^3J_{cis}$
HC=CH (ethylene)	38	+19.1	+11.5
HC(=O)—NH (formamide)	135	+13.4	+1.7
	223	17.4	(4.2)*
	224	19.0	9.0
$H_2P—PH_2$	128, 129	+10.5	+6.8

* For  см. see Ref. 225

These data yield the region corresponding to the stereochemical relation between $^3J_{NHCH}$ and the angle θ bounded by the extreme curves in Fig. 17. The average values for this region may be fitted by the equation [240,241]

$$^3J_{NHCH} = 9.4\cos^2\theta - 0.5\cos\theta + 0.9\sin^2\theta. \quad (18)$$

Table 17. The vicinal constants $^3J_{HH}$ averaged over the rotational states for heteroatomic fragments with an X–Y single bond.

Fragment	Compound	⟨J⟩	Refs.	Fragment	Compound	⟨J⟩	Refs.
H—C—C—H	CH_3CH_3	+8.0	38	H—Si—P—H	H_3SiPH_2	5.1	236
H—C—P—H	CH_3PH_2	+8.2	226, 227	H—Si—As—H	H_3SiAsH_2	5.1	236
H—C—S—H	CH_3SH	+7.45	170	H—Ge—P—H	H_3GePH_2	4.8	236
H—C—P⁺—H	$(CH_3)_3P^+H$	5.48	228	H—Ge—As—H	H_3GeAsH_3	4.8	236
H—C—N⁺—H	$(CH_3)_3N^+H$	5.15	229	H—Ge—Ge—H	$H_3GeGeH_2(CH_3)$	3.9	237
H—C—O—H	CH_3OH	+5.08	230	H—Si—Si—H	H_3SiSiH_3	4.0	238
H—C—O⁺—H	$CH_3O^+H_2$	3.6	231	H—C—CH=C	$CH_3CH=CH_2$	+6.40	98
H—C—Ge—H	CH_3GeH_3	+4.22	133	H—C—CH=O	CH_3CHO	+2.83	48
H—C—Si—H	CH_3SiH_3	+4.68	232, 233	H—C—CH=O⁺	$CH_3CH=O^+H$	3.5	239
H—C—Sn—H	CH_3SnH_3	+2.7	233, 234	H—C—NH⋯	$CH_3NHCH(=O)$	+4.9	135
H—C—Pb—H	$(CH_3)_3PbH$	+1.47	234	H—C—N⁺H=	$CH_3N^+H=C(CH_3)_2$	5.0	223
H—B . . . P—H	$H_3B \ldots PH_3$	8.0	235				

The free rotation model with allowance for the maximum values of the constants $^3J_{NHCH}$ for the angle $0° \leqslant \theta < 90°$ (8.9 Hz for 5,6-dihydrouracils [254] and 8.0 Hz for valinomycin [250]) yielded narrower ranges of the coefficients:

$$8.9 \leqslant A \leqslant 9.8,\ 0 \leqslant B \leqslant (A - 8.9), \text{ and } C = 9.8 - A,$$

represented by the shaded region in Fig. 17. The equation corresponding to the average values for this region is of the form [242]:

$$^3J_{NHCH} = 9.6\cos^2\theta - 0.3\cos\theta + 0.5\sin^2\theta. \quad (19)$$

Comparison of Eqns. (18) and (19) shows that the result is almost independent of the choice of model for rotation relative to the N–C$^\alpha$ peptide bond.

The $^3J_{NHCH}(\theta)$ stereochemical relation has served as a basis of the conformational analysis of peptides and depsipeptides [240–244,255–258]. The dihedral angle θ determines the rotational state of the N–C$^\alpha$ bond, one of the two single bonds in the peptide fragment –CON–C$^\alpha$–CO.

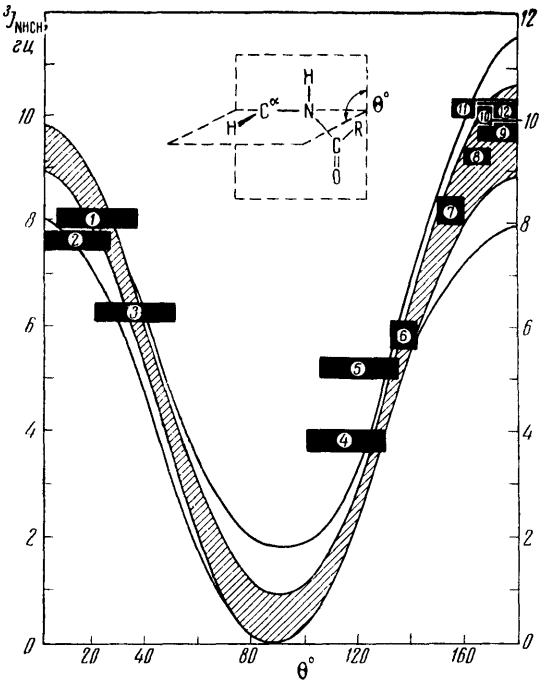


Figure 17. Stereochemical relation between the vicinal constant for the NH–CH peptide fragment and the dihedral angle θ. [240–244] The extreme curves bound the region calculated for the discrete-rotation model. The shaded region corresponds to the free-rotation model. The filled rectangles denote the experimental data for aminoacid residues: 1) D-valine of valinomycin in a non-polar medium [249]; 2) L-valine of valinomycin in a polar medium [249,250]; 3) L-valine of valinomycin in a non-polar medium [249]; 4) D-phenylalanine of gramicidin S in a polar medium [251]; 5) L- and D-valine of lincomycin in a complex with K^+ ion [249,250]; 6)–8) L-ornithine (1, 2, and 3) of alumichrome A in water [252] (X-ray diffraction analysis of ferrichrome-A) [253]; 9) L-ornithine of gramicidin S in a polar medium [251]; 10) D-valine of valinomycin in a polar medium [249,250]; 11) and 12) L-valine and L-leucine of gramicidin S in a polar medium [251].

The angle θ may be converted into the conventional angle [259] φ for the N–C$^\alpha$ bond by means of the following relations:

for L-aminoacid residues, $\varphi = 240 \pm \theta$.
for D-aminoacid residues, $\varphi = 120 \pm \theta$.

The preferred rotational states found from the $^3J_{NHCH}(\theta)$ relation have served as a basis for the determination of the conformations in solution of important biologically

active peptides and depsipeptides such as valinomycin[249,250,258], enniatin B[258,260], gramicidin S[251,258], antamanide[258,261], actinomycin D[262], oxytocin[263], alumichrome A[252], α-chymotrypsin substrates[264], and complexes of valinomycin and enniatin B with alkali metal cations. The data for valinomycin, gramicidin S, and alumichrome A, which have been reliably confirmed by data obtained by other methods, in particular by theoretical conformational and X-ray diffraction analysis, are plotted in Fig. 17.

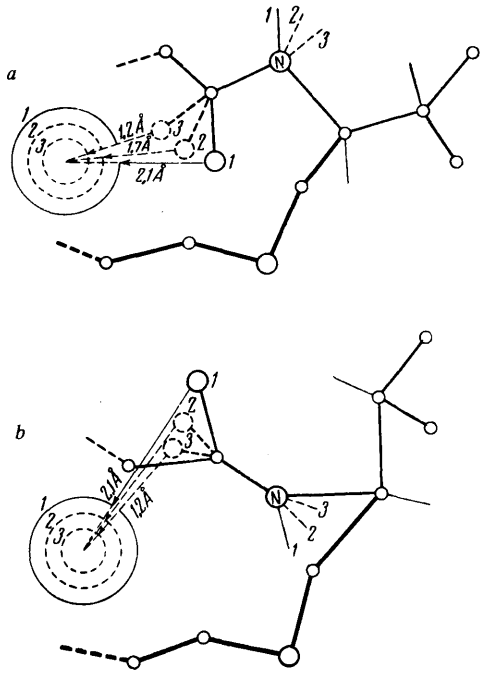
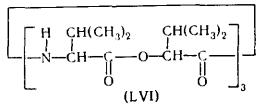


Figure 18. Effect of the dimensions of the complex cation on the orientation of the amide group of (tri-*N*-desmethyl)enniatin B in conformations P_1 (*a*) and P_2 (*b*).

As an example of studies on the conformations of cyclic antibiotics, one may quote the determination of the conformation of an analogue of enniatin B—(tri-*N*-desmethyl)-enniatin B (LVI)—in the formation of complexes with alkali metal cations[260].



(LVI)

Examination of molecular models showed that complexes may be formed when the cation enters the cavities in two conformations P_1 and P_2. With increasing diameter of the cation, an increase of the size of the inner cavity, formed by the carbonyl groups involved in ion–dipole interaction with the cations, may be expected (Fig. 18). Evidently the effective size of the cavity for a given ring size is determined by the orientation of the carbonyl groups. In a complex with a cation having a smaller diameter, the carbonyl oxygen should be closer to the centre of the molecule than in a complex with a larger cation. The change in the conformation of the complex with increasing size of the cation may be compared with the opening of a flower bud. Fig. 18 shows that such a change in the orientation of the carbonyl groups inevitably leads to the rotation of the CONH plane, which causes a change in the orientation of the N–H and C^{α}–H bonds, i.e. in the angle θ.

Table 18. The dihedral angles and the constants $^3J_{NHCH}$ for the complexes of (tri-*N*-desmethyl)enniatin B with univalent cations[260].

Calculation					Experiment		
	P_1		P_2				
diameter of cavity, A	θ,°	J, Hz	θ,°	J, Hz	cation	diameter of cation, A	$^3J_{NHCH}$, Hz
1.7	120	2.9	0	8.9	Li^+	1.40	4.9
2.7	130	4.6	10	8.6	Na^+	1.96	6.4
3.2	140	6.2	20	7.8	K^+	2.66	7.9
3.7	150	7.4	30	6.6	Rb^+	2.98	7.9
4.2	165	9.0	45	4.3	Cs^+	3.30	8.5

Analysis of molecular models shows that, with increase of the size of the inner cavity, the angle θ increases in the range 120–170° for conformation P_1 and in the range 0–60° for conformation P_2 (Table 18). It follows from the stereochemical relation for $^3J_{NHCH}$ that, with increase of the diameter of the cation, the constant should increase in the first case and decrease in the second. The experimental data for the complexes (LVI) with Li^+, Na^+, K^+, Rb^+, and Cs^+ demonstrate reliably that conformation P_1 obtains (Fig. 19). The knowledge of the steric structure of biologically active substances permits a more profound study of the mechanism of the action of these compounds, in particular the mechanism of the selective transport of cations across cell membranes.

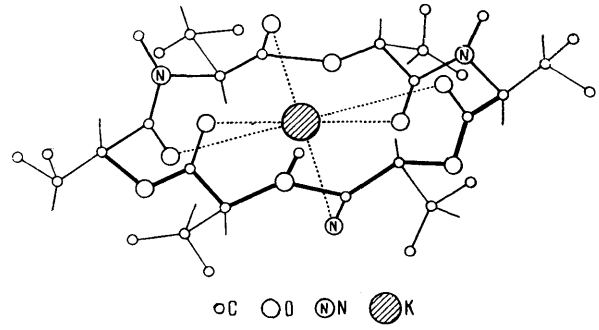


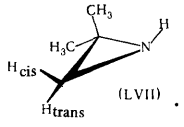
Figure 19. Conformation of the complex of enniatin B with the potassium ion.

The following relation has been found for six- and five-membered rings with a *cis*-amide bond (in contrast to compounds with a *trans*-amide bond)[265]:

$$^3J_{NHCH} = 9.3\cos^2\theta - 3.5\cos\theta + 0.3\sin^2\theta\ .$$

It differs appreciably from Eqns. (18) and (19), particularly in the range $0° < \theta < 60°$. Possibly the difference can be accounted for by the specificity of the electronic structure of the nitrogen atom, which is reflected in the value of the overlap integral $K(\sigma\sigma')$ for an electronic structure of type (XXXIII), in the *trans*-amide bond and in relatively strained systems with a *cis*-amide bond.

The measurement of the ^3J(NH–CH) constants for amines is very difficult owing to the high mobility of the NH proton and requires careful elimination of catalytic acid and basic impurities. The data for 2,2-dimethylaziridine (LVII), $^3J_{cis} = 7.5$ Hz and $^3J_{trans} = 10.2$ Hz,[266] which indicate a dependence of the constant on the dihedral angle, are noteworthy. In ammonium salts the proton exchange involving the N^+H group is significantly retarded, which facilitates the measurements of the constants for the coupling of the N^+H–CH protons particularly in highly acidic media.



(LVII).

A definite indication of the dependence of this constant on the stereochemical factor has been obtained[267] for protonated benzylamines $C_6H_5CH_2N^+HRR'$. Approximate analysis showed that, for the CH–N^+H fragment, the constant $^3J_{trans,\ 180°} > 9.45$ Hz and $^3J_{gauche,\ 60°} < 3.15$ Hz.[267]

The constant for the HO–CH fragment in alcohols was found to depend on the stereochemical factor[268]:

$$^3J_{HCOH} = 10.4\cos^2\theta - 1.5\cos\theta + 0.2\ .$$

Owing to conformational factors, $^3J_{HCOH}$ for the equatorial OH group in cyclohexanols is higher by 1.0–1.5 Hz than for the axial group[230,269].

Incomplete data indicate the existence of a similar relation for the HS–CH fragment with $^3J_{gauche} < 4.03$ Hz and $^3J_{trans} > 14.9$ Hz.[270,271]

Valence bond theory predicts[17], on the basis of hyperfine structure constants of ESR spectra, the following relations for the HN–CH and HO–CH fragments:

$$^3J_{HNCH} = 12\cos^2\theta + 0.2, \qquad (20)$$

$$^3J_{HOCH} = 10\cos^2\theta - 1.0. \qquad (21)$$

The agreement with experiment for the HN–CH fragment is fairly satisfactory except that Eqn. (20) does not reflect the difference for dihedral angles of 0° and 180°. An additional discrepancy for the HO–CH fragment is that the predicted negative sign of $^3J_{HOCH}$ for $\theta = 90°$C is not confirmed by experiment.

Deviating somewhat from the subject of the review, we may mention that stereochemical relations, described by equations of type (7)–(9), have been established for the interaction of the vicinal H and ^{19}F(HC–CF) nuclei[110,272,273]:

$$^3J_{HF} \simeq 37.5\cos^2\theta - 6.5\cos\theta,$$

and H and ^{31}P(HC–CP) nuclei[274-279]:

$$^3J_{HP} \simeq 25\cos^2\theta - 9\cos\theta.$$

There are also important grounds for the expectation that analogous relations should hold for the (^{31}P–O–C–H),[277-282] (^{14,15}N–C–C–H),[276,283-285] (^{13}C–C–C–H),[286] and (^{199}Hg–C–C–H)[287] vicinal constants. Special emphasis must be laid on the importance of a future determination of the stereochemical characteristic of the constant $^3J_{15}$NCCH for the HC^{α}–CO–^{15}N peptide fragment, which would make it possible to determine the rotational conformation of the peptide chain at the C^{α}–C(O) bond (angle ψ). NMR spectroscopy would then make it possible to establish completely the conformation of peptides, since the rotational state of the NH–C^{α}H bond (angle φ) may be determined from the constant $^3J_{HNCH}$ (see above).

It has been shown theoretically for the H–C–C–X fragments, where X = B, C, N, O, or F, that the $^3J_{HX}$ interaction constants are positive because the contribution by orbitals not involved in valence bonds is decisive.

Without exaggeration, one may claim that the stereochemical relations for vicinal fragments are of the greatest importance for conformational analysis by the NMR method. The determination of the relations for new fragments leads to many possible applications of a physicochemical method as powerful as NMR spectroscopy in the study of conformational states of a wide variety of compounds.

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Summarising the present state of the theoretical and empirical relations, one may conclude that the geminal and vicinal H–H spin–spin coupling constants are extremely sensitive to fine details of the electronic and steric structures of molecules§. In a comprehensive approach, the H–H constant constitutes an effective research tool, but this NMR spectroscopic parameter must be employed with caution, bearing in mind the complete set of effective factors involved. Probably at present the empirical approach to relations governing the interaction constants is more promising than direct theoretical calculations, which necessarily involve serious approximations. However, the theoretical approach makes it possible to find the "guide lines" for a systematic arrangement of experimental data.

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§As the NMR spectroscopic technique is improved, more distant spin–spin interactions, via four and more chemical bonds, are acquiring increasing importance for structural and conformational analysis. A number of interesting reviews have been devoted to such interactions[44,289,290]. The dependence of $^4J_{HH}$ on the steric structure of the H–C–C–H fragment, determined on the basis of experimental data[10,291] significantly complements the vicinal constant $^3J_{HH}$ in conformational analysis by the NMR method[107,108,292,293].

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Determination of the Effective Charges of Anions in Media of the Ionic Type by the Positron Method

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The essential features of the positron method for determining the effective charges of anions in ionic solids are presented, and papers dealing with its application are reviewed. Values of the charges of the anions are given for more than 100 compounds (alkali metal halides, oxides, etc.). In contrast to earlier work, the effective charges of the anions given in this review were determined independently of other methods. Various regular features of the behaviour of the charges in the compounds studied are noted. The bibliography contains 67 references.

The experimental and theoretical study of the annihilation of positrons with the electrons of a substance has revealed a number of possible applications of the effects associated with the annihilation in the study of electronic states in solids[1-5]. Examples illustrating the fruitful nature of the application of the positron-annihilation method include the determination of the energy and topology of the Fermi surface in metals and alloys, the detection of the change in the momentum distribution of electrons in metals and alloys in their plastic deformation, the study of the magnetic structure of ferromagnetic materials, etc. In ionic media, the positron-annihilation method can be used successfully to study the nature of chemical bonds and in particular to determine the effective charges on atoms, produced on the formation of a particular compound. In this respect the positron method may provide a valuable supplement to existing methods such as Szigeti's method, the X-ray spectral method, etc. The present paper presents the essential features of the positron method for the determination of the effective charges of anions in media of the ionic type, based on the "optical" positron model of Gol'danskii and Prokop'ev[6]. To illustrate the method, the values of the charges of the anions are given for more than 100 compounds.

To determine the effective charges of the anions it is possible to use either of two fundamental characteristics of the annihilation: the angular distribution of the annihilation quanta or the lifetimes of the positrons with respect to annihilation.

The annihilation of positrons with the electrons of a substance is most commonly accompanied by the emission of two gamma-quanta at an angle of 180° to one another (in the system of the centre of gravity of the annihilating pair). If the centre of gravity of the pair is moving relative to the observer at a velocity v, the angle between the direction of movement of the photons decreases by an amount of the order of v/c, where c is the velocity of light. The experimental assembly (Fig. 1) is used to determine the deviation from 180° of the angle of separation of the photons (the angle θ). The annihilation quanta are recorded by means of two detectors including NaI(Tl) scintillation crystals with photomultipliers, the signals from which are transferred to a coincidence circuit. Between the detector and the specimen containing the source (^{22}Na or ^{64}Cu isotopes), on each side, there are placed lead screens with narrow slits, one of which—screen 1—is fixed rigidly to the movable detector. The distribution of the pairs of gamma-quanta with respect to θ is studied by measuring the count rate of coincidences in the signals from the detectors as a function of the angle of rotation of one of the detectors relative to the specimen. Since this distribution in fact lies within a small range of

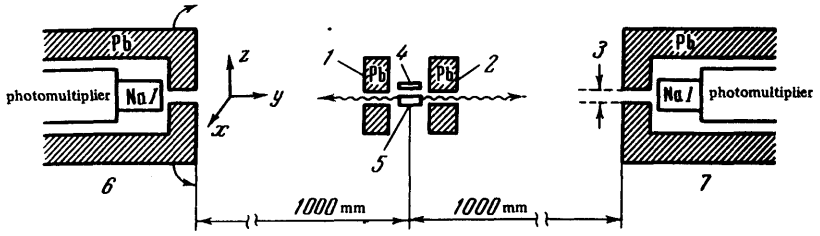

Figure 1. Typical assembly with parallel-slit geometry for the observation of the angular correlation of annihilation quanta: *1*) and *2*) screens; *3*) 1 mm slit; *4*) positron source; *5*) specimen; *6*) moveable detector; *7*) fixed detector.

angles (usually $\theta \lesssim 20$ mrad), it may be assumed that a pair of gamma-quanta moving apart at an angle $(\pi - \theta)$ has a projected momentum on the z axis (see Fig. 1) equal to $p_z = m_0 c\theta$ (m_0 is the rest mass of the electron). The typical form of the $I(\theta)$ curves giving the angular distribution of the annihilation quanta is shown in Fig. 2.

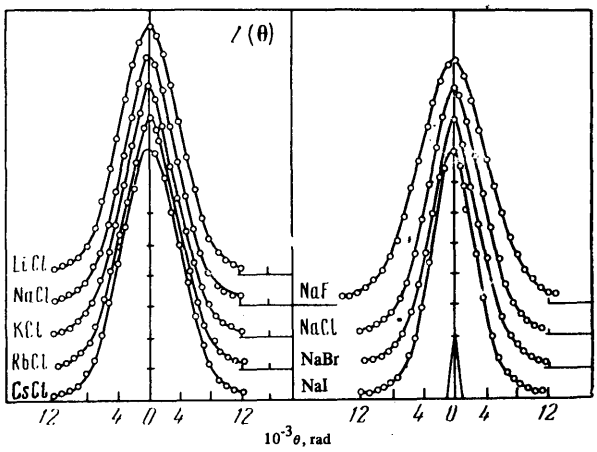

Figure 2. Curves giving the angular correlation of annihilation quanta in alkali metal halide crystals[8].

Observation of the angular correlation of the annihilation quanta gives direct information on the momentum distribution of the annihilating pairs (or electrons, if the movement of the positron can be neglected) in the substance. This is possible since the experimentally observed count rate for the coincidences of the gamma-quanta $I(\theta)$ is related to the momentum distribution density function† $\rho(p)$ for the centres of inertia of the annihilating pairs by the expression[7,8]:

$$I(\theta) = I\left(\frac{p_z}{m_0 c}\right) = \text{const} \int_{p_z}^{\infty} p\rho(p)\,dp; \quad \rho(p) \propto -\frac{1}{\theta}\frac{dI}{d\theta}. \qquad (1)$$

† The momentum distribution $N(p) = 4\pi p^2 \rho(p)$ is often considered instead of the function $\rho(p)$.

Information on the mechanisms of the interaction of a positron with the surrounding electron medium can also be obtained by measuring the lifetimes of the positrons in the substance with respect to annihilation. The lifetime is determined using an assembly (Fig. 3) including a delayed-coincidence circuit. The container with the substance being studied, surrounding the positron source—the ^{22}Na isotope—is placed between two detectors. The moment of generation of the positron is detected by recording the gamma-quantum (detector 1) with energy 1.28 MeV, the emission of which accompanies the β^+-decay of the ^{22}Na nuclei. The moment of annihilation is determined from the production of annihilation quanta with energy 0.511 MeV (detector 2). Fig. 4 gives a typical spectrum of the lifetime distribution of positrons with respect to annihilation in alkali halide crystals. The presence of several decay components with different average lifetimes in the annihilation time spectrum indicates that the mechanism of the annihilation of positrons in ionic crystals is complex. The average lifetimes of the relatively long-lived components are determined from the slope of the plot of the logarithm of the coincidence count rate against the delay time at long delay times.

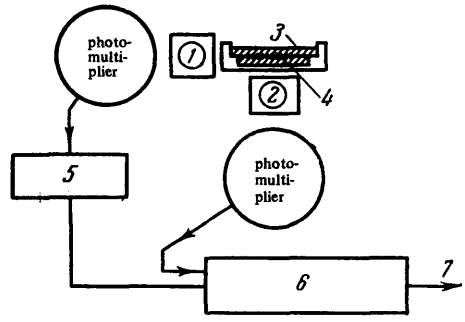

Figure 3. Basic scheme of an assembly for measuring the lifetimes of positrons in condensed media[1]: *1*) and *2*) stilbene crystals; *3*) specimen; *4*) positron source; *5*) delay line; *6*) ~ 10^{-9} s coincidence circuit; *7*) output.

A fairly large number of papers have now been published on the study of the angular distribution of the annihilation quanta and the lifetime distribution of the positrons

with respect to annihilation in different ionic media; halides, oxides, sulphides, and other metal compounds (see, for example, Refs. 1–3 and 8–26). Analysis of experimental results on the study of the annihilation of positrons in ionic crystals shows that the annihilation is preceded by the formation of combined states of the positron, the chief of which are quasi-atomic formations of the e^+–anion type and states of the positronium type (positronium formation is detected from the appearance of a narrow component in the correlation curves and long-lived components in the annihilation time spectra with decay times of the order of 10^{-9} s or more). It has also been noted that if positronium formation is not forbidden energetically, its probability is usually greatly increased by the presence in the medium of defects; of pores (gel), vacancies (irradiated crystals), regions of lower density (glass), etc. Here we shall be interested only in compounds of the e^+–anion type. The formation of these compounds in ionic crystals is preceded by the thermalisation of the positrons, that is their deceleration to thermal velocities. The thermalisation of positrons in ionic crystals is brought about as a consequence of ionisation energy losses, the excitation of electrons into the conduction zone, and by interaction with longitudinal optical phonons. Estimates[27,28] have shown that as a result of all these processes, the positrons are decelerated to thermal velocities in times of the order of 10^{-12} s. Since the shortest lifetime of positrons with respect to annihilation in ionic crystals amounts to several 10^{-10} s,[1,9,22–24,26] it may be assumed that almost all the positrons are able to undergo thermalisation before annihilation. Some of the positrons naturally enter the target and annihilate in flight, that is in the thermalisation process, but experimental results[29–32] and theoretical estimates[27] show that the proportion amounts to only 1–3%.

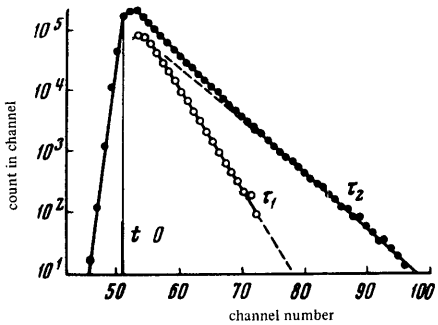

Figure 4. Positron lifetime distribution with respect to annihilation in lithium chloride[9] (one channel = 0.88×10^{-10} s, $\tau_1 = 2.36 \times 10^{-10}$ s, $\tau_2 = 4.35 \times 10^{-10}$ s).

The thermalised positron annihilates in the free state or is captured beforehand by the nearest negative ion. The probability of annihilation of free positrons in media of the ionic type is negligibly small compared with the probabilities of the two-photon annihilation of combined positrons[33]. Thus the annihilation characteristics of ionic crystals in the absence of appreciable positronium yield will be determined chiefly by the properties of the e^+–anion system.

Negative ions (F^-, Cl^-, Br^-, I^-, O^{2-}, S^{2-}, Se^{2-}, and Te^{2-}) have filled electron levels with the structure of inert gas atoms. The positron moves in the field of the nucleus and the electrons of the anion. In this instance we are dealing with a many-electron problem. If however we neglect the deforming action of the positron on the electron levels of the ion, we can regard the movement of the positron in the e^+–anion system as movement in a field of central forces; this is analogous to the model of the optical electron in alkali metal atoms. The "optical" positron model was first proposed by Gol'danskii and Prokop'ev[6]. In this model it is assumed that the positron moves in the Coulombic field of the anion, of the type $U(r) = -\eta e/r$, where $(-\eta e)$ is the effective charge of the anion in the crystal. Since the inner levels of the anion are not accessible to the positron as a consequence of the strong Coulombic repulsion by the nucleus, the wave function of the ground state of the positron in the e^+–anion quasi-atom has been given in the form[6] $r \cdot \exp(-\alpha r)$, where α is a variable parameter. For a combined positron, the correlation of the annihilation radiation is determined by the relative probability[34]:

$$P(k_z) = \frac{\int_{k_z}^{\infty}\int_0^{2\pi} \omega(k)\, k dk d\theta}{\int_0^{\infty}\int_0^{2\pi} \omega(k)\, k dk d\theta}, \qquad (2)$$

where $\omega(k)$ is the probability of annihilation, with the emission of two gamma-quanta with a total momentum $p = nk$, averaged with respect to the spins of the initial states of the electrons and the positron and summed over the polarisations of the radiated photons:

$$\omega(k) = \pi r_0^2 c \sum_{i=1}^{m} \left[h^{-\frac{3}{2}} \int e^{-ikr} \varphi_i(r)\, \chi(r)\, dr\right]^2. \qquad (3)$$

Here, r_0 is the classical radius of the electron, and $\varphi_i(r)$ and $\chi(r)$ the one-electron and positron wave functions respectively for the compound of the e^+–anion type. The summation in Eqn. (3) is carried out over all electrons involved in the annihilation.

The lifetime of a combined positron can be calculated from the equation[35]

$$\tau = 5 \cdot 10^{-10} \frac{\rho_0}{\rho}, \text{ s}, \qquad (4a)$$

where $\rho_0 = (8\pi a_0)^{-1}$ is the electron density at the positronium atom, averaged with respect to the spin states of the electron and positron, and

$$\rho = K \cdot \sum_{i=1}^{m} \int \varphi_i^2(r)\, \chi^2(r)\, dr. \qquad (4b)$$

Here, K is a factor which takes account of the change in the wave functions of the electrons not involved in the annihilation; to a good approximation, it may be assumed that $K = 1$.[33,36]

If we choose Slater exponents as the wave functions of the electrons of the anion, we can use Eqns. (2)–(4) to establish in analytical form the relationship between the chief characteristics of the annihilation of the positron with the electrons of the anion‡ and the effective charge of the anion in the crystal. Within the framework of the "optical" model of the positron, this relationship has the

‡ Usually, only the annihilation of positrons with the electrons of the outer ns^2, p^6-levels of the anions is considered.

following form[6]: the angular correlation of the annihilation quanta for the annihilation of a positron with an *nl* electron of an anion is

$$P_{nl}(k_z) = \frac{\int_{k_z}^{\infty} S_{nl}^2 k^{2l+1} dk}{\int_0^{\infty} S_{nl}^2 k^{2l+1} dk}, \quad (5)$$

where

$$S_{nl} = k^{-l} \int_0^{\infty} r^{n^*+2} e^{-(\alpha+\beta)r} j_l(kr)\, dr, \quad (6)$$

and $j_e(kr)$ represents the spherical Bessel functions (the form of various functions S_{nl} and P_{nl} has been published[6]); the half-width of the correlation curves (the total width at half the height of the curve $P_{ns,p} = 0.25\, P_{ns} + 0.75\, P_{np}$) is

$$\Gamma_{ns,p} = C^{\Gamma}_{ns,p}(\alpha + \beta), \text{ mrad} \quad (7)$$

and, finally, the lifetime of the positron (with allowance for the factor 4π omitted in Ref. 6) is

$$\tau_{ns,p} = 2{,}5 \cdot 10^{-10}\, C^{\tau}_{ns,p}\, \frac{(\alpha+\beta)^{2n^*+3}}{\alpha^5 \cdot \beta^{2n^*+1}}. \quad (8)$$

The following symbols are used in Eqns. (5)–(8): $\alpha = 3/2\eta$, $\beta = Z - \sigma/n^*$ is the Slater exponent (Z is the charge of the nucleus, σ is the screening number, and n^* is the effective principal quantum number), and $C^{\Gamma}_{ns,p}$ and $C^{\tau}_{ns,p}$ are constants, the values of which are determined entirely by the quantum number n. The calculated values of the constants $C^{\Gamma}_{ns,p}$ and $C^{\tau}_{ns,p}$ are given in Table 1.

Table 1. Calculated values of the coefficients $C^{\Gamma}_{ns,p}$ and $C^{\tau}_{ns,p}$ in Eqns. (7) and (8)*.

n	2	3	4	5
n^*	2	3	3.7	4
$C^{\Gamma}_{ns,p}$	3.52	2.86	2.59	2.48
$C^{\tau}_{ns,p}$	$\frac{1}{80}$	$\frac{3}{448}$	$\frac{1}{215}$	$\frac{1}{240}$

* The values of the constant $C^{\tau}_{ns,p}$ for $n = 2$, 3, and 5 were taken from Ref. 6.

The form of the theoretical curves for the angular correlation of the annihilation quanta and the nature of the dependence of the lifetimes of the positrons on the magnitude of the effective charge of the anion are shown in Figs. 5 and 6. The decrease in the half-width of the correlation curves and the increase in the lifetime of the positrons with increase in the number n, that is the principal quantum number of the outermost level of the anions, following from the "optical" model of the positron, and also numerical estimates of these characteristics of the annihilation, show good agreement with results of the measurement of the angular distribution of the annihilation quanta[8] and the lifetimes of the positrons[9] in alkali metal halide crystals.

The direct comparison of the theoretical and experimental curves giving the angular correlation of the annihilation quanta is of interest. The result of this comparison for the oxides of the alkaline earth metals is shown in Fig. 7.

Because of the appreciable scatter in the published values of the charges of the oxygen ion in oxides, the theoretical curves in Fig. 7 were calculated in such a way that their half-width was equal to the half-width of the experimental $I(\theta)$ curves. Comparison of the theoretical and experimental correlation curves is also necessary for the detection of the possible presence, on the curves, of a narrow component due to the annihilation decay of parapositronium atoms. When parapositronium atoms are formed, the calculated and experimental $I(\theta)$ curves do not coincide (see, for example, Fig. 8).

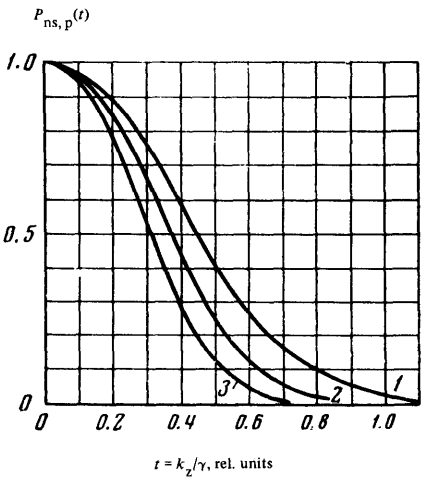

Figure 5. Theoretical angular correlation curves for annihilation quanta: *1*) $P_{2s,p}(k_z/\gamma)$, *2*) $P_{3s,p}(k_z/\gamma)$, *3*) $F_{5s,p}(k_z/\gamma)$, where $\gamma = \alpha + \beta$.

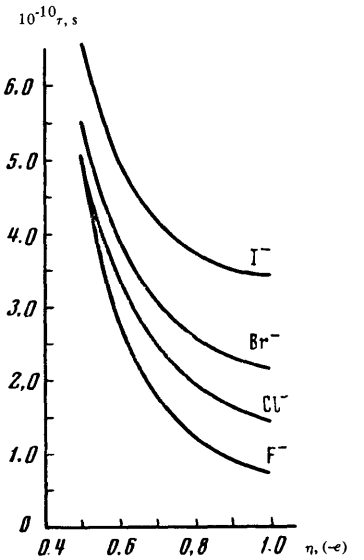

Figure 6. Dependence of the lifetimes of the positrons on the effective charge of the anion η in the "optical" positron model.

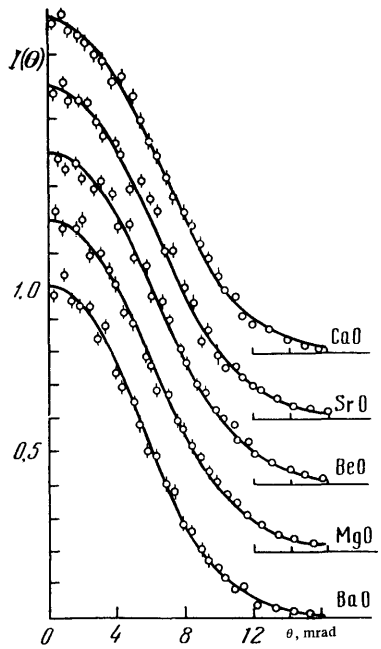

Figure 7. Theoretical (continuous line) and experimental (points) angular correlations for annihilation quanta in alkaline earth metal oxides (BeO and MgO were sintered, the others were in powder form).

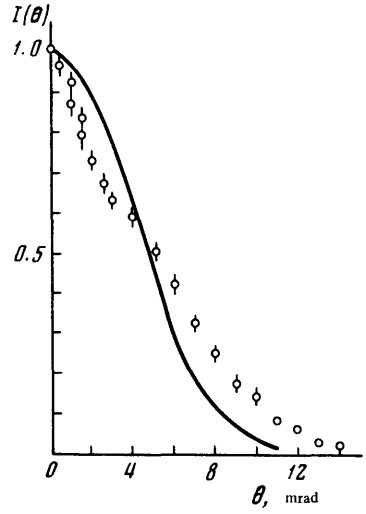

Figure 8. Theoretical (continuous line) and experimental (points) angular correlations for annihilation quanta in zirconium oxide.

We can now proceed directly to the problem of determining the effective charges of atoms from the chief characteristics of the annihilation of positrons in media of the ionic type. The possibility of determining the effective charges of anions from the half-width of correlation curves was first demonstrated for the example of metal oxides[10]. Values have been obtained for the effective charges of F^-, Cl^-, and O^{2-} ions in crystals of various alkali metal halides and quartz from the short lifetimes of positrons with respect to annihilation[37]. It may be noted that in Ref. 10, as in later papers[12,14,16-18], the constants $C^{\Gamma}_{ns,p}$ in Eqn. (7) were given empirical values chosen to give best agreement between the calculated charges and the values of the charges determined by other methods. Thus for example the semi-empirical value of $C^{\Gamma}_{2s,p}$ for the oxides is ~ 3.78,[10] which is slightly greater than the theoretical value $C^{\Gamma}_{2s,p} = 3.52$ (see Table 1). This difference is not so significant, however, if we allow for the accuracy of the determination of the effective charges and the scatter in the results obtained by different methods.

Table 2. Half-width of the correlation curves (~ ±0.2 mrad) and effective charge of the oxygen ion in metal oxides*.

Oxides	Γ, mrad	$\eta, -e$	Oxides	Γ, mrad	$\eta, -e$	Oxides	Γ, mrad	$\eta, -e$
BeO**	13.8	1.33	Sb_2O_3	11.8	0.95	Co_2O_3	13.0	1.18
MgO**	12.8	1.14	Sc_2O_3	12.1	1.01	NiO	12.2	1.03
MgO***	12.1[19]	1.01	TiO_2	12.4	1.07	CuO	12.4	1.07
CaO	14.4	1.45	V_2O_5	11.4	0.88	ZnO	12.2	1.03
SrO	14.2	1.41	Cr_2O_3	14.8	1.52	ZrO_2	12.6	1.10
BaO	12.0	0.99	MnO	13.0	1.18	Nb_2O_5	12.6	1.10
Al_2O_3***	15.3	1.62	Mn_3O_4	13.4	1.26	MoO_3	13.5	1.27
SiO_2***	12.8	1.14	MnO_2	13.0	1.18	La_2O_3	12.8	1.14
SiO_2	11[1]	0.80	FeO**	12.7	1.12	Ce_2O_3	13.4	1.26
GeO_2	11.9	0.97	Fe_3O_4**	13.7	1.31	HfO_2	13.0	1.18
SnO_2	14.4	1.45	Fe_2O_3**	14.3	1.43	Ta_2O_5	12.2	1.03
PbO	12.0	0.99	Co_3O_4	14.0	1.37	WO_3	13.6	1.29

* For the oxides for which the correlation curves have a narrow component, Table 2 gives the half-widths of the broad components;
** sintered;
*** single crystals; the other oxides were taken in the form of powders.

We shall use the theoretical values of the constants $C^{\Gamma}_{ns,p}$ throughout. The effective charges on the anions in various ionic crystals, calculated from the half-widths of the correlation curves (see Eqn. (7) and Table 1), are given in Table 2 (see also Table 5). In those instances where the correlation curves show the presence of a narrow component (for example La_2O_3, TiO_2, GeO_2, ZrO_2, HfO_2, and PbO), the effective charge was determined from the half-width of the broad component. The broad component from the correlation curves can be separated by the "parabola" method, based on the fact that the theoretical $I(\theta)$ curve in the "optical" positron model has the form of a parabola for angles $\theta < 4$ mrad. The narrow component lies in the part of the experimental $I(\theta)$ curve above the parabola (Fig. 9) and the part of the experimental curve remaining after the subtraction of the narrow component is the broad component. When determining the charges of ions from the half-widths of the correlation curves for those compounds in which positronium formation is possible, it should be noted that the best results can be obtained for specimens in the form of single crystals or specimens obtained by sintering powders: in this instance the correlation curves do not have a narrow component[11].

Improved results can also be achieved by carrying out the measurements under vacuum conditions; this produces a marked decrease in the intensity of the narrow component (see, for example, Refs. 11 and 38). The agreement between the effective charge of the oxygen anion, calculated from the half-width of the correlation curves, and the charges found by other methods [39-51]—Szigeti's method, the X-ray spectral method, etc. [52]—is illustrated in Table 3.

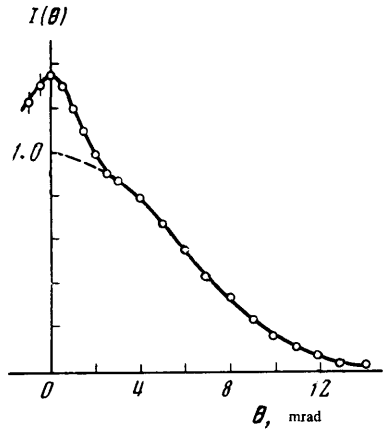

Figure 9. Separation of the broad component from the correlation curve for zirconium oxide by the "parabola" method (the parabola is given by the broken line).

The results in Table 2 lead to various conclusions regarding the magnitude of the effective charge on the oxygen ion in simple metal oxides. The effective charge of the oxygen ion in metal oxides: a) is generally much smaller than its formal value ($-2e$); b) does not change monotonically in the series of alkaline earth metal oxides; c) for the same oxidation state (transition metal oxides), it increases from the start of a period and then decreases towards its end (see, for example, the nickel group), the maximum charge corresponding to the group VI atom (for example the Cr atom); departures from this rule are shown by oxides of the A_3O_4 type (A = Mn, Fe, or Co), for which the charge increases on going from Mn to Co; d) for the same oxidation state (transition metal oxides), in a group of the Mendeleev Table, it increases or remains constant with increase in the atomic number (for example, from Ti to Hf, from V to Ta, and from Mo to W); and e) with increase in the oxidation state, the effective charges of the metal atoms in manganese and iron oxides increase, whereas in cobalt oxides they coincide, within the limits of the formal error in the measurements ($\sim \pm 0.04\ e$) (see Table 4).

Table 4. Effective charge on the metal atom in oxides of manganese, iron, and cobalt.

Manganese oxides (powders)	η, $+e$	Iron oxides (sintered)	η, $+e$	Cobalt oxides (powders)	η, $+e$
MnO	1.18	FeO	1.12	—	—
Mn_3O_4	1.68	Fe_3O_4	1.75	Co_3O_4	1.83
—	—	Fe_2O_3	2.15	Co_2O_3	1.76
MnO_2	2.36	—	—	—	—

Another interesting feature is that the values of the charges on the iron atoms correspond to the fact that the lattice of the oxide Fe_3O_4 contains iron atoms in different oxidation states Fe^{II} and Fe^{III}, in the ratio 1 : 2. The following point must be made regarding conclusion (e): according to results obtained by the X-ray spectral method [47], in compounds of "multivalent" elements the effective charges do not increase, but on the contrary decrease, with increase in the formal valency. A possible reason for this discrepancy is [12] the different physical significance attached to the concept of effective charge in the different methods (see note on p. 229 of Ref. 43).

Table 3. Comparison of the effective charges of the oxygen ion in metal oxides, determined by different methods.

Method and references	Oxides														
	BeO	MgO	CaO	SrO	BaO	Al_2O_3	SiO_2	TiO_2	MnO	FeO	Fe_2O_3	NiO	ZnO	ZrO_2	WO_2
Annihilation of positrons	1.33	1.01 1.14	1.45	1.41	0.99	1.62	0.80 1.14	1.07	1.18	1.12	1.43	1.03	1.03	1.10	1.29
Szigeti's method [39]	—	1.76	1.56	1.16	—	—	—	1.30	—	—	—	—	—	—	—
Ditto [40]	—	1.20	1.56	1.16	—	—	—	—	—	—	—	—	—	—	—
» [41]	1.1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
» [42]	—	1.20	1.18	1.22	—	—	—	—	—	—	—	—	—	—	—
» [43]	—	—	—	—	—	—	—	—	—	—	—	—	1.06	—	—
X-Ray spectral method [44]	—	1.01	—	—	—	1.02	0.98	—	—	—	1.05	—	—	—	—
From heats of sublimation [45]	—	1.08	—	—	—	0.82	0.84	0.80	—	1.03	—	1.00	0.88	0.84	0.56
From heats of formation [46]	—	1.48	1.62	1.60	—	—	—	—	—	—	—	—	1.20	—	—
From interatomic distances [47]	1.18	1.42	1.32	1.40	1.36	—	—	1.02	1.34	1.32	—	1.30	1.24	1.10	—
Theoretical calculation [48]	—	1.56	1.66	1.68	—	—	—	—	—	—	—	—	1.32	—	—
Ditto [49]	—	—	1.46	1.18	0.91	—	—	—	—	—	—	—	1.21	—	—
» [50]	—	1.0 1.1	1.2 1.5	1.2 1.3	1.0 1.1	—	—	—	—	—	—	—	—	—	—
» [51]	1.06	1.20	1.36	1.40	1.44	—	—	—	—	—	—	—	1.08	—	—

As noted above, the effective charges on anions can be determined from the lifetimes of positrons (see Eqn. (8) and Table 1). The effective charges of anions in ionic crystals, determined in this way, agree well with the values found by other methods (Table 5). In the calculation of the charges given in Table 5, the lifetimes of the positrons were given the shortest value, usually denoted by τ_1, except for the bromides and iodides of copper, silver, gold, and thallium, where we used the times τ_2, since for these compounds the values of τ_1 lie much lower than the corresponding $\tau(\eta)$ curves calculated from the "optical" positron model. We used the published values of the lifetimes of the positrons for the alkali metal halides[9], the alkaline earth metal halides[22], copper, silver, gold, and thallium halides[23], crystalline and fused quartz[53], vanadium oxide[26], and nitrides[24]. The half-widths of the correlation curves were determined from published graphs for the alkali metal chlorides and sodium halides[8], LiF,[54] KI, AlN,[19] FeS, and Na_2S.[55]

Table 5. Effective charges of the anions in ionic compounds, determined by the positron-annihilation and other methods.

Ion	Compound	Positron lifetimes*		Angular correlation*		Values of η ($-e$) found by Szigeti's method, the X-ray spectral method, etc.						
						references						
		$10^{-10}\tau$, s	η, $-e$	Γ, mrad	η, $-e$	39	52	40	44	45	47	51
F^-	LiF	1.31±0.07	0.78	12.0	0.65	0.87	0.83	0.80		0.73	0.67	0.76
	NaF	1.93±0.10	0.67	10.5	0.37	0.93	0.94	0.83	0.58	—	—	—
	KF	1.80±0.09	0.69	—	—	—	0.96	0.82	—	—	—	—
	RbF	1.55±0.08	0.73	—	—	—	0.93	—	—	—	—	—
	CsF	1.45±0.08	0.75				0.88	—				
	MgF_2	1.70±0.09	0.70	—	—	—	—	—	—	—	0.68	—
	CaF_2	1.79±0.09	0.69	—	—	0.74	—	—	—	0.69	0.66	—
	SrF_2	1.74±0.09	0.70	—	—	0.65	—	—	—	—	0.69	—
	BaF_2	1.76±0.09	0.70	—	—	0.70	—	—	—	—	0.68	—
Cl^-	LiCl	2.36±0.12	0.72	9.2	0.87	—	0.72	0.67	—	—	—	—
	NaCl	3.13±0.16	0.61	8.6	0.73	0.74	0.74	0.75	0.92	0.79	—	0.64
	KCl	2.75±0.14	0.66	8.3	0.66	0.80	0.79	0.80	—	0.83	—	—
	RbCl	1.99±0.10	0.79	8.6	0.73	0.84	0.87	0.84	—	0.83	—	—
	CsCl	2.02±0.11	0.79	8.9	0.79	0.84	0.87	0.86	—	—	—	—
	$BaCl_2$	2.93±0.15	0.59	—	—	—	—	—	—	—	—	—
	CuCl	1.81±0.09	0.84	—	—	1.10	0.98	1.00	—	—	—	—
	AgCl	1.81±0.09	0.84	—	—	—	0.69	0.71	—	0.77	—	—
	TlCl	1.97±0.10	0.79	—	—	1.08	0.88	1.10	—	0.65	—	—
Br^-	LiBr	2.97±0.15	0.71	—	—	—	0.68	0.74	—	—	—	—
	NaBr	2.92±0.15	0.72	7.4	0.60	0.69	0.71	0.70	0.83	0.77	0.86	0.60
	KBr	3.47±0.17	0.64	—	—	0.76	0.77	0.76	—	—	—	—
	CsBr	3.39±0.17	0.65	—	—	0.79	0.81	0.80	—	—	—	—
	$CaBr_2$	2.62±0.13	0.78	—	—	—	—	—	—	—	—	—
	$SrBr_2$	2.72±0.14	0.76	—	—	—	—	—	—	0.74	—	—
	CuBr	3.81±0.15	0.60	—	—	0.995	0.96	0.86	—	—	0.63	—
	AgBr	3.47±0.15	0.64	—	—	—	0.66	0.67	—	—	0.73	—
	TlBr	3.65±0.15	0.62	—	—	—	0.84	1.06	—	—	—	—
I^-	LiI	3.27±0.17	~1	—	—	—	0.55	0.50	—	—	—	—
	NaI	3.28±0.18	~1	6.8	0.62	0.71	0.70	0.71	0.75	—	—	0.54
	KI	4.01±0.20	0.72	7.1	0.71	0.69	0.70	0.73	—	0.79	0.80	—
	RbI	4.25±0.21	0.68	—	—	0.89	0.81	—	—	—	—	—
	CsI	3.55±0.20	0.86	—	—	—	0.74	—	—	—	—	—
	SrI_2	3.87±0.19	0.75	—	—	—	—	—	—	—	—	—
	CuI	3.79±0.15	0.77	—	—	—	0.91	—	—	—	0.60	—
	AgI	3.70±0.15	0.80	8.5	1.08	—	0.70	—	—	0.79	0.72	—
	AuI	3.86±0.20	0.75	—	—	—	—	—	—	—	—	—
	TlI	3.76±0.15	0.78	—	—	—	0.83	—	—	—	—	—
O^{2-}	SiO_2 (cryst.)	2.0±0.33	0.68	—	—	—	—	—	0.98	0.65	—	—
	SiO_2 (fused)	3.5±0.5	0.56	—	—	—	—	—		—	—	—
	V_2O_3	1.94±0.13	0.69									
S^{2-}	Na_2S	—	—	8.3	0.91	—	—	—	0.96	—	—	—
	FeS	—	—	10.3	1.38	—	—	—	0.71—0.96	—	—	—
N^{3-}	BN	2.64±0.08	0.66	—	—	—	—	—	—	—	1.62	0.76
	AlN	2.90±0.10	0.63	11.1	1.15	—	—	—	1.32	—	—	1.20

* The references to the papers from which the values of τ and Γ were taken are given in the text.

The data given in Tables 2 and 5 (see also below) confirm again the view, recently developed by Syrkin and his school[56,57], that inorganic compounds do not contain multiply-charged anions; the charges of anions in compounds are generally much smaller than their formal values.

Table 6. Comparison of the half-widths of the correlation curves, the effective charge of the oxygen ion, and the melting points of molybdates and tungstates.

Molybdates	Γ, mrad	η, $-e$	M.p., °C	Tungstates	Γ, mrad	η, $-e$	M.p., °C
Li_2MoO_4	12.4	1.07	705	Li_2WO_4	10.8	0.77	738
Na_2MoO_4	13.1	1.20	688	Na_2WO_4	12.9	1.16	698
K_2MoO_4	12.3	1.05	926	K_2WO_4	11.3	0.86	926
Rb_2MoO_4	12.4	1.07	929	Rb_2WO_4	11.2	0.84	959
Cs_2MoO_4	12.2	1.03	925	Cs_2WO_4	11.1	0.82	958
$LiSc(MoO_4)_2$	12.8	1.14	820	$LiSc(WO_4)_2$	11.4	0.88	975
$NaSc(MoO_4)_2$	13.5	1.27	920	$NaSc(WO_4)_2$	13.2	1.22	820
$KSc(MoO_4)_2$	12.9	1.16	1100	$KSc(WO_4)_2$	12.2	1.03	1120
$RbSc(MoO_4)_2$	12.3	1.05	1110	$RbSc(WO_4)_2$	11.7	0.93	1190
$CsSc(MoO_4)_2$	11.6	0.91	1120	$CsSc(WO_4)_2$	11.3	0.86	1250
$Sc_2(MoO_4)_3$	12.4	1.07	—	$Sc_2(WO_4)_3$	12.2	1.03	—

The positron method can be used to determine effective charges not only in binary inorganic compounds, but also in more complex compounds, for example in mixed metal oxides[17] and in multi-component inorganic glasses[13,16]. The possibility of using the "optical" positron model to determine the charges of anions in glasses is based on the fact that this model does not assume the existence of long-range order. In complex compounds, when the anion can occupy several non-equivalent positions in the lattice, the charge found for the anion will represent a value averaged over these positions. As an example of the determination of the effective charge of anions in complex compounds, Table 6 gives the charges of the oxygen ion in molybdates and tungstates, calculated from the half-widths of the correlation curves (see Eqn. (7) and Table 1). The correlation curves for these compounds, with the exception of lithium tungstate (Li_2WO_4), do not contain a narrow component. A noteworthy feature is the correlation between the change in the magnitude of the charge on the oxygen ion and the melting points of the alkali metal molybdates and tungstates and the double molybdates and tungstates of the alkali metals and scandium (in each of the four groups of compound, they change in opposite fashion in the series of atoms Li–Cs): the maximum charge corresponds to the minimum melting point in the compounds containing sodium atoms. It would appear that the compound $NaSc(MoO_4)_2$ does not obey this rule, but the study of the structure of this compound shows a polymorphic transformation at 600°. It may therefore be stated that the "melting point" of the low-temperature modification of $NaSc(MoO_4)_2$ must be lower than the melting point of the $LiSc(MoO_4)_2$ crystal. The above correlation between the relative change in the effective charge on the anion and the melting point is apparently a general characteristic of analogous compounds containing alkali metal atoms. An example confirming this conclusion is provided by the alkali metal fluorides and chlorides[17]. In this instance, in contrast to the situation for the molybdates and tungstates, the maximum melting point corresponds to the sodium halides.

Interesting results were obtained in the study of the behaviour of the effective charge on anions in the crystal–glass transition[13,16,18]. Table 7 gives the half-widths of the correlation curves and the effective charges of the oxygen ion for a number of three-component glasses, where, in contrast to the situation for one- and two-component glasses, positronium formation is not detected from the results of measurements of the angular correlation and the lifetimes of the positrons. Comparison of the values of the charges on the oxygen ion in corresponding crystalline oxides (Table 2) and glasses (Table 7) shows that the effective charge on the oxygen ion decreases systematically in the crystal–glass transition§. This conclusion is also confirmed[18] for binary compounds of the (IV–V) and (IV–VI) type. Thus the change to the vitreous state is accompanied by a redistribution of the valency electrons which increases the proportion of the covalent component in the chemical bonds.

Table 7. Half-widths of the correlation curves and effective charge on the oxygen ion in various oxygen-containing glasses.

Composition of glass, mole %	Γ, mrad	η, −e
76.2 SiO_2·19.0 Li_2O·4.8 SnO_2	10.6	0.72
76.2 SiO_2·19.0 Na_2O·4.8 SnO_2	11.2	0.84
76.2 SiO_2·19.0 K_2O·4.8 SnO_2	11.6	0.91
84.3 B_2O_3·13.7 Na_2O·2.0 Fe_2O_3	12.0	0.99
76.2 B_2O_3·19.0 Na_2O·4.8 SnO_2	11.8	0.91
63.5 CaO·31.7 Al_2O_3·4.8 SnO_2	11.5	0.89

In tin-containing glasses with the equimolar composition, an increase in the effective charge of the oxygen ion is observed when one alkali metal ion is replaced by another in the order Li–K (see Table 7). In this instance the change in the charge on the oxygen ion is confirmed[13] by measurements of the chemical shift of the Mössbauer absorption line; the chemical shift in glasses with the composition indicated is negative relative to crystalline tin(IV) oxide, and its absolute value increases on going from Li to K, indicating[58] an increase in the ionic character of the Sn–O bonds in this order. In alkali silicate glasses with the equimolar composition, as in mixed metal oxides, a correlation is observed between the change in the effective charge and various macroscopic properties. Thus the increased magnitude of the charge on the oxygen ion on going from the lithium silicate glass to the potassium silicate glass corresponds to an increase, in the same sense, in the coefficient of thermal expansion and a decrease in the micro-hardness of the glass.

Determination of the effective charge on the oxygen atom in water (the half-width of the broad component of the correlation curve is approximately 10 mrad[59]) gives the value $-0.6\,e$, which is almost twice the calculated value of $-0.26\,e$[60]; this is possibly due to the approximate nature of the "optical" positron model for the description of the characteristics of annihilation positrons in water.

§ The "positron" effective charge of the oxygen ion in alkali metal oxides is not known, but the value calculated from the heats of sublimation for Na_2O is $-1.10\,e$.[45]

The "optical" positron model cannot be used to determine the charge of the H^- ion in metal hydrides, since in the hydrides the positron is apparently present simultaneously in the field of several H^- ions; this is indicated by the dependence of the lifetimes of the positrons on the density of the hydrides[61]. A more rigorous calculation of the characteristics of the annihilation, with allowance for the distribution of electron density in the LiH molecule by the MO method, carried out[62] for the LiH crystal, gives the value $-0.60\,e$ for the charge of the H^- ion, this is fairly close to the published value of $-0.52\,e$.[63] Thus the above results indicate that the positron-annihilation method can be regarded as a new *independent* method for determining the effective charges of the anions in compounds of the ionic type.

In conclusion it may be noted that the determination of the charges of anions is not the only possible application of the positron-annihilation method in the chemistry of ionic compounds. Recent results[25,64–67] show that the annihilation characteristics of positronium atoms, for example in highly dispersed oxide powders, depend markedly on the physicochemical properties of their surfaces and the filling of the pores. It can already be stated that further studies in this direction will make it possible to use the positron-annihilation method to study adsorption phenomena.

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Modern Views on the Nature of Inorganic Peroxy-compounds

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A general account is given of the literature data on the molecular oxygen anions O_2^{2-}, O_2^-, and O_3^- characterising the structures of simple peroxy-compounds: peroxides, superoxides, and ozonides. The principal studies published in recent years dealing with the structure of complex peroxy-compounds are briefly summarised. The nomenclature for organic peroxy-compounds proposed by other authors is critically discussed and a scheme is put forward for classification and nomenclature based on the latest data on the structures of such compounds.
The bibliography includes 93 references.

Until recently, in order to define the concept of "an inorganic peroxy-compound" it was thought sufficient to indicate compounds corresponding to this concept and containing the peroxo-group, the so called "oxygen bridge".

Detailed studies of the structures and properties of many compounds corresponding to the above concept, begun in the 1930's with active participation of Soviet scientists, showed that the term "inorganic peroxy-compounds" is applicable to a very wide class of compounds and combines at least nine groups of compounds differing in the type of bond not only between the "oxygen bridge" and the atoms of the elements constituting the peroxy-compound but also in the type of bond between the oxygen atoms in the bridge itself.

Some workers, including Hein[1], tend to regard all inorganic peroxy-compounds as complex, dividing them into three groups: polyoxides, peroxo-acids, and peroxy-hydrates. However, the authors include in the group of polyoxides, together with H_2O_2, H_2O_3, and H_2O_4, also peroxy-compounds the crystal lattices of which consist of metal ions (belonging mainly to subgroups IA and IIA of the Periodic System) and the corresponding molecular anions O_2^{2-} (peroxides), O_2^- (superoxides), and O_3^- (ozonides).

It has been shown recently[2] that compounds of this type, for example Rb_2O_2, dissociate completely in the $LiNO_3-KNO_3$ eutectic mixture into ions according to the mechanism $M_2O_2 \rightarrow 2M^+ + O_2^{2-}$ and RbO_2 dissociates[3] according to the mechanism $RbO_2 \rightarrow Rb^+ + O_2^-$.

In the neutral molecule of hydrogen peroxide H_2O_2, the peroxide ion O_2^{2-} does not exist as such. This means that hydrogen atoms are not attracted to any appreciable degree by the peroxo-group via electrostatic forces. Hydrogen peroxide is the first member of the homologous series of hydrogen polyoxides H_2O_2, H_2O_3, H_2O_4, ..., the molecules of which comprise, like sulphanes, zig-zag chains of oxygen atoms joined by single bonds with a length of about 1.5 Å.

The change in the type of bond in the peroxo-group on passing from hydrogen peroxide to other peroxy-compounds depends mainly on the change in the electronegativity of the element forming the peroxy-compound. The negative dissociation energy of the O_2^{2-} ion and the high energy required to complete the process $O_2 \rightarrow O_2^{2-}$ are the reasons why this ion can be stabilised only by highly electropositive elements (Li–Cs, Ca–Ba). To some extent this applies also to O_2^- and O_3^- ions.

To a first approximation, one may assert that the linkage between atoms of elements having an electronegativity lower than that of hydrogen and the "oxygen bridge" formed by the above molecular anions is predominantly ionic. The peroxy-compounds of elements with an electronegativity higher than that of hydrogen contain a peroxo-group (both as such and in the form of H_2O_2 molecules and HO_2 radicals). The peroxo-group may be present in the compound both as a bidentate ligand and as a "bridge".

On the basis of the differences in the structures of inorganic peroxy-compounds, it is useful to retain in their classification the subdivision into simple and complex compounds and to isolate in a special group the hydrogen polyoxides despite the clear genetic relation between H_2O_2 and metal peroxides.

For a deeper understanding of the structure of inorganic peroxy-compounds, it is necessary to examine in somewhat greater detail the electronic structure of molecular oxygen anions.

Molecular Oxygen Anions

In order to represent the electronic structure of the above molecular anions, it is necessary to recall that the oxygen molecule has an unusual structure, the details of which have still not been completely elucidated. The former representation of the double-bonded oxygen structure O=O in which the two oxygen atoms complete their stable octets by exchanging two electrons [:Ö: :Ö:] has been disproved by spectroscopic and magnetic measurements. The oxygen molecule is paramagnetic, which implies the presence of unpaired electrons. Therefore the oxygen molecule has been regarded as a kind of biradical, the structure of which may be represented by the electronic scheme [:Ö–Ö:] with an even number of electrons (twelve) but with only one single bond and two unsaturated valences. Two electrons are unpaired, which is the reason for the paramagnetism of the oxygen molecule. The low reactivity of oxygen in relation to that of free radicals is evidence against this scheme. Moreover, experimental data show that the dissociation energy of the oxygen molecule into atoms is 118 kcal mole^{-1}, which greatly exceeds the value necessary to dissociate a simple covalent bond. Hence it follows that in this case the unpaired electrons stabilise the bond between the oxygen atoms. This unusual case has been treated[4,5] as a three-electron bond. On the basis of these hypotheses, the oxygen molecule in the ground $^3\Sigma$ state can be approximately described by the formula [:O⋯O:] with one single and two three-electron bonds. The O=O bond length is 1.207 Å.[6]

The structure of the oxygen molecule may be represented as follows in terms of the molecular orbital method:

$$[KK(z\sigma)^2(y\sigma^*)^2(x\sigma^*)^2(w\pi)^4(v\pi^*)^2].$$

Consequently in the ground state of the oxygen molecule there are four bonding electrons in excess relative to the antibonding electrons and the bond order is two.

The addition of a single electron to the oxygen molecule leads to the formation of the singly-charged negative ion O_2^- which enters into the composition of superoxides. The electronic structure of the O_2^- ion may be represented by the formula $[:\ddot{O}\!\!-\!\!\ddot{O}:]$, [5,7] and in terms of the molecular orbital method by the formula

$$[KK(z\sigma)^2(y\sigma^*)^2(x\sigma)^2(w\pi)^4(v\pi^*)^3].$$

The electron adds to the antibonding orbital and the bond order diminishes by 1/2. Evidently the singly-charged negative superoxide ion has an odd number of electrons (thirteen) with one single and one three-electron bond†. This is consistent with the paramagnetism and colour of the peroxy-compounds containing this ion. More detailed information about the electronic structure of the O_2^- ion in the free state and in the lattices of alkali metal halides has been given by Zeller et al. [8]

The electron affinity of the oxygen molecule ($O_2 + e \rightarrow O_2^-$) determined by a thermochemical method [9] proved to be 0.87 ± 0.13 eV, i.e. the addition of an electron to the oxygen molecule involves an energy change of 20 ± 3 kcal mole^{-1}. However, the value of $E_{O_2^-}$ determined by other methods is much lower.

The dissociation energy of the O_2^- ion into O^- and O has been estimated from the Raman spectra of KO_2 as 2.99 eV, i.e. about 69 kcal mole^{-1}. [10] Consequently the O_2^- ion is less stable than the oxygen molecule. The O–O bond length in the O_2^- ion is greater than in the oxygen molecule. Earlier a value of 1.28 Å was adopted [10] but subsequent studies showed that it is in the range 1.82–1.35 Å. [12] The O_2^- ion has the form of an ellipsoid of rotation, the length of the major axis of which is 4.55 Å. The radius of each oxygen atom in O_2^- may be assumed to be 1.59 Å. [13] The major half-axis of the O_2^- ion is therefore 2.27 Å and the minor half-axis (or the transverse radius) is 1.52 Å. [7]

The absorption spectrum of O_2^- ions in an aprotic solvent has a maximum at 240 nm. [14]

The addition of two electrons to the oxygen molecule or of one electron to the O_2^- ion is not accompanied by evolution of energy, as in the formation of the O_2^- ion, but by its absorption,

$$O_2 + 2e \rightarrow O_2^{2-} - 110 \text{ kcal mole}^{-1},$$
$$O_2^- + e \rightarrow O_2^{2-} - 130 \pm 3 \text{ kcal mole}^{-1},$$

and the formation of the doubly charged negative O_2^{2-} ion [15,16], which forms part of peroxides‡.

In contrast to the O_2^- ion, which is known to occur in a free state [18] and which is capable of prolonged existence in aprotic solvents [19], the O_2^{2-} ion is known only in the crystal lattices of peroxides, where it is stabilised by cations with large radii. The appearance of the O_2^{2-} ion in aqueous solution is also possible: $H_2O_2(\text{liq.}) \rightarrow 2H^+ + O_2^{2-} - 56$ kcal mole^{-1}, but not in the gas phase, since in the latter case the formation of O_2^{2-} is exothermic: $H_2O_2(\text{gas}) \rightarrow 2H^+ + O_2^{2-} - 886$ kcal mole^{-1}. The electronic structure of O_2^{2-} may be represented by the formula $[:\ddot{O}\!\!-\!\!\ddot{O}:]^{2-}$, [4,20]§ and in molecular orbital terms by

$$[KK(z\sigma)^2(y\sigma^*)^2(x\sigma)^2(w\pi)^4(v\pi^*)^4].$$

The addition of two electrons to the antibonding orbital leads to a decrease of the bond order to unity. Evidently the doubly charged negative peroxide ion has an even number of electrons (fourteen) and one single bond. This is consistent with the diamagnetism and the lack of colour of peroxy-compounds containing this ion. The dissociation energy of the O_2^{2-} ion has been estimated as -125 kcal mole^{-1}, [21] while according to other data [22] it is -53.4 kcal mole^{-1}. Consequently the O_2^{2-} ion is less stable than the O_2^- ion and the oxygen molecule. The O–O bond length in O_2^{2-} is 1.40 Å, i.e. longer than in the O_2^- ion and in the oxygen molecule. Like O_2^-, the O_2^{2-} ion has the shape of an ellipsoid of rotation but with a somewhat less extended major axis, whose length is 4.19 Å. The radius of both O^- and O_2^{2-} is 1.35 Å. The major half-axis of the O_2^{2-} ion is therefore 2.09 Å and the minor half-axis (or the transverse radius) is 1.23 Å. [21,23]

The probable distribution of electrons in the three perpendicular 2*p* orbitals according to the quantum-mechanical representation of the electronic structure of the oxygen molecule and O_2^- and O_2^{2-} ions is illustrated schematically in Fig. 1. [24]

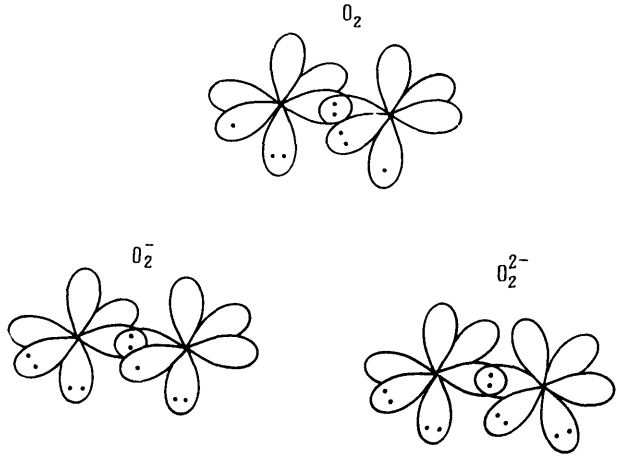


Figure 1. Schematic illustration of the probable distribution of electrons in three perpendicular 2*p* orbitals according to the quantum-mechanical representation of the electronic structure of the oxygen molecule and the O_2^- and O_2^{2-} ions.

In order to represent the electronic structure of the O_3^- ion, one must recall that the structure of ozone $:\!\overset{:O:}{\underset{:O:-:O:}{\diagup\diagdown}}$ proposed previously is in conflict with its enthalpy of formation, which amounts to +34.0 kcal mole^{-1}. If this structure is adopted, then ΔH_{298} for the formation of ozone

† The pernitride ion $[:\ddot{N}\!\!-\!\!\ddot{N}:]^{3-}$ has a similar electronic structure.

‡ The affinity of the oxygen molecule for two electrons quoted by Vedeneev et al. [17] (-175 ± 15 kcal mole^{-1}), obtained with the aid of the Born–Haber cycle on the basis of an approximate estimate of the lattice energies of alkaline earth metal peroxides, is inaccurate.

§ The O_2^{2-} has a structure which is isoelectronic with that of the fluorine molecule and is analogous to the structure of the disulphide ion $[:\ddot{S}\!\!-\!\!\ddot{S}:]^{2-}$.

should be 77.9 kcal mole^{-1}. According to Pauling [4,6], the electronic structure of the ozone molecule may be represented by a formula with eighteen electrons (Table 1). Then the structure of one of the terminal oxygen atoms in the ozone molecule resembles that of the fluorine atom; it completes its octet by sharing one electron pair with a neighbouring oxygen atom. Such an atom may be regarded as a negative ion $:\ddot{O}\cdot^-$ forming one covalent bond. The central atom may be regarded as a positive oxygen ion $:\dot{O}^+$ forming three covalent bonds: one single bond with the left-hand side oxygen atom and one double bond with the right-hand side oxygen atom. The angle at the vertex is 116°4′ according to Trambarulo [25] and 127°3′ according to Hughes [26].

Table 1. Principal characteristics of the bond types in the molecules of oxygen and ozone and their molecular anions.

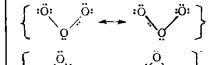
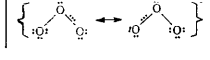
Formula	Electronic structure	O–O bond length, A	Bond dissociation energy, kcal mole^{-1}	Electron affinity E, kcal mole^{-1}
O_2	:O ⋮⋮ O:	1,207	118	20±3
O_2^-	[:O ⋮⋮ O:]$^-$	1.32—1.35	69	130±3
O_2^{2-}	[:Ö–Ö:]$^{2-}$	1.49	—125	—
O_3		1.278	25.1	44±10
O_3^-		(1.19—1.22)	—	—

Table 1 presents two structures for the ozone molecule. This implies that the two terminal oxygen atoms are equivalent. Using the terminology of the resonance theory, one may say that each bond in the ozone molecule is a hybrid of a single and a double bond.

The addition of one electron to the ozone molecule results in the evolution of energy, $O_3 + e \rightarrow O_3^-$ + 66.5 kcal mole^{-1}, [25,27] or, according to later data, +44 ± 10 kcal mole^{-1}, [28] and the formation of the singly-charged negative ion O_3^- which enters into the composition of ozonides. The electron structure of the O_3^- ion may be represented by the formula quoted in Table 1. Evidently the singly-charged negative ozonide ion has an odd number of electrons (nineteen), in agreement with the paramagnetism and colour of compounds containing it. The dissociation energy of the O–O bond in the O_3^- ion is unknown, but it is probably lower than the dissociation energy of this bond in the ozone molecule itself, giving O_2 and O, which amounts to 25.1 kcal mole^{-1}. [9] Consequently in the series of molecular oxygen anions, the O_3^- anion is least stable, though, according to not altogether reliable data [29,30], its O–O bond length is smaller than in the other ions discussed above and even in the oxygen molecule itself. It is 1.19–1.22 Å, [29,30] while in ozone it is 1.278 Å [25] or, according to later data [26], 1.260 Å. The angle at the vertex of the O_3^- ion is 100°. [29]

Table 1 presents the principal characteristics of the bond types in oxygen and ozone molecules and their molecular anions.

Simple Inorganic Peroxy-compounds

Inorganic peroxy-compounds, the crystal lattices of which contain the above oxygen anions O_2^{2-}, O_2^-, O_3^- and also the hydroperoxide anion HO_2^- should be classified as simple peroxy-compounds.

Simple inorganic peroxy-compounds can be divided into four groups: (1) peroxides, the crystal lattices of which contain the peroxide ions O_2^{2-}; (2) superoxides incorporating the superoxide ions O_2^-; (3) ozonides incorporating the ozonide ion O_3^-; (4) hydroperoxides.

The crystal lattices of hydroperoxides, which have the general formula EOOH, contains the hydroperoxide ion HO_2^-. In these compounds the peroxo-group is linked by an ionic bond to the atom of the element E and by a covalent bond to the hydrogen atom. The ionic character of hydroperoxides has been demonstrated experimentally only for the compound NH_4OOH. [31,32] It is also confirmed by the fact that hydrogen peroxide is a weak acid with $K = [H^+][HO_2^-]/H_2O_2 = 2.24 \times 10^{-12}$.

It is noteworthy that certain hydroperoxides may be regarded as peroxyhydrates and others as peroxo-acids. For example, NaOOH may be represented as the peroxyhydrate $Na_2O_2.H_2O_2$, and the compound $(OH)_3TiOOH$ may be regarded as a peroxo-acid.

Compounds in which the peroxo-group is linked to the atom of the element forming the peroxy-compound by a coordinate bond involving the π bonding orbitals of the O_2^{2-} ion should be included among complex peroxy-compounds, which will be described in detail in the next section. Complex peroxy-compounds include also peroxide hydrates, adducts of peroxides and salts with hydrogen peroxide, and compounds containing in the inner sphere H_2O_2 molecules or HO_2 radicals.

A characteristic property of peroxy-compounds, both simple and complex, is their capacity to form hydrogen peroxide on interaction with dilute solutions of acids and also to evolve oxygen readily in an active form on thermal decomposition or under the influence of water and other chemical agents. The "superoxide" oxygen evolved by peroxides has come to be referred to as "active". Other inorganic compounds which can serve as sources of oxygen, for example nitrates, chlorates, perchlorates, permanganates, and certain oxides [33], do not evolve oxygen under the action of water; they do so only on heating to high temperatures and in the presence of catalysts. Potassium dichromate, manganese dioxide, and lead dioxide evolve oxygen only on interaction with concentrated sulphuric acid solutions.

The difference in the type of bond between the oxygen atoms in the "bridges" of peroxides and hydroperoxides on the one hand and in superoxides and ozonides on the other is clearly revealed on hydrolysis. Peroxides and hydroperoxides are hydrolysed according to the equations $M_2O_2 + H_2O \rightarrow 2MOH + H_2O_2$ and $MOOH + H_2O \rightarrow MOH + H_2O_2$ (where M is the metal atom) with formation of hydrogen peroxide, which is quantitatively titrated with acid permanganate. The formation of hydrogen peroxide on hydrolysis of peroxides and hydroperoxides indicates a clear genetic relation between these compounds and hydrogen peroxide. Therefore peroxides and hydroperoxides have long been regarded as salts of hydrogen peroxide with two and one metal atoms.

Superoxides are hydrolysed with formation of an intermediate HO_2 radical (the hydroperoxyl) according to the equations

$$\begin{array}{l} 2MO_2 + 2H_2O \rightarrow 2MOH + 2HO_2, \\ 2HO_2 \rightarrow H_2O_2 + O_2, \\ \hline 2MO_2 + 2H_2O \rightarrow 2MOH + H_2O_2 + O_2, \end{array}$$

Consequently two-thirds of the active oxygen, constituting the "superoxide oxygen", is evolved as O_2 and can be determined gas-volumetrically and one-third of the active oxygen, which constitutes the "peroxide oxygen", is evolved as H_2O_2 and can be titrated with acid permanganate. Ozonides are hydrolysed without the formation of H_2O_2 according to the equation $MO_3 + H_2O \rightarrow MOH + OH + O_2$.

The reactions occurring on hydrolysis of superoxides and ozonides reveal a clear genetic relation, noted by Kazarnovskii, between superoxides and the H_2O radical and between ozonides and the hypothetical radical HO_3 (the hydro-ozonyl).[34]

The term peroxide was introduced in the Russian nomenclature by D.I. Mendeleev, who wrote, emphasising the lack of similarity in the reactions of the peroxides MO_2 and the salt-forming oxides of the same composition, that "the concept of peroxides is indefinite if one includes among them not only H_2O_2, Na_2O_2, and BaO_2 but also MnO_2 and PbO_2".[35] The definitions of "peroxide" quoted in the textbook of Gess [Hess?][36] and Shcheglov[37] suffer from this lack of clear-cut significance. Unfortunately certain contemporary chemists both in the USSR and abroad continue to employ the term peroxides for quadrivalent lead and manganese oxides the molecules of which contain the oxide ion O^{2-} with the electron structure $[:\ddot{O}:]^{2-}$. The nitrogen (IV) oxide N_2O_4, in the molecule of which there is no peroxo-group and the oxygen atom is linked covalently to the nitrogen atom, is also incorrectly called a peroxide.

The principal feature distinguishing peroxide from oxides of the type MO_2 is the reaction with dilute acids. As mentioned above, the former form H_2O_2, and the latter can, for example, evolve chlorine from hydrochloric acid.

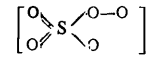
The term hydroperoxide (gidroperekis') was adopted in the Russian literature as the translation of the German term Hydroperoxyd[38].

The term superperoxide (nadperekis') was introduced into the Russian nomenclature in 1948 [39] and is more apt than the term "tetroxide" adopted previously[40], since it has been shown[4,7] that there is no O_4^{2-} ion in the molecules of these compounds. The term superperoxide has become firmly established in the Russian chemical nomenclature[41-43]. In 1947 the term "dioxide" was proposed for these compounds[44], as in the German nomenclature[45], and later the term "superoxide" ["superoksid"][46], a translation of the corresponding English term, was suggested by Neuman[47]. This term was adopted[48] in 1953 in the English, French (superoxyde), German (Superoxyd), and Italian (superossido) nomenclature, but in 1957 the International Union of Pure and Applied Chemistry approved the terms hyperoxide and hyperoxyde[49,50] on the basis of the term Hyperoxyd proposed by Remy[51] for the German nomenclature. While there names are justified by the fact that in the above languages we have the terms oxide, oxyde, Oxyd, and ossido and also peroxide, peroxyde, Peroxyd, and perossido, in the Russian nomenclature the terms "superoksid" (superoxide) and "giperoksid" (hyperoxide) are in no way justified, since the terms "okis'" (oxide) and "perekis'" (peroxide)[52] have been generally adopted for the lower degrees of oxidation and not "oksid" (oxide) and "peroksid" (peroxide), as suggested by some workers[53-56]. Moreover the Russian suffix "nad" corresponds to the Latin suffix super and the Greek suffix $\upsilon\pi\epsilon\rho$. Therefore the term "nadperekis'" (superperoxide) is quite acceptable¶. Evidently, on the basis of the same considerations, the term "nadokis'" (superoxide) was proposed[52]. However, it is close in significance to the term "perekis'" (peroxide) and does not reflect the fact that the relevant compounds contain more active oxygen than a peroxide. The proposed term "superoksid" (superoxide) for peroxides of the type M_2O_2 is quite inappropriate[56].

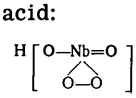
The term "inorganic ozonide" was introduced by Kazarnovskii[57] and has been adopted by the International Union of Pure and Applied Chemistry[49,50].

Complex peroxy-compounds may be divided into five groups.

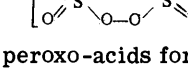
1. Peroxo-acids and their salts, in which the peroxo-group† enters into the composition of the complex anion. Mononuclear peroxo-acids and their salts are known, for example, peroxomonosulphuric acid:



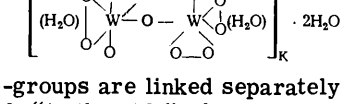
and peroxomononiobic acid:



as well as polynuclear peroxo-acids and their salts. In these compounds the atoms of elements in Groups IV–VI of the Periodic System—the non-metals carbon, nitrogen, phosphorus, and sulphur or the metals titanium, vanadium, chromium, niobium, molybdenum, tantalum, and tungsten—usually function as the coordinating species. In polynuclear peroxo-acids formed by non-metals, the atoms of the coordinating element are linked via a peroxo-group, as, for example, in peroxodisulphuric acid:



In polynuclear peroxo-acids formed by transition elements, the linkage between the atoms of the coordinating element is formed via one oxygen atom, as, for example, in potassium tetraperoxotungstate[59,60] or tetraperoxomolybdate[61]:

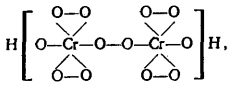


The peroxo-groups are linked separately by two covalent π bonds "to the side" of each atom of the coordinating element. The O–O bond length is 1.50 Å in the tungsten compound[60] and 1.48 Å in the molybdenum compound[61]. The peroxy-complexes of titanium[62], in which the O–O bond length is 1.45 Å, have the same structure.

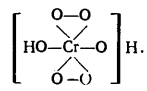
¶ If the term "oksid" (oxide) proposed by the authors of projects for the Russian nomenclature[53,54] and Kazarnovskii[55] is approved, the above remarks concerning the term "superoksid" (superoxide) will be no longer valid and the terms "perekis'" (peroxide) and "gidroperekis'" (hydroperoxide) should be replaced by "peroksid" (peroxide) and "gidroperoksid" (hydroperoxide).

† At the XXIInd Congress of the International Union of Pure and Applied Chemistry, the term "peroxido-group" was adopted instead of "peroxo-group"[58].

The presence of a linkage between the atoms of the coordinating element via an "oxygen bridge" in polynuclear peroxo-acids of certain other transition elements appeared controversial. For example, until recently [63] it was believed that there exist polynuclear peroxochromates with the composition $M_2[Cr_2O_{12}]$ to which the formula of pentaperoxodichromic acid was attributed:



However, according to later data [64,65], the mononuclear structure of oxomonohydroxodiperoxochromic acid was established for this compound:

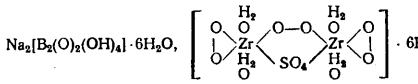


The O–O bond length in derivatives of chromium peroxo-acids is 1.40–1.47 Å. [65] The O–O bond length in peroxoacid derivatives of non-metals, for example, in the compounds $(NH_4)_2S_2O_8$ and $Cs_2S_2O_8$, is 1.46 Å. [66]

2. Peroxy-complexes which are not peroxoacids or their derivatives. These can also be divided into mononuclear and polynuclear. The mononuclear compounds may contain the peroxo-group in the inner sphere, for example $M_2[Nb(O-O)Cl_5]$, and $M_2[Mo(O-O)_2OCl_4]$, and may be combined in the subgroup of peroxo-complexes. It is noteworthy that, whereas the oxo-group always behaves as a monodentate ligand, the peroxo-group, owing to the greater length of the O–O bond, can behave as a bidentate ligand and can promote the formation of compounds with a coordination number of seven and particularly eight. This possibility diminishes in the series Cr < Mo ≃ W and V < Nb ≃ Ta. The possibility of the existence of a peroxo-ligand and other ligands around the central atom of the complex depends both on the nature of the central atom and on the conditions in the medium where the compound is synthesised. It depends on the pH of the solution and on the oxidation–reduction properties of the ions involved in the reaction.

Mononuclear peroxy-complexes also include compounds with hydrogen peroxide molecules in the inner sphere, for example $[Fe(H_2O)_5(H_2O_2)]^{3+}$. Compounds of this kind constitute the group of perhydro-complexes. Finally hydroperoxy-radicals may be coordinated in the inner sphere, as, for example, in $K_3[Co(CN)_5OOH]$. Compounds of this type constitute the subgroup of hydroperoxo-complexes.

Compounds of the type



$[(NH_3)_5Co-O-O-Co(NH_3)_5](NO_3)_5$ and others

may serve as an example of polynuclear peroxy-complexes which are not peroxo-acids.

The bond length in the first compound is 1.47 Å [67] and in the last 1.45 ± 0.06 Å. [68] In contrast to derivatives of binuclear peroxo-acid derivatives of transition elements, in these compounds the linkage between the metal atoms is formed via an "oxygen bridge".

The comparatively recently discovered complex peroxy-compounds formed by the addition of oxygen to certain reactive d^8 and d^{10} complexes of iridium, rhodium, platinum, palladium, and nickel are of some interest. For example, the iridium complex $IrO_2Cl(CO)(PPh_3)_2$, in which the O–O distance is 1.30 ± 0.003 Å, i.e. close to the O–O distance in the O_2^- anion, has been isolated [69–71]. However, this compound is diamagnetic like all other similar derivatives. It is interesting to note that the O–O bond length in iridium complexes of this kind and their capacity for combination with oxygen increase with increasing capacity of the other ligands to lose electrons.

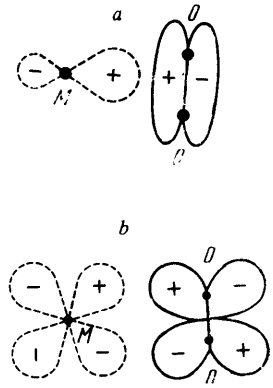


Figure 2. *a*) Transfer of π electrons from the donor (oxygen) to free *d* orbitals of the metal; *b*) transfer of *d* electrons from the metal to the antibonding orbital of the donor.

For example, in the iodide complex $IrO_2I(CO)(PPh_3)_2$, the O–O distance is 1.51 Å, i.e. close to the O–O distance in the O_2^{2-} anion, while in the phosphine chelate complex $IrO_2(PAr_2)_4$ [probably $IrO_2(P_2Ar_4)$, (Ed. of Translation)] the distance is 1.66 Å, i.e. greater by 0.17 Å than in the O_2^{2-} molecular anion. The reason for the increase of the O–O bond length should probably be sought in the fact that these compounds have a metal–oxygen bond $(L)_nM\leftarrow\overset{O}{\underset{O}{\|}}$ of the π type [72]. In this bond type, one may expect a transfer of π electrons from the donor (oxygen) to the free *d* orbitals of the metal, as shown schematically in Fig. 2*a*, and also a transfer of the *d* electrons of the metal to the antibonding orbital of the donor, as shown schematically in Fig. 2*b*. The overall effect is the transfer of electrons from the bonding to the antibonding orbital of the donor via the metal. This is reflected in a decrease of bond energy and consequently in an increase of bond length. The stronger the linkage between the donor and the metal, the greater the bond length.

The most important property of these complexes is their capacity to oxidise substrates under unusually mild conditions [73].

3. Peroxide hydrates—adducts of peroxides and water of crystallisation, for example $CaO_2.8H_2O$.

4. Peroxyhydrates—molecular compounds, resembling hydrates, containing hydrogen peroxide of crystallisation, for example $CaO_2.2H_2O_2$ and $K_2CO_3.3H_2O_2$.

The analogy between the peroxyhydrates of peroxides and their hydrates is not rigorous. In the former the hydrogen peroxide molecules are linked to O_2^{2-} ions by strong hydrogen bonds, forming infinite chains. The nature of peroxyhydrates of peroxides is close to that of compounds of the type KF.HF.[74] Molecular compounds with H_2O_2 are also formed by ammonia and certain organic compounds with basic properties.

5. Hydrates of peroxyhydrates—molecular compounds containing both water and hydrogen peroxide of crystallisation, for example $BaO_2.H_2O_2.2H_2O$ and $Na_2SO_4.0.5H_2O_2.H_2O$.

The term "peroxoacid" ("peroksokislota") is the English term recommended by the International Union of Pure and Applied Chemistry[48]. The necessity to introduce into the Russian nomenclature this term, in the place of the previously adopted "nadkislota" ("peracid") proposed by Mendeleev[75] arose due to the following considerations.

For example, the compound $H_2S_2O_8$ is at present called persulphuric acid (nadsernaya kislota) in the Russian nomenclature. The terms "sulphuric acid" ("sernaya kislota" and "sulphurous acid" ("sernistaya kislota") have been adopted for oxyacids of sulphur. They emphasise that in the first compound sulphur is in the hexavalent state and in the second in the quadrivalent state. The term "persulphuric acid" is unwittingly associated with the idea that in this compound sulphur has a valence higher than six, which is not the case. Moreover, the compound H_2SO_5 is nowadays called monopersulphuric acid (mononadsernaya kislota). It would be quite logical to assume, as rightly pointed out by Gussein-zade[76], that the prefix "mono" indicates the number of peroxo-groups in the compound, since otherwise it should be referred to as permonosulphuric acid (nadmonosernaya kislota). In fact, in the above example the prefix "mono" indicates the number of sulphur atoms. Like the preceding compound, $H_2S_2O_8$ contains one peroxo-group but two sulphur atoms, which is not reflected in its name (persulphuric acid). The use of the terms "peroxomonosulphuric" and "peroxodisulphuric" for the compounds H_2SO_5 and $H_2S_2O_8$ removes this inconsistency. If in any other peroxoacid the number of peroxo-groups is greater than unity, as, for example, in peroxochromic acid H_3CrO_8 where there are four such groups, it should be designated as a tetraperoxoacid, i.e. tetraperoxomonochromic acid.

As regards the nomenclature of peroxoacid salts, it is noteworthy that the terms persulphates, percarbonates, perborates, etc. which persist in the chemical literature, are very inapt and lead to the incorrect idea that they resemble the salts of certain oxygen-containing acids, such as perchlorates, permanganates, perrhenates, etc., where the prefix "per" indicates merely the highest degree of oxidation of the element and not the presence of the peroxo-group. Certain salts of oxygen-containing acids (for example, perchlorates and permanganates) also serve as sources of oxygen in thermal decomposition. However, in contrast to the thermal decomposition of peroxoacid derivatives, their decomposition involves a change in the valence of the elements forming these compounds. For example, whereas in the thermal decomposition of potassium peroxodisulphate according to the equation $K_2S_2O_8 \rightarrow K_2SO_4 + SO_3 + 0.5O_2$ sulphur retains a valence of six in the decomposotion products, in the thermal decomposition of potassium perchlorate or permanganate according to the equations $KClO_4 \rightarrow KCl + 2O_2$ and $2KMnO_4 \rightarrow K_2MnO_4 + MnO_2 + O_2$, the chlorine in the decomposition products has passed from the heptavalent to the univalent state and the manganese from the heptavalent to the hexavalent and quadrivalent state. The terms peroxosulphates, peroxocarbonates, etc. are correct for peroxoacid salts. According to crystal structure data[67], infrared and NMR spectroscopy[77], and magnetic measurements[78,79], "perborates" may be divided into two groups: those containing water may be referred to as diperoxodiborotetrahydroxo-salts and the anhydrous compounds may be designated by the term peroxoborates.

The general term peroxy-complexes is not open to objection. The term peroxyhydrate has also been recommended by the International Union of Pure and Applied Chemistry[48]. It is to be preferred to the terms "perhydrate"[90] and "hydroperoxate" proposed by American workers[81].

The difference in the type of bond between the "oxygen bridge" and the element forming the peroxy-linkage in peroxoacids and their salts compared with peroxides, superoxides, and ozonides is also shown in hydrolysis. For example, in the hydrolysis of peroxodisulphuric acid $H_2S_2O_8$ or peroxodisulphate salts, peroxomonosulphuric acid H_2SO_5 is formed initially without the formation of hydrogen peroxide, according to the equation $H_2S_2O_8 + H_2O \rightarrow H_2SO_5 + H_2SO_4$ and then peroxomonosulphuric acid yields hydrogen peroxide according to the equation $H_2SO_5 + H_2O \rightarrow H_2SO_4 + H_2O_2$. However, at room temperature the hydrolysis is very slow and involves considerable loss of active oxygen. Although on heating the rate of reaction does increase, there is a simultaneous increase of the amount of oxygen evolved. Consequently, the quantitative determination of active oxygen in these compounds cannot be achieved by permanganate titration and iodometric titration is employed.

Peroxy-complexes which are not peroxoacids or derivatives of peroxoacids hydrolyse in most cases with formation of hydrogen peroxide, but certain mononuclear peroxy-complexes, for example $[(NH_3)_5Co-O-O-Co(NH_3)_5]^{5+}$ are extremely stable in relation to water and give rise to H_2O_2 only in an acid medium.

When peroxyhydrates react with water, hydrogen peroxide of crystallisation passes to the solution and may be determined quantitatively by permanganate titration in an acid medium.

A new class of peroxides—organometallic peroxides—the composition of which includes one or several metal atoms, peroxy-groups, and organic residues, are of special interest[82]. For example silicon, germanium, tin, and lead are capable of forming symmetrical peroxides of the type R_3MOOMR_3, in which the linkage between the atoms of the element is achieved via an "oxygen bridge".

Table 2 presents a scheme for the classification and nomenclature of inorganic peroxy-compounds proposed by the author of this review[83-85] and supplemented by taking into account the latest data on their structure.

The methods of synthesis of each group of peroxy-compounds quoted in Table 2 are different. Hydroperoxides are synthesised mainly via alkoxides in an anhydrous medium. Peroxides are synthesised by the reaction of oxides with oxygen or via solutions of the hydroxides and hydrogen peroxide. Superoxides are synthesised mainly via the metals, by their combustion in oxygen at the normal pressure, and also by the action of oxygen on peroxides at the normal or elevated pressure. Ozonides are obtained by the reaction of ozone with hydroxides or superoxides with subsequent extraction by liquid ammonia. Peroxoacids and the peroxoacid salts of

Table 2. Classification and nomenclature of inorganic peroxy-compounds.

Type	Group			Formula
Simple	Hydrogen polyoxides			H_2O_2, H_2O_3, H_2O_4
	Hydroperoxides			M^IOOH
	Peroxides			$M^I_2O_2$
	Superoxides			M^IO_2
	Ozonides			M^IO_3
	Peroxoacids and their salts	Mononuclear		$[E^{IV}O_4]^{2-}$; $[E^VO_5]^{3-}$; $[E^{VI}O_5]^{2-}$; $[E^{VI}O_6]^{2-}$
		Polynuclear	With peroxo-bridges	$[O_2E^{IV}-O-O-E^{IV}O_2]^{4-}$; $[O_2E^V-O-O-E^VO_3]^{4-}$; $[O_2E^{VI}-O-O-E^{VI}O_2]^{2-}$
			With oxo-bridges	$[(O-O)_2OE^{VI}-O-E^{VI}O(O-O)_2]^{2-}$
Complex	Peroxy-complexes	Mononuclear	Peroxo-	$[M(O-O)_x(L)_y]^n$
			Perhydro-	$[M(H_2O_2)_x(L)_y]^n$
			Hydroperoxo-	$[M(HO_2)_x(L)_y]^n$
				$n=0,\pm1,2,3\ldots$
		Polynuclear		$[(L)_yMO-OM(L)_y]^n$
	Peroxide hydrates			$M^I_2O_2\cdot xH_2O$
	Peroxyhydrates	of peroxides		$M^I_2O_2\cdot xH_2O_2$
		of salts		$M^I_nEO_m\cdot x\cdot H_2O_2$
	Peroxyhydrate hydrates	of peroxides		$M^I_2O_2\cdot xH_2O_2\cdot yH_2O$
		of salts		$M^I_nEO_m\cdot x\cdot H_2O_2\cdot yH_2O$
Organometallic	Hydroperoxides			$R_nM(OOH)_m$
	Substituted hydroperoxides			$R_nM(OOR)_m$; $M(OOR)_n$
	Peroxides	Homoradical		R_nMOOMR_n
		Heteroradical		$R_nMOOMR^1_n$
		Heteroelemental		R_nMOOCR_n

M = metal, E = element, L = ligand, and R = organic group.

typical elements are synthesised predominantly by the electrolytic method. The peroxoacids of transition elements and their salts are synthesised via solutions of oxygen-containing acids of these elements and of hydrogen peroxide. Peroxy-complexes which are not derivatives of peroxoacids are obtained mainly with the aid of solutions of hydrogen peroxide, but in many cases oxidation with molecular oxygen is employed. The addition of molecular oxygen to the coordinating element in compounds of certain transition metals may be represented schematically as follows:

$$M^{n+} + O_2 \xrightarrow{I} M^{n+}(O_2) \xrightarrow{II} M^{n+2}(O_2^{2-}).$$

Oxygen carriers are formed reversibly via mechanism I, while mechanism II involves the irreversible formation of peroxy-complexes where the metal passes to a higher valence state and in the case of binuclear complexes μ-peroxo-compounds are produced.

Peroxyhydrates and their hydrates are formed exclusively from hydrogen peroxide solutions. Organometallic compounds form organometallic peroxo-derivatives on reaction with peroxy-compounds or on oxidation with molecular oxygen.

The difference between the structures of inorganic peroxy-compounds is responsible for the difference between their physical properties and reactivities and hence for the possibility of employing them under a wide variety of conditions.

The above data concerning the radical differences between the molecular oxygen anions and the different states of the peroxo-group in complex peroxy-compounds demonstrate that inorganic peroxy-compounds cannot be characterised by the words "these are compounds incorporating an oxygen bridge". Additional evidence showing that this definition is not altogether satisfactory comes from the elucidation of the structure of the compound F_2O_2, which has been incorrectly called[15] fluorine peroxide. It has been established[86,87] that in the oxygen fluoride F_2O_2 the fluorine atoms are joined by the "oxygen bridge" O–O, although this compound does not exhibit the properties of peroxides. The O–O bond length in this compound (1.22 Å) differs little from the bond length in the oxygen molecule. On coming into contact with ice, F_2O_2 (m.p. 64.3°) explodes with evolution of oxygen[88]. The energy of the dissociation of F_2O_2 into 2OF is 62.3 ± 20 kcal mole^{-1}.[89]

The so called dioxygenyl compounds incorporating the O_2^+ ion, for example the compounds $O_2^+PtF_6^-$[90] and $O_2^+BF_4^-$[91] are not peroxides either. The formation of the O_2^+ ion is accompanied by the evolution of 286 kcal mole^{-1} and the energy of dissociation into $O^+ + O$ is 153.48 ± 0.05 kcal mole^{-1}.[92] The interatomic distance in the O_2^+ molecular ion, which is formed on removal of one electron from the $\nu\pi^*$ level, is reduced to 1.1227 Å compared with 1.2074 Å in the oxygen molecule, while, as stated above, on formation of peroxide anions the above distance increases owing to the introduction of additional electrons in the same level[93].

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Methods for the Preparation of Refractory Compounds of Transition Metals and Prospects for Their Development

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The principal methods for preparing borides, carbides, silicides, nitrides, and oxides of transition metals in Groups IV-VI are surveyed. Distinctions between the concepts "method" and "process" of preparation are examined. The main parameters of methods and processes—temperature, time, chemical reactions, etc.—are summarised in tables. General theoretical schemes for preparation from solutions in melts and by the electrolysis of melts and solutions in melts are discussed in detail. Several prospects for the development and utilisation of the above methods of preparation are indicated. A list of 377 references is included.

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I. INTRODUCTION

The refractory compounds of transition metals are their binary compounds with boron, carbon, nitrogen, oxygen, and silicon (the sulphides, selenides, phosphides, and certain other transition-metal compounds can also be included to some extent).

The vigorous development of various branches of modern technology, such as nuclear power, space technology, various direct methods of transformation into electrical energy, etc.—all this requires the application of considerable quantities of various refractory compounds. Their preparation sometimes presents considerable difficulties, for various reasons—high cost or inadequate purity of the initial products, low yield, poor reproducibility and danger of some methods of preparation, and also the poor quality of the products.

Nevertheless, modern technology demands increased reliability in objects made of refractory compounds, with stable properties (both invidivual and combined) under the most severe operating conditions. In many cases only single crystals of these compounds are able to exhibit such properties, and their production becomes an important technical problem. It can be solved in two ways—(*a*) by obtaining single crystals from the ready made compounds (by Czochralski crystal pulling, zone melting, gas transport, etc.), and (*b*) by growing them in the course of preparing the compounds (from the gas phase, from solution, etc.)—neither of which has yet been significantly investigated in its application to borides, carbides, nitrides, oxides, or silicides of transition metals. Development of the first procedure is restricted by the high temperatures of the molten compounds, their great reactivity and the lack of suitable inert materials for the crystallisers, and also the incongruent melting of several of the compounds. Development of the second procedure is made difficult by the problems of controlling the complicated mechanisms of the crystallisation of refractory compounds either from the gas phase or from solutions in and also by the absence of definite information on the structure of such solutions. The state of these procedures, especially the second, is evidence of the need for its further theoretical and experimental investigation, and the necessity of developing and improving methods for the preparation of refractory compounds.

The present Review surveys methods for the preparation of refractory compounds of transition metals in Groups IV–VI and the prospects for developing these methods both in general and in application to the growth of single crystals.

II. PRINCIPAL METHODS FOR THE PREPARATION OF REFRACTORY COMPOUNDS

The main existing methods for the preparation of refractory compounds have been quite fully classified in monographs and volumes of papers[1-26]. An analysis of these classifications suggests a somewhat modified classification—(1) direct synthesis from the elements, (2) preparation from solutions in melts, (3) electrolysis of melts and solutions in melts, (4) metallothermic reduction of metal oxides, (5) reduction of oxides and other compounds by non-metals and their compounds, and (6) gas-phase preparation.

This classification is based on combining most logically and completely the principles of adequacy of the initial components and the type (kinetic mechanism†) of the chemical reactions. Thus, for example, the state of aggregation of the reactants (gaseous, liquid, or solid) alone does not indicate the specific character of individual methods (electrolysis, preparation from molten solutions), and either of the above principles separately is an insufficient condition of classification: adequacy of the initial components does not distinguish metallothermic reduction of

† The kinetic mechanism must be taken as meaning a definite number and sequence of stages of chemical reactions, leading to the formation of definite chemical compounds.

oxides from their reduction by non-metals, and the same type of reaction identifies direct synthesis from the elements with synthesis from solutions in melts, gas-phase synthesis with reduction of oxides, etc.

It is also necessary to make a clear distinction between two concepts—method and process of preparation—which differ in extent; this distinction is by no means always made in the scientific literature. It can be concluded from the definitions [27-33] that, although in all cases "method" and "process" are actually equated, nevertheless a wider range of phenomena and even a set of phenomena are covered by a method [29-31,33]. Hence we consider the concept "method" to be more general that that of "process", which is a particular case of a "method". The mixing of these ideas, which is often met in the literature, leads to confusion and uncertainty, and does not promote a correct classification, in particular of modes of preparation. In this connection the following definitions may be suggested for these concepts.

Method of preparation is the accomplishment of a chemical reaction between elements or chemical compounds of certain classes by a definite kinetic mechanism.

Process of preparation is a particular embodiment of a method, i.e. the actual accomplishment of a chemical reaction with a definite kinetic mechanism under given specific conditions—with given reactants, a given technical operation of the method, and given state of aggregation of the reactants and products.

Let us examine the above methods for the preparation of refractory compounds, in particular information on their discovery, development, chemical reactions, conditions of preparation, industrial applications, use for the production of single crystals, virtues, defects, and development prospects. The sets of chemical reactions and the conditions of preparation in Tables 1–6 have been compiled from the original papers, in which the methods and processes were first developed. References to more than one worker as the first to discover or develop a given process are explained by significant and fundamental modifications of a process effected by subsequent investigators. It is noteworthy also that all methods of preparing nitrides and oxides are in fact variants of a semi-gaseous method (owing to the gaseous state of nitrogen and oxygen under the conditions of preparation); in view of the above conditions of classification, however, they are not included among the gas-phase preparations (Table 6), but are placed in the appropriate tables.

Tables 1–6 have been compiled not only from periodicals and special publications but also from all the available most general reviews and monographs on the preparation and technology of refractory compounds [1-26]. Among papers of the same type we have considered only those in which processes were developed for the first time, which are the most characteristic and representative, or which are concerned with the larger number of refractory compounds.

III. DIRECT SYNTHESIS FROM THE ELEMENTS

This method consists essentially in the reaction between a transition metal (M = Ti, Zr, Hf, V, Nb, Ta, Cr, Mo, W) and a non-metal (Nm = B, C, N, O, Si)

$$xM + yNm \rightarrow M_xNm_y$$

which can be effected with the components in various states of aggregation (gaseous G, liquid L, solid S). This is a redox reaction: both transition metals and non-metals can function as oxidants and reductants. Electronic processes in the formation of a chemical bond in the "molecules" of refractory compounds are especially complicated by the presence of valency d-electrons in transition metals. These and s-electrons, together with the s- and p-electrons of the non-metals, are involved in the formation of conduction bands and valency bands when the refractory compounds are formed in the condensed phase. The topography of the electron density in the solid phase of such compounds is extremely complicated: according to some workers [34,35] it is characterised by greater density either on the cores of the metal atoms, which when isolated have about 5 or 10 valency d-electrons, or on the cores of the non-metal atoms, whose electronic structure (valency electrons) is close to sp^3 or s^2p^6.

The time τ and the temperature limits T of homogenisation of refractory compounds in their direct synthesis are determined by the exponential relation $\tau^{-1} = K \exp(-Q/RT)$, where Q is the activation energy of homogenisation. The uppermost temperature limits are determined by the temperatures at which the compounds decompose, but in practice they are governed by the limit at which the materials from which the apparatus is made remain inert. Relatively little study has yet been made of the use of ultrahigh pressures in direct synthesis, but they show some promise for obtaining new modifications of such compounds, possessing more extreme properties [36,37].

Table 1 lists the main characteristics of existing processes for the direct synthesis of borides, carbides, nitrides, and silicides [38-67].

The process of melting the elements together was first used for the synthesis of silicides by Berzelius [68] and later by Moissan [40], who used it also to obtain borides [39] and carbides [38]. Sintering or saturation was first applied to the synthesis of nitrides [67,69,70] and then also for borides [42-44,46], silicides [48,54], and carbides [47]. The process of hot extrusion was first tried for the preparation of silicides [54]; carbides [52,53] and borides [51] were obtained later. The above processes were first developed in various forms by many investigators: the smelting of borides [42-45], carbides [56], and silicides [58], the sintering of borides [49], carbides [47,57], and silicides [59,60], the saturation of nitrides [57,71-77], and also the hot extrusion of borides [55], carbides [52,53], and silicides [11,14,62-66] have continued to be improved until the last decade. Oxides, which are produced from ores [78-86] and various compounds [87-92], are synthesised by the present method only under special conditions (in a plasma [93], in an electric discharge [94]) or in order to obtain special deposits (films [95]).

Application of method in industry. (1) Fusion for tungsten carbide [56,96]; with arc melting shows promise for obtaining all clasess of compounds [97]. (2) Sintering (saturation) for borides [13], carbides [16], silicides [11], and nitrides [20,98]. (3) Hot extrusion mainly for higher borides [13,55], carbides [14], and silicides [14].

Growth of single crystals. Kiessling used this method by sintering chromium boride (20 days). [42-44]

Advantages of method. (1) Possibility of obtaining large quantities of refractory compounds. (2) Production by hot extrusion of ready-made articles of borides, carbides, and silicides, including those fused to

Table 1. Direct synthesis from the elements.

Compounds	Process	Synthetic reaction	Refs	Conditions of preparation				Ref
				t, °C	time	medium	pressure	
Borides	melted together	$M_L + Nm_{L,S} \rightarrow MNm_L$ (assumed)		1200—2000	0.5 h	vacuum	—	42—44
			38—41	~3000	5—40 min	vacuum, air	—	45
	sintered	$M_S + Nm_S \rightarrow MNm_S$ (assumed)						
			46—48	1300—2050	10—30 min	rarefied Ar	—	42—44, 49, 50
	hot extrusion	$M_{S,L} + Nm_{S,L} \rightarrow MNm_S$(assumed)				H_2, vacuum		
			51—54	1350—2850	0.5 min	air	~202 kg cm^{-2}	55
Carbides	melted together	$M_L + Nm_S \rightarrow MNm_{L,S}$ (assumed)				H_2, vacuum		
			32—41	~3000	a few min	town gas	—	56
				1200—2000	1 h	H_2	—	47
	sintered	as with borides	46—48	1700—2000	30 min	H_2	—	57
	hot extrusion	$M_{S,L} + Nm_S \rightarrow MNm_S$ (assumed)	51—54	$T<T$ below m.p.	not stated precisely	air	~100 kg cm^{-2}	52, 53
Silicides	melted together	$M_L + Nm_L \rightarrow MNm_L$ (assumed)						
			38—41	≥2000and<	~10 min	Ar, He	—	58
				1600—2100	3—68 min	Ar	—	59
	sintered	as with borides	46—48	1000—1200	0.5—2 h	Ar	—	60
	hot extrusion	$M_{S,L} + Nm_L \rightarrow MNm_{S,L}$ (assumed)		1000—1600	1.5—8 min	air, vacuum, H_2	~200 kg cm^{-2}	61—66
			51—54	1300—2100	2—10 min	air, vacuum, H_2	~220—250 kg cm^{-2}	11, 14
Nitrides	saturation	$M_S + N_{2,G}(NH_{3,G}) \rightarrow MN_S(+H_{2,G})$	57,67	1100—1200	2 h	N_2, N_2+H_2	—	57

100% density [99]. (3) Simplicity of apparatus for the synthesis. (4) Comparatively short times of synthesis. (5) Possibility of obtaining carbides in fibre form [100].

Disadvantages of method. Difficulty of obtaining exact composition of borides and silicides (especially the lower compounds), and limiting composition of carbides and nitrides.

Prospects for development and exploitation of method. (1) Preparation of initial components before the synthesis—pickling of powder grains of transition metals, boron, and silicon to remove oxides and activate the surface, followed by vacuum drying; thorough grinding and mixing of initial stoichiometric mixtures, and also their degasification before synthesis in a high vacuum; and selection of individual heating schedules for filled and extruded intermediate products. (2) The creation in vacuum synthesis of an attenuated inert atmosphere in the reaction apparatus to prevent dissociation of the refractory compounds [101-103]. (3) The use of plasma [104,105] and other [106,107] processes for synthesis by this method.

IV. PREPARATION FROM SOLUTIONS IN MELTS

This method consists essentially in the interaction of atoms of transition metals and non-metals or of molecules of their compounds dissolved in salt or metallic melts. Three different cases may be encountered: (1) the soluble components (elements or their compounds) do not form compounds with either salt or metallic solvents; (2) both or at least one component forms compounds with metallic solvents; (3) both or at least one component forms compounds with salt solvents. These processes can be represented by the following schemes, in which the first two stages may involve dissolution of the components, whereas the third stage (underlined) involves their interaction.

Case (1)

(*a*) Both components dissolve

For elements (partly McKenna's process, synthesis of carbides—Table 2) we have

$$\begin{gathered} M_S + Solv \rightarrow M_{diss} \\ Nm_{S,G} + Solv \rightarrow Nm_{diss} \\ \underline{M_{diss} + Nm_{diss} \rightarrow MNm_{diss}} \end{gathered} \quad (1.1)$$

For compounds (partly Gruber's synthesis of borides—Table 2) the equations are

$$\begin{gathered} MEl'_S + Solv \rightarrow MEl'_{diss} \\ NmE''_S + Solv \rightarrow NmEl''_{diss} \\ \underline{MEL'_{diss} + NmEl''_{diss} \rightarrow MNm_{diss} + El'El''_{diss}} \end{gathered} \quad (1.2)$$

Here Solv denotes the solvent, salt or metallic, in the molten, liquid state (the symbol L is omitted), diss denotes "dissolved", and El′ and El″ are elements combined with the transition metal and with the non-metal respectively.

Transition metals, non-metals, and their compounds may interact with or dissolve in the molten solvents while in any state of aggregation. However, the gaseous and liquid states of metals ($M_{L,G}$) their compounds ($MEl'_{L,G}$), and compounds of non-metals ($NmEl''_{L,G}$), as well as the liquid state of non-metals (Nm_L), are in practice unrealisable, although theoretically possible, in this method of synthesis from solutions in melts.

The state of aggregation of refractory compounds formed from solutions in melts will be determined by the state of the initial components and their behaviour towards the solvent: the products will be dissolved when both initial components either dissolve in or interact with the solvent (even if one component is in the gas phase); if, however, at least one component is insoluble, the products will also occur in the solvent in the solid phase [108].

(*b*) One component dissolves

For the elements (the zinc process, the synthesis of silicides—Table 2)

$$\begin{array}{l} M_S + Solv \rightarrow M_{diss}(M_S) \\ Nm_{S,G} + Solv \rightarrow Nm_{S,G}(Nm_{diss}) \\ \hline M_{diss}(M_S) + Nm_{S,G}(Nm_{diss}) \rightarrow MNm_{S,diss}(MNm_S) \end{array} \quad (1.3)$$

For compounds (copper silicide process, synthesis of silicides, (*a*)—Table 2)

$$\begin{array}{l} MEl'_S + Solv \rightarrow MEl'_{diss}(MEl'_S) \\ NmEl''_S + Solv \rightarrow NmEl''_S(NmEl''_{diss}) \\ \hline MEl'_{diss}(MEl'_S) + NmEl''_S(NmEl''_{diss}) \rightarrow MNm_S + El'El''_S \end{array} \quad (1.4)$$

Case (2)

(*a*) Both components interact

For the elements (zinc process, synthesis of borides and nitrides—Table 2)

$$\begin{array}{l} M_S + Solv^M \rightarrow MSolv^M_{diss} \\ Nm_{S,G} + Solv^M \rightarrow Solv^M Nm_{diss} \\ \hline MSolv^M_{diss} + Solv^M Nm_{diss} \rightarrow MNm_{diss} + Solv^M \end{array} \quad (2.1)$$

For compounds‡

$$\begin{array}{l} MEl'_S + Solv^M \rightarrow MSolv^M_{diss} + Solv^M El'_{diss} \\ NmEl''_S + Solv^M \rightarrow Solv^M Nm_{diss} + El''Solv^M \\ \hline MSolv^M_{diss} + Solv^M Nm_{diss} \rightarrow MNm_{diss} + Solv^M \end{array} \quad (2.2)$$

where $Solv^M$ is a metallic solvent.

(*b*) One component interacts while the other simply dissolves or is even insoluble

For elements (zinc process, synthesis of silicides and carbides or the copper silicide process, synthesis of silicides, (*b*)—Table 2)

$$\begin{array}{l} M_S + Solv^M \rightarrow MSolv^M_{diss} \\ Nm_{S,G} + Solv^M \rightarrow Nm_{diss}(\text{or } Nm_{S,G}) \\ \hline MSolv^M_{diss} + Nm_{diss} \rightarrow MNm_{diss} + Solv^M \\ (\text{or } MSolv^M_{diss} + Nm_{S,G} \rightarrow MNm_{S,G} + Solv^M) \end{array} \quad (2.3)$$

$$\begin{array}{l} M_S + Solv^M \rightarrow M_{diss} \ (\text{or } M_S) \\ Nm_{S,G} + Solv^M \rightarrow NmSolv^M_{diss} \\ \hline M_{diss} + NmSolv^M_{diss} \rightarrow MNm_{diss} + Solv^M \\ (\text{or } M_S + NmSolv^M_{diss} \rightarrow MNm_S + Solv^M) \end{array} \quad (2.4)$$

‡ It must be emphasised that synthesis in cases (2) and (3) requires that the refractory compound should be very stable (this can be assessed by means of the enthalpy, the energy of the chemical bond, and other parameters) in comparison with the products formed by interaction of the transition metal and the non-metal with the solvent. Transition metals and non-metals, when they interact with the solvent, function to different extents as donors and acceptors of electrons, which governs the possibility of their interaction in the melts after the compounds they form have dissociated into oppositely charged ions. For example

$$\begin{array}{l} MSolv^M \rightleftharpoons M^+ + Solv^{M-} \\ NmSolv^M \rightleftharpoons Nm^- + Solv^{M+} \\ M^+ + Nm^- \rightarrow MNm \end{array} \quad \text{or} \quad \begin{array}{l} MSolv^2 \rightleftharpoons M^+ + Solv^{2-} \\ NmSolv^1 \rightleftharpoons Nm^- + Solv^{1+} \\ M^+ + Nm^- \rightarrow MNm \end{array}$$

For compounds

$$\begin{array}{l} MEl'_S + Solv^M \rightarrow MSolv^M_{diss} + El'Solv^M_{diss} \\ NmEl''_S + Solv^M \rightarrow NmEl''_{diss} \ (\text{or } NmEl''_S) \\ \hline MSolv^M_{diss} + NmEl''_{diss} \rightarrow MNm_{diss} + Solv^M El''_{diss} \\ (\text{or } MSolv^M_{diss} + NmEl''_S \rightarrow MNm_S + Solv^M El''_S) \end{array} \quad (2.5)$$

$$\begin{array}{l} MEl'_S + Solv^M \rightarrow MEl'_{diss} \ (\text{or } MEl'_S) \\ NmEl''_S + Solv^M \rightarrow NmSolv^M_{diss} + Solv^M El''_{diss} \\ \hline MEl'_{diss} + NmSolv^M_{diss} + MNm_{diss} + El'Solv^M_{diss} \\ (\text{or } MEl'_S + NmSolv^M_{diss} \rightarrow MNm_S + El'Solv^M_S \end{array} \quad (2.6)$$

Case (3)

(*a*) Both components interact

For elements [134]

$$\begin{array}{l} M_S + Solv^1Solv^2 \rightarrow MSolv^2_{diss} + Solv^{1+} \\ Nm_{S,G} + Solv^1Solv^2 \rightarrow NmSolv^1_{diss} + Solv^{2-} \\ \hline MSolv^2_{diss} + NmSolv^1_{diss} \rightarrow MNm_{diss} + Solv^1Solv^2 \end{array} \quad (3.1)$$

For compounds [117]

$$\begin{array}{l} MEl'_S + Solv^1Solv^2 \rightarrow MSolv^2_{diss} + El'Solv^1_{diss} \\ NmEl''_S + Solv^1Solv^2 \rightarrow NmSolv^1_{diss} + El''Solv^2_{diss} \\ \hline MSolv^2_{diss} + NmSolv^1_{diss} \rightarrow MNm_{diss} + Solv^1Solv^2 \end{array} \quad (3.2)$$

where $Solv^1Solv^2$ is a salt solvent in which $Solv^{1+}$ is the cation and $Solv^{2-}$ the anion.

(*b*) One component interacts

Similarly to case (2*b*) we have for the elements

$$\begin{array}{l} M_S + Solv^1Solv^2 \rightarrow MSolv^2_{diss} + Solv^{1+} \\ Nm_{S,G} + Solv^1Solv^2 \rightarrow Nm_{diss}(\text{or } Nm_{S,G}) \\ \hline MSolv^2_{diss} + Nm_{diss} \rightarrow MNm_{diss} + Solv^{2-} \\ (\text{or } MSolv^2_{diss} + Nm_{S,G} \rightarrow MNm_{S,diss} + Solv^{2-}) \end{array} \quad (3.3)$$

$$\begin{array}{l} M_S + Solv^1Solv^2 \rightarrow M_{diss} \ (\text{or } M_S) \\ Nm_{S,G} + Solv^1Solv^2 \rightarrow NmSolv^1_{diss} + Solv^{2-} \\ \hline M_{diss} + NmSolv^1_{diss} \rightarrow MNm_{diss} + Solv^{1+} \\ (\text{or } M_S + NmSolv^1_{diss} \rightarrow MNm_S + Solv^{1+}) \end{array} \quad (3.4)$$

For compounds

$$\begin{array}{l} MEl'_S + Solv^1Solv^2 \rightarrow MSolv^2_{diss} + El'Solv^1_{diss} \\ NmEl''_S + Solv^1Solv^2 \rightarrow NmEl''_{diss} \ (\text{or } NmEl''_S) \\ \hline Msolv^2_{diss} + NmEl''_{diss} \rightarrow MNm_{diss} + El''Solv^2_{diss} \\ (\text{or } MSolv^2_{diss} + NmEl''_S \rightarrow MNm_S + El''Solv^2_S) \end{array} \quad (3.5)$$

$$\begin{array}{l} MEl'_S + Solv^1Solv^2 \rightarrow MEl'_{diss} \ (\text{or } MEl'_S) \\ NmEl''_S + Solv^1Solv^2 \rightarrow NmSolv^1_{diss} + El''Solv^2_{diss} \\ \hline MEl''_{diss} + NmSolv^1_{diss} \rightarrow MNm_{diss} + El'Solv^1_{diss} \\ (\text{or } MEl'_S + NmSolv^1_{diss} \rightarrow MNm_S + El'Solv^1_S) \end{array} \quad (3.6)$$

The above possible variants in the synthesis of refractory compounds from molten solutions are merely the simplest and relate to ternary systems. Synthesis in multicomponent systems is greatly complicated by parallel and exchange processes. Real mechanisms of synthesis are far more complicated than the schemes presented

Table 2. Formation from molten solutions.

Compounds	Process	Synthetic reaction	Ref.	Conditions of preparation					Ref.
				t, °C	time, h	protective medium	rate of cooling, deg min^{-1}	solvent	
Borides	in molten iron	$B_{diss}(BFe_{diss}) + Ti_{diss}(TiFe_{diss}) \rightarrow TiB_{diss} + (Fe_L)$ (assumed)	112	400—2000	not stated	not stated	1—100	mineral acids	112
	in molten Na (K)	$B_{diss}(BEl_{diss}) + M_{diss}(MEl_{diss}) \rightarrow MB_{diss} + El_{diss}(NaEl_{diss})$ (assumed)	113	650—1100	2—10	air	—	H_2O	113
	Zn process	$B_{S,diss} + MZn_{diss} \rightarrow MB_{S,diss} + Zn_L$	111	>907	1—4	Ar, vacuum	100—1000	HCl (1 : 1), HNO_3 (1 : 10)	111
Carbides	McKenna's	in molten Al(Na) assumed that: $C_{diss}(AlC, NiC)_{diss} + M_{diss}(AlM, NiM)_{diss} \rightarrow MC_{diss} + Al(Ni)_L$	115	~2000	not stated	not stated	Ar, vacuum	HCl, HNO_3, 3HCl+HNO_3	115
	Zn process	$C_S + MZn_{diss} \rightarrow MC_S + Zn_L$	111	>907	1—4	Ar, vacuum	100—1000	HCl (1 : 1), HNO_3 (1 : 10) NaOH (10%)	111
Silicides	Lebeau's	in molten Cu assumed that: (a) $Cu_L + Si_{diss} + MO_S \rightarrow MSi_{diss} + CuO_S + SiO_{2S}$ (b) $Si_{diss}(CuSi_{diss}) + M_{S,diss}(MCu_{diss}) \rightarrow MSi_{diss,S} + (Cu_L)$	109, 116	~1300	2	H_2	7.5	HNO_3 (10%, (warm)	109
	Zn process	$Si_{diss} + MZn_{diss} \rightarrow MSi_{diss} + Zn_L$	111, 114	>907	1—4	Ar, vacuum	100—1000	HCl (1 : 1), HNO_3 (1 : 10)	111—114
Nitrides	in molten chlorides	$MO(MCl_n) + Ca_3N_2 + CaCl_2 \rightarrow MN + CaO + CaCl_2$	117	450—1200	1	Ar	not stated	H_2O	117
	Zn process	$N_{G,diss} + MZn_{diss} \rightarrow MN_{diss} + Zn_L$	111	>907	1—4	N_2, Ar	100—1000	HCl (1 : 1), HNO_3 (1 : 10)	111

here, owing to reversibility of the dissolution and interaction stages with many refractory compounds, dissociation and solvation of dissolved components and products, and also the actual conditions of synthesis—composition and nature of components, technical design factors, and operating schedules.

The formation of homogeneous products and the overall yield of the reaction (provided that the products can be separated from the solvent without decomposition) are governed by the behaviour of the solvent towards the initial components: if it shows greater affinity for one of them, excess of this component is required in the melt [109]. The affinity of the solvent for the reactants can be assessed by means of thermodynamic calculations, by computing and comparing the chemical potentials of the components in the solvent and in the resulting refractory compound [109]. Furthermore, the necessary excess of one metal or non-metal in the melt, in the synthesis of refractory compounds of several transition metals or non-metals from the elements, can be established experimentally (by a series of experiments on the homogeneity of the product), and then the required excess can be calculated for other metals or non-metals by setting up the proportion $\Delta m/u_1 = \Delta m_X/u_2$, where Δm is the experimental excess of one component over the other in the melt, u_1 the total energy of the valency band of this element [110]—a quantity which is proportional to the sum of the successive ionisation potentials of the atom (this sum could also be used for these purposes, but with less accuracy)—Δm_X is the unknown excess of the other metal or non-metal, and u_2 is the total energy of its valency band. The basis of such a calculation is the dependence of all properties of the atoms of dissolved components (including their behaviour towards the solvent) on the energy characteristics of their valency electrons. The usefulness of such a calculation is confirmed in the practical synthesis of borides and silicides of transition metals from solution in molten zinc. The excess of transition metals necessary for homogeneous synthesis [109] and calculated from the above relation can be applied to the preparation of homogeneous borides and silicides (both polycrystalline powders and single crystals). In the separation of the refractory compounds from zinc this excess is easily removed by hydrochloric or nitric acid, since the intermetallic compounds which it forms with zinc (so called zincides) dissolve readily in these acids [111].

The chief characteristics of existing processes for the synthesis of borides, carbides, nitrides, and silicides by this method are given in Table 2. [109,111-117]

The first attempts to isolate carbides from steel were made in 1887. [118] The prepartion of carbides has since been improved by Williams [119], Moissan [120], and others [111,121]. Silicides were obtained long ago by Lebeau [116] using this method§; other processes for their synthesis were developed considerably later [122]. Borides [111-113] and nitrides [111,117,123] have been prepared quite recently. Development of the above processes for the synthesis of borides [112,113], carbides [115], silicides [109,114], and nitrides [117] has not yet reached industrial proportions. Oxides are not synthesised by this method because it is unprofitable; but it is possible in principle, and can be used in practice to grow single crystals [123-125].

Application of method in industry. (1) The Lebeau, McKenna, etc. processes are inapplicable because of low yield and high cost for borides and silicides, small-scale application may be possible to obtain complex and pure carbides [8,126] and nitrides [117]. (2) The zinc process is not applicable because of the low yield and the cost; in the synthesis of nitrides control of the process is complicated.

Growth of single crystals. This application is possible and promising for borides [108,111-127], carbides [128], silicides [66,108,109,127,129], and nitrides [108,127,130].

§ The variety of processes in this method is determined not only by the technical conditions of crystal growth but also by the nature of the solvent and its behaviour towards the solutes.

Advantages. (1) Comparative simplicity of synthetic processes. (2) Possibility of obtaining pure, alloyed, and complex (mixed) compounds. (3) Possibility in individual cases of regenerating easily sublimate solvent metals [111,127].

Disadvantages. (1) Low yield and high cost of production, caused by the consumption of salt and metal solvents. (2) Possibility of contamination of the products with the solvent. (3) Need for vigorous stirring of molten solutions in order to obtain homogeneous compounds.

Prospects of development and exploitation. (1) Use of vibrational agitation of solutions in melts to intensify synthetic processes. (2) Choice of solvents of low boiling point so that boiling can be used to agitate the molten solution. (3) Investigation of structure of solutions in melts in order to study the kinetics of the synthesis and the mechanism of the growth of single crystals [131] of refractory compounds. (4) Use of ultrahigh pressures (by analogy with the production of diamond) in treatment of the systems and their solutions in melts in order to grow single crystals and obtain new modifications of refractory compounds. (5) Use for the application of coatings of refractory compounds on steel, various metals, and alloys [132,133].

This method has not yet become widespread for the preparation of refractory compounds. Work on synthesis in metallic melts—(1.1), (1.2), (2.1), and (2.2)—has been concerned mainly with semiconductor and intermetallic systems [134,135]. The interesting use of amalgam metallurgy has enabled, in particular, silicides [136] and nitrides [123] of rare-earth metals to obtain at 400–600°C, although the solubility of transition metals in mercury is insignificant, and they hardly react at all with such non-metals as boron and silicon [135,137]. Furthermore, considerable theoretical and practical interest attaches also to the search for new, and the investigation of already known, low-temperature polymetallic solvents (such as Newton's, Rose's, Wood's, and Guthrie's alloys [138]) for transition metals and non-metals, that are comparatively cheap, of low viscosity, and capable of simple recovery. Salt solvents are more rarely used [139] for synthetic purposes—(1.1), (1.2), (3.1), (3.2), etc.—mainly for growing single crystals of oxides and various salts by the recrystallisation of already prepared compounds [123–125,140] and also for the application of coatings [144]. Nevertheless, synthesis in salt solvents from the elements or from compounds may be of considerable interest with appropriate selection and investigation of the systems [143,144], because of the solubility of metals in melts of their own and other salts [142].

Structural investigations on solutions in melts (both salt and metallic) are of great value for synthetic purposes, since the information obtained will provide a more detailed and a clearer picture of the processes occurring in such solutions and enable them to be controlled [134,145].

V. ELECTROLYSIS OF MELTS AND SOLUTIONS IN MELTS

This method consists essentially in the formation of refractory compounds as a result of primary or secondary electrode processes either on the cathode or on the anode. In the electrolysis of melts (only the initial one-component systems are implied) the presence of any other component in the system already represents a solution of one in the other, i.e. a solution in a melt formation of the refractory compound is always the primary¶ electrode process, but in the electrolysis of solutions in melts it may be either the primary or a secondary process.

1. Electrolysis of Melts

This form of electrolysis consists in the passage of an electric current through molten salts (or in the present case molten refractory compounds), which are strong electrolyes. It seldom finds practical application in the preparation of refractory compounds [146]. Formation of a refractory compound can take place either on the cathode, on the anode, or on both at the same time, in a single electrolytic cell, e.g. in the electrolysis of silica (silicides and oxides on the surfaces of transition-metal electrodes). The lower temperature limits are governed by the melting points of the compounds undergoing electrolysis, but in practice many factors—the possible occurrence of synthesis on the electrodes, the intensity of vaporisation or decomposition of the electrolyte, the stability of the cell towards the melt, etc—determine the temperature of electrolysis. All the classes of refractory compounds under consideration can be obtained by the present form of electrolysis. One of the components in the synthesis should form an electrode (metal or non-metal, including the possibility of gas cathodes for nitrogen and oxygen; furthermore, the non-metal cannot form the anode, since the metal which is to be discharged on it cannot have a negative charge in a melt of its binary compound, but this is hypothetical).

The following types of dissociation are undergone by salts in melts

$$MEl' \rightarrow M^{n_1^+}El'^{n_1^-} \text{ (or } n_1El^{1-}\text{), e.g. } TiS_2, VF_3, WO_3$$

$$NmEl'' \rightarrow Nm^{n_2^+} + El''^{n_2^-} \text{ (or } n_2El''^{1-}\text{), e.g. } B_4C, SiO_2, SiC$$

$$El''Nm \rightarrow Nm^{n_2^-} + El''^{n_2^+} \text{ (or } n_2El''^{1+}\text{), e.g. } CaO, K_2O, Ca_3N_2, CaC_2$$

The reactions at the electrodes (synthesis of borides, carbides, silicides, nitrides, oxides) are—at the cathode

$$\begin{aligned} Nm^{+n_2} + M_{cath}^{(n_2^-)} &\rightarrow MNm^0 \\ M^{n_1^+} + Nm_{cath}^{(n_1^-)} &\rightarrow Mnm^0 \end{aligned} \qquad (4.1)$$

and at the anode

$$Nm^{n_2^-} + M_{anode}^{(n_2^+)} \rightarrow MNm^0 \qquad (4.2)$$

where n_1 and n_2 are the valencies of metals and non-metals, EL′ and EL″ are elements with which they form compounds, and the zero denotes the electrically neutral state of molecules (atoms). The charge on an atom of the electrode (in parentheses), at which an ion of the other component is discharged, will always equal the ionic charge: $n_2 = (\pm n_2)$; $\pm n_1 = (\pm n_1)$.

The refractory compounds prepared in this way may form coatings or deposits on the electrodes or may settle as a slime at the bottom of the cell.

¶ The process is primary if it is assumed that on discharge the ions at once form lattice points of the refractory compound but, having been converted into neutral atoms, do not interact with the electrode surface, do not migrate along the surface, and also do not diffuse inside the electrode.

2. Electrolysis of Solutions in Melts

This form of electrolysis consists in passing a current through a molten strong electrolyte containing the dissolved reactants. The latter may be present either in the electrically neutral atomic or molecular state or as ions, but if one component is in a neutral state, the other must be ionised. Only the electrolysis of solutions in salt melts is used in practice for the preparation of refractory compounds (Table 3), for metallic electrolytes have not yet found widespread use.

Formation of a compound by discharge of the ion of one component on an electrode made of the other component must be regarded as the primary electrode process; in all other cases the synthesis of the refractory compound is a secondary electrode process. We shall examine possible synthetic reactions at electrodes on the assumption that both ions and complexes (complex ions) of the individual components may take part in the reactions.

(1) Reactions on cathode (borides, carbides, silicides, and nitrides)

For ions (Meerson and Smirnov's preparation of borides, Andrieux and Dodero's preparation of silicides—(Table 3) we have

$$\begin{gathered} M^{n_1^+} + n_1 e \rightarrow M^0 \\ Nm^{n_2^+} + n_2 e \rightarrow Nm^0 \\ M^0 + Nm^0 \rightarrow MNm^0 \end{gathered} \tag{4.3}$$

and for complexes

$$\begin{gathered} MEl'^{n_1^+} + n_1 e \rightarrow MEl'^0 \\ NmEl''^{n_2^+} + n_2 e \rightarrow NmEl''^0 \\ MEl'^0 + NmEl''^0 \rightarrow MNm^0 + El'El''^0 . \end{gathered} \tag{4.4}$$

It should be noted that variant (4.3), and also (4.7) and (4.11), are not applied in practice to the preparation of nitrides (these processes are possible only if ammonia dissolves and dissociates in the melts, and also nitrogen dissolves). Nitrides can be obtained on the cathode by dissolving ammonium, etc. halides, nitrates, carbonates, and other salts in the solvent melts with their subsequent dissociation to form the ammonium ion (4.4) or by simply dissolving them—(4.7) and (4.11).

Refractory compounds formed on the cathode are in the solid phase. The following possibilities can be envisaged for the synthesis.

(*a*) One component is an ion, while the other is present in a complex:

$$\begin{gathered} M^{n_1^+} + n_1 e \rightarrow M^0 \\ NmEl''^{n_2^+} + n_2 e \rightarrow NmEl''^0 \\ M_0 + NmEl''^0 \rightarrow MNm^0 + El''^0 \end{gathered} \tag{4.5}$$

$$\begin{gathered} MEl'^{n_1^+} + n_1 e \rightarrow MEl'^0 \\ Nm^{n_2^+} + n_2 e \rightarrow Nm^0 \\ MEl'^0 + Nm^0 \rightarrow MNm^0 + El'^0 \end{gathered} \tag{4.6}$$

(*b*) One component is an ion (or is present in a complex), while the other component is unionised (undissociated), i.e. occurs in the melt either in the dissolved state or in the solid state (gaseous in the case of nitrogen) as the cathode and is negatively charged (Weiss and Andrieux's preparation of carbides—Table 3): for ions

$$\begin{gathered} M^{n_1^+} + n_1 e \rightarrow M^0 \\ Nm_{diss} + M^0 \rightarrow MNm^0 \\ NmEl''_{diss} + M^0 \rightarrow MNm^0 + El''_{diss} (ZrB_2 \text{ (Ref.147)}, \end{gathered} \tag{4.7}$$

$$M^{n_1^+} + Nm_{cath}^{(n_1^-)} \rightarrow MNm^0 \tag{4.8}$$

$$\begin{gathered} Nm^{n_2^+} + n_2 e \rightarrow Nm^0 \\ M_{diss} + Nm^0 \rightarrow MNm^0 \\ MEl'_{diss} + Nm^0 \rightarrow MNm^0 + El'_{diss} \end{gathered} \tag{4.9}$$

$$Nm^{n_2^+} + M_{cath}^{(n_2^-)} \rightarrow MNm_2^0 \tag{4.10}$$

and for complexes [148,149]

$$\begin{gathered} MEl'^{n_1^+} + n_1 e \rightarrow MEl'^0 \\ MEl'^0 + Nm_{diss} \rightarrow MNm^0 + El'^0 \\ MEl'^0 + NmEl''_{diss} \rightarrow MNm^0 + El'El''_{diss} \end{gathered} \tag{4.11}$$

$$MEl^{n_1^+} + Nm_{cath}^{(n_1^-)} \rightarrow MNm^0 + El'^{n_1^-} \tag{4.12}$$

$$\begin{gathered} NmEl''^{n_2^+} + n_2 e + NmEl''^0 \\ NmEl''^0 + M_{diss} \rightarrow MNm^0 + El''^0 \\ NmEl''^0 + MEl'_{diss} \rightarrow MNm^0 + El'El''_{diss} \end{gathered} \tag{4.13}$$

$$NmEl''^{n_2^+} + M_{cath}^{(n_2^-)} \rightarrow MNm^0 + El''^{n_2^-} \tag{4.14}$$

Variants (4.11) and (4.13) are possible also as parallel reactions near the cathode. Furthermore, parallel processes are possible also in the bulk electrolyte, such as interaction between ions (complexes) and dissolved atoms (compounds) with the formation of refractory compounds:

$$\begin{gathered} M^{n_1^+} + NmEl''_{diss} \rightarrow MNm_{diss} + El''^{n_1^+} (\text{or } n_1 El''^{1+}) \\ MEl^{n_1^+} + NmEl''_{diss} \rightarrow MNm_{diss} + El'El''^{n_1^+} \\ MEl^{n_1^+} + Nm_{diss} \rightarrow MNm_{diss} + El'^{n_1^+} (\text{or } n_1 \times El'^{1+}) \end{gathered} \tag{4.15}$$

$$\begin{gathered} Nm^{n_2^+} + MEl'_{diss} \rightarrow MNm_{diss} + El'^{n_2^+} (\text{or } n_2 \times El'^{1+} \\ NmEl''^{n_2^+} + MEl'_{diss} \rightarrow MNm_{diss} + El'El''^{n_2^+} \\ NmEl''^{n_2^+} + M_{diss} \rightarrow MNm_{diss} + El''^{n_2^+} (\text{or } n_2 \times El''^{1+}) \end{gathered} \tag{4.16}$$

(2) Reactions on anode (nitrides and oxides)

Here the following possibilities arise in connection with the synthesis.

(*a*) The transition metal is the anode, on which both ions and complexes of the non-metal can be discharged [150]:

$$\begin{gathered} Nm^{n_2^-} + M_{anode}^{(n_2^+)} \rightarrow MNm^0 \\ NmEl''^{n_2^-} + M_{anode}^{(n_2^+)} \rightarrow Mnm^0 + El''^{n_2^-} (\text{or } n_2 \times El''^{1+}) \end{gathered} \tag{5.1}$$

(*b*) Synthesis may occur in the anolyte, with atoms (compounds) of the metal dissolved in the melt, after discharge of an ion (complex) of the non-metal. For ions we have

$$\begin{gathered} Nm^{n_2^-} - n_2 e \rightarrow Nm^0 \\ Nm^0 + M_{diss} \rightarrow MNm^0 \\ Nm^0 + MEl'_{diss} \rightarrow MNm^0 + El'_{diss} \end{gathered} \tag{5.2}$$

and for complexes

$$NmEl''^{n-}_3 - n_2e \rightarrow NmEl''^0$$
$$NmEl''^0 + M_{diss} \rightarrow MNm^0 + El''_{diss} \quad (5.3)$$
$$NmEl''^0 + MEl'_{diss} \rightarrow MNm^0 + El'El''_{diss}$$

(*c*) Parallel reactions are possible in the bulk electrolyte between ionised and dissolved components (variants analogous to (4.15) and (4.16) follow here, but in the latter case the signs of the ions should be changed).

The above alternative schemes representing the synthesis of refractory compounds at an electrode show neither secondary processes nor processes occurring at the opposite electrode. Furthermore, purely chemical redox processes (other than formation of the refractory compound) occurring at the electrodes are also omitted. Consideration of all these processes would introduce considerable complications into the already numerous schemes. Actual examples of several of these processes (both main and secondary processes) are given in Table 3.[10,151-157]

This method was first used by Andrieux[151,152] to prepare borides, after which he and other investigators employed it to obtain carbides[151,152,154] and silicides[158]. Following this, the method was developed for the preparation of borides[153,154,156], carbides[154,156], and silicides[157,159]. Nitrides have not yet been obtained by this method, but their synthesis is theoretically possible both on the cathode and on the anode. With regard to oxides, papers have appeared on the surface passivation of titanium and niobium in molten alkali-metal carbonates and nitrates[150,160] (corresponding to (5.1), second case). Such passivation leads to the production of oxide and nitride deposits possessing specific properties.

It should be noted that the preparation of refractory nitrides and oxides by this method is inefficient, and can be of value only for the application of oxide and nitride films and coatings[161,167]. In the view of several workers[10,153] this method may be of intrinsic interest for borides, carbides, and silicides (while it retains its value for the application of coatings[133,162,163]), especially with continuous electrolysis.

Industrial application. This has been prevented by the low yield and by the complexity of the electrolysis and of the separation of the products from the electrolyte. Application is promising especially for borides[10] and silicides[148].

Growth of single crystals. The process has not been used for this purpose. Coarsely crystalline deposits can be obtained[148].

Advantages. (1) Simplicity of equipment and availability of starting materials; (2) low temperatures; (3) possible use to obtain refractory coatings[133,162-164] and films[150].

Disadvantages. (1) The impurity of the products and the laboriousness of purifying cathodic deposits; (2) difficulty of obtaining either higher or lower (with respect to the non-metal) compounds of strictly defined composition; (3) uneconomic.

Development and use prospects. (1) Development of continuous processes of electrolysis; (2) selection of easily fusible, cheap, and technically pure electrolytes and initial components; (3) investigation of structure of electrolyte and processes of electrolysis.

Further development of this method of synthesis will depend in considerable measure on investigations of the structure of melts and solutions in melts and also on investigations of the mechanism of the processes involved in synthesis on electrodes and in the electrolyte. Such researches have recently become increasingly widespread[143,144,155].

VI. METALLOTHERMIC REDUCTION OF METAL OXIDES

This method consists in reduction of metal and nonmetal oxides (or of metal oxides in the presence of nonmetals) with aluminium (magnesium and other metals in

Table 3. Electrolysis of alloys and molten solutions.

Compounds	Electrolytic bath	Ref.	Synthetic reaction	Ref.	Conditions of preparation					Ref
					t,°C	time	protective medium	electrolysis conditions	solvent of electrolyte	
Borides	$1/n(1-40)MO+2(1-3)B_2O_3+$ $+CaO(MgO,(Li, Na)_2O)+$ $+CaF_2(MgF_2,(Li, Na,F)$	151, 152	on cathode $Ca^{2+}(Mg, Na, Li)+2e(MO, B_2O_3)\rightarrow$ $\rightarrow Ca(CaO+M, CaO+B)$ $M+B\rightarrow MB$	151, 152	960—1000	1—2 h	air	4—10 V, 20—25 amp	HCl (dil.), H_2O	10, 151, 152
	$MO+2B_2O_3+CaO+CaF_2$	153	on cathode $M^{n+}+ne\rightarrow M$ $B^{3+}+3e\rightarrow B$; $M+B\rightarrow MB$	153	900—1200	>25 min	air	~6 V, ~2 amp	H_2O	153
Carbides	$Na(K)_2O\cdot B_2O_3+Na(K)_2CO_3+$ $+1/nMO+Li(Na,(Mg, Ca)_{1/2})F$ higher carbides deposited at higher $MO:CO_2$ ratios	154	in melt $Na_2CO_3\rightleftarrows$ $\rightleftarrows 2Na^+(Na_2O)+CO_3^{2-}(CO_2)$ $CO_3^{2-}\rightleftarrows CO_2+O_2^{2-}$							
			on cathode $M^{n+}+ne\rightarrow M$ $CO_2+2e\rightarrow C+2O^{2-}$; $M+C\rightarrow MC$ possible reactions on electrodes $CO_2+C\rightarrow 2CO$; $Na_2CO_3+2C\rightarrow$ $\rightarrow 2Na^++3CO$ possible reactions on cathode (1) $M+CO\rightarrow MC+O$ (2) $M+CO_2\rightarrow MC+M_xO_y$	154, 155	760—800	20—30 min	air	1.5—4 V, 20 amp	H_2O, HCl (dil.) (warm)	154, 156
Silicides	$2K(Na)\cdot SiF_4+MF_n(1/nMO$ or $K(Na)_2MO_4)$	151, 152 157	on cathode $M^{n+}+ne\rightarrow M(Na^++e\rightarrow Na)$ $Si^{4+}+4e\rightarrow Si$; $M+Si\rightarrow MSi$ at cathode (1) $Si+MO\rightarrow MSi+SiO_2$ (2) $M+SiO_2\rightarrow MSi+MO$ possible reactions at cathode and in bulk (1) $M^{n+}+SiF_4\rightarrow MSi+4F^-$ (2) $Si^{4+}+MF_n\rightarrow MSi+nF^-$	157	900—1200	~15 min	air	~6 V, ~20 amp	H_2O, Na(K)OH(5%)	151, 152, 157

the presence of compounds that evolve oxygen) to form refractory compounds:

$$MO + NmO(Nm + Al(Mg, Ca; + BaO_2, + NaNO_3) + S \rightarrow MNm_{molt} + Al(Mg)_x S_y O_z (Al_2O_3, MgO, etc.)$$

where the product MNm is in the molten state. The products of the reaction are also multicomponent compounds—slags (sulphur, etc. is sometimes added to the initial mixture to improve their fusibility)—together with oxides of the reducing metals (aluminium, magnesium, etc.).

This method of preparation involves a set of typical redox reactions, in which the starting materials always take part in the solid phase, whereas the products often melt at the resulting high temperatures (3000°C and above, especially when aluminium is used). It is the most explicit and simplest of all the methods of preparation, but the poor quality of the products and their lack of uniformity of composition, together with the difficulty of isolating them from the slags, prevent its widespread practical application for the production of refractory compounds. Furthermore, not all classes of these compounds can be obtained by this method, and carbides have been obtained only recently [165,166]. Nitrides and oxides cannot in principle by prepared by this method: nitrogen can occur only in the gas phase under the given conditions, and nitrides can therefore be formed only on the surface of the reduced metal (usually molten) in an atmosphere of pure nitrogen. In the presence of oxygen the reducing metal will burn in its atmosphere, almost without interacting at all with the metal oxides.

The main characteristics of the processes for the metallothermic preparation of borides, carbides, and silicides are set out in Table 4. [166,168-178] This method was first applied to the preparation of borides and silicides in 1905, [168,169] and only quite recently has it been used for carbides [165,166]. Many investigators have developed the method for the preparation of borides [170-173], silicides [174-176], and carbides [166].

The high temperatures make this method quite specific and industrially hazardous [24], and the impossibility of controlling the process results in compounds of variable composition. Nevertheless, several papers indicate that this is a promising method for the production of refractory compounds [24,172,173,176,179]. Further improvement is evidently possible by working very accurately through all the fine details of technology for each particular compound on both laboratory and manufacturing scales.

Industrial application. None, but promising [166,172,173,176,180].

Growth of single crystals. It has not been used for this purpose. But crystals are obtained as a consequence of the dissolution of the resulting borides, silicides, and carbides in the slags or aluminium and their subsequent crystallisation (up to 1 mm with silicides). [166,170,171,177]

Advantages. (1) Economical—little or no external supply of energy required for the process; (2) technology simple, raw material cheap [172,173]; (3) possibility of obtaining large quantities of the compounds [172,173,176].

Disadvantages. (1) Heavy contamination of the compounds with difficultly removable impurities (aluminium and magnesium borides and silicides, the monoxide of the metal, silica, etc.); (2) uncontrollability of the process and its well known danger with large quantities of reactants; (3) comparatively high cost of reducing metals.

Development and use prospects. (1) Accurate calculation of proportions of components in the initial charge and precise working out of industrial schedules for each specific compound [179]; (2) development of continuous cycles of preparation and utilisation of the energy evolved (heat and light).

VII. REDUCTION OF OXIDES AND OTHER COMPOUNDS BY NON-METALS AND THEIR COMPOUNDS

This method consists in reducing oxides (or other compounds) of transition metals by non-metals and their compounds:

$$MO(MEl', MEl'O, MEl'El'') + Nm(NmEl', NmO, NmEl'El'') \rightarrow MNm_S + NmO(El'_2, El'O, El''O, El'El''),$$

where El′ and El″ may be either metals or non-metals, MEl′ may represent a hydride, carbide, sulphide, chloride, or other compound of the metal, MEl′El″ and MEl′O are salts, NmEl′ is a hydride, carbide, or other compound of the non-metal, and NmEl′El″ is a hydrocarbon derivative, a complex, etc. (Table 5). As in the preceding method (Table 4) the preparation involves a set of redox reactions (in individual cases also exchange

Table 4. Metallothermic reduction of metal oxides.

Compounds	Synthetic reaction	Ref.	Conditions of preparation				Ref.
			t, °C	time, min	medium	solvent for products	
Borides	$MO+B_2O_3(B)+Al(Mg;+BaO_2)+S \rightarrow MB+$ + slags [$Al(Mg)_xS_yO_z$—sulphides, oxides multicomponent cpds.]	168—171	2000—3000	~2—3	air	HCl, HNO_3, 3HCl+HNO_3	168—171
	$M_nO_m+nB_2O_3+(m+3n)Mg \rightarrow MB_2+$ $+(m+3n)MgO$	172, 173	1150—1200	not stated	Ar	H_3PO_4(1:10), HCl(1:1)	172, 173
Silicides	$MO+SiO_2(Si)+Al(Mg;+NaNO_3)+S \rightarrow MSi+$ + slags [$Al(Mg)_xS_yO_z$—sulphides, oxides, multicomponent cpds.]	168, 169, 174—176	2000—3000	~2—3	air	HCl, K(Na)OH(5—10%), HNO_3(20%)	174—177 178
Carbides	ore (wolframite, schellite $CaWO_4$, $Fe_2O_3(WO_3)_3$)+Al+CaC_2+Fe_2O_3 $\rightarrow$ $\rightarrow WC+Al_2O_3$+ slags	166	2455—3040—700	not stated	air	not stated or absent	166

Table 5. Reduction of oxides and other compounds by non-metals and their compounds.

Compounds	Process	Synthetic reaction	Ref.	Conditions of preparation				Ref.
				t, °C	time	medium	other conditions	
Borides	reduction of oxides by non-metals	$MO+B\rightarrow MB+BO$	181—183	1500—1800	1—2 h	H_2, vacuum	—	182, 183
		$MO+B_2O_3+C\rightarrow MB+CO$	184—187	1700—2000	30 min	H_2	vacuum for purification	187
				1800—2050	not stated	H_2, CO	in stages above $t°$	185, 186
	reduction of oxides by cpds. of non-metals with C and other elements	$MO(M)+B_4C+C+(B_2O_3)\rightarrow MB+CO$	12, 188, 189	~2000	~15 min	H_2	pelleted at 7.5 tons cm^{-2}	188
				1200—1900	0.25—2 h	vacuum	0.02-4.2 mmHg	189
	reduction or interaction of other compounds	$MH(MC)+B(B_4C)+(B_2O_3)\rightarrow MB+H_2(C, B_4C, CO)$	55	1350—2850	0.5 min	air	pelleted at ~202 kg cm^{-2}	55
Carbides	reduction of oxides by non-metals	$MO_n+C\rightarrow MO_{n-1}+CO$	16, 47, 57	1100—1900	not stated	H_2	—	47
		$MO_{n-1}+C\rightarrow MO_{n-2}+CO$						
		$MO_n+C\rightarrow MC+nCO$		1700—2000	30 min	H_2	—	57
	reduction of oxides by cpds. of non-metals with C and other elements	$MO+CH_4+H_2\rightarrow MC+H_2O$	190	1600—2000	0.5—3 min	H_2	—	191
		$MO+CCl_4+H_2(CHCl_3)\rightarrow MC+HCl+H_2O$	191		(5—80 min)			
	reduction or interaction of other compounds	$K_2O{\cdot}MO+C\rightarrow MC+K_2CO_3$	192	not stated	not stated	CO	—	195
		$MS_2+C\rightarrow MC+CS_2$	193, 194					
		$MO{\cdot}SiO_2+C\rightarrow MC+SiC+CO$	195					
Silicides	reduction of oxides by non-metals	$MO+Si\rightarrow MSi+SiO$	60, 196	1350—1600	30—60 min	vacuum	pelleted at 1-1.5 ton cm^{-2}	60
	reduction of oxides by cpds. of non-metals with C and other elements	$MO+SiC\rightarrow MSi+CO$	197	~2000—3000	5—6 h	air, CO	—	197
		$MO+SiO_2+C\rightarrow MSi+CO$	198	1600—1900—2200	5—10—60 min	air, CO	pelleted at 800 kg cm^{-2}	198
	reduction or interaction of other compounds	$K_2MF_n+Si\rightarrow MSi+KF+SiF_4$	48					
		$MH+Si\rightarrow MSi+H_2$	199					
		$MO{\cdot}SiO_2+C\rightarrow MSi+MC+CO$	195, 200	see above conditions for carbides				195
Nitrides	reduction of oxides by non-metals	$MO+N_2+C(H_2)\rightarrow MN+CO(H_2O, CN)$	201—204	1200—1300	2—3 h	N_2, CO, H_2	—	203
				1200—1250	3 h	N_2, N_2+H_2	rise in temp. for 3 h	204
	reduction of oxides by cpds. of non-metals with C and other elements	$MO+NH_3\rightarrow MN+H_2O$	130, 204, 205	1200—1300—800	not stated	NH_3	—	130
				1250—1350	3 h	NH_3	1150° for 1 h rise in temp. for 3 h	204
	reduction or interaction of other compounds	$NH_4MO_n+NH_3\rightarrow MN+H_2O(H_2)$	206	125—1000—1100	4—8 h	NH_3	—	206
		$MCl_n{\cdot}nNH_3\rightarrow MN+HCl$ и др.	207 and 208, 209					

reactions). The reactants and products may be in different states of aggregation, but are predominantly in the solid phase.

Several specific processes may be encountered depending on the reactants used in this method. The chief characteristics of the most important processes are listed in Table 5.[12,16,47,48,55,57,60,130,181-209].

This method was first applied by Johnston in 1831,[210] when silicides were obtained by reducing oxides by non-metals. These products were prepared later also by Moissan[211]. Carbides[38,212,213], nitrides[201,202], and borides[181,184,214] have since been obtained by this process. Reduction of oxides by compounds of the non-metals with carbon and other elements was first applied to the preparation of nitrides[205], and then of silicides[1,215], borides[216,217], and carbides[190,191,218]. The process of reduction or reaction of other compounds was employed initially to obtain nitrides[203,204,207-209,219-222], and then carbides[192,213], silicides[48,199,200], and borides[55,223,224]. Credit for developing the above processes is due to many workers. Thus the reduction of metal oxides was developed initially for nitrides[203,204] and carbides[47,57], and later for silicides[60,196] and borides[182,183,185-187]. The reduction of oxides by compounds of non-metals with carbon and other elements was also elaborated for the above classes of compounds—silicides[197,198], nitrides[130,204], carbides[191], and borides[188,189]. All these classes of compounds have been obtained also by developing the reduction or reaction of other compounds—borides[55] carbides[195,225], silicides[195], and nitrides[209,226].

Industrial application. (1) Reduction of oxides by non-metals applicable to the preparation of borides[227-230], carbides[231-233], silicides[234,235], and nitrides[8-14]; (2) reduction of oxides by compounds of non-metals with carbon and other elements applicable to the preparation of borides[12,13,189,227,236] and nitrides[8,10,12,14,237,238], and promising for carbides[191,239] and silicides[197,198]; (3) reduction or interaction of other compounds promising for the production of all classes of refractory compounds, especially for carbides[225,240,241], silicides[195,200], and nitrides[206,226].

Growth of single crystals. The method has not been applied and is not applicable owing to the solid-phase mechanism of the formation of borides, carbides, and silicides, However, it is theoretically possible to obtain crystalline powders of these compounds[242].

Advantages. (1) Possibility of obtaining large quantities of refractory compounds; (2) use of oxides and other readily available compounds of metals and non-metals for the preparation[243-252].

Disadvantages. (1) Contamination of products by metal and non-metal oxides and also by other compounds; (2) impossibility of preparing molybdenum and tungsten compounds in a vacuum owing to the volatility of their oxides.

Development and use prospects. Improvement of individual stages of the preparation in actual processes and their variants, e.g. for borides[253,254], carbides[231,255], silicides[235,256], and nitrides[257]; possibility of obtaining new materials[258-260].

Borides, carbides, nitrides, and silicides can be obtained by this method. Oxides are prepared only by the decomposition or interaction of complex compounds[261-273], when oxide coatings can be produced[274].

The availability and cheapness of the initial components make this method, together with direct synthesis from the elements, the most widely used and generally applicable in industry[88,227,231,275].

Further development of the method will be concerned mainly with improving the technical conditions in each process or with modifying the processes to yield products of higher quality, as has been done e.g. in the preparation of borides by reducing oxides with non-metals [276].

VIII. GAS-PHASE PREPARATION

This method consists essentially in the decomposition of chemical compounds followed by interaction of their constituent parts in the gaseous (vapour) state (both the ions and radicals and the atoms and molecules to which they are reduced) to form the refractory compounds. Preparation is possible also by the decomposition of one compound containing either one or both components of the reaction. In the former case the second component (this applies more to metals than to non-metals) should be present in the reaction volume in the elementary state, usually in the solid phase. In all cases a reducing atmosphere is necessary in the apparatus, for both the reduction and the removal of pyrolysis products. The general process can be represented

$$MHal_n\,[M, M(NmEl)_n, M(C_xH_yO_z)_n] + NmHal_n\,(Nm, NmEl) + H_2 \rightarrow$$
$$\rightarrow MNm_{G,S} + HHal\ (+ NmEl, C_xH_yO_z)$$

where Hal = F, Cl, Br, I; NmEl = CO, and also CO_2, NH_3, hydrocarbons, etc.; and $C_XH_yO_Z$ is a carbohydrate.

Gas-phase formation consists of a series of mainly ionic and atomic (molecular) reactions in the gas phase, although in individual cases (when one component is present in the solid phase) the reaction may have a topochemical mechanism.

The main characteristics of the gas-phase method for borides, carbides, silicides, nitrides, and oxides are listed in Table 6, [218,277-288] which shows that all the classes of refractory compounds under consideration can be prepared by this method.

The gas-phase method was first used to obtain silicides [277,282,283], and other classes of compounds—carbides [218,278,280-282], nitrides [278,281,282], borides [277,278], and oxides [278]—were obtained later. Campbell, Powell, et al. [279] must be regarded as the first workers to develop the method for all classes of compounds. It may be remarked merely that an attempt to develop this method for the preparation of borides was made somewhat earlier [289]. The necessary conditions for the deposition of refractory compounds from the gas phase can be formulated from the results in Ref. 290.

Industrial application. The method is used, and is promising for borides [291], carbides [290,292-297], silicides [298-303], nitrides [304], and oxides [305-316].

Growth of single crystals. Used for borides [317], carbides [318], silicides [319], nitrides [320], and oxides [321,322].

Advantages. (1) Possibility of obtaining single crystals; (2) possibility of obtaining coatings (including multicomponent coatings) on various materials; (3) possibility of relatively easy study of the kinetics of gas-transport reactions [323,324], etc. and the mechanism of the growth of single crystals.

Disadvantages. (1) Non-uniform phase composition of products; (2) complexity of apparatus and processes involved; (3) difficulty of obtaining large quantities of single-phase products.

Development and use prospects. (1) Possibility of obtaining especially pure and alloyed single crystals [325]; (2) possibility of obtaining articles having a complicated shape [326] and also articles from monocrystalline deposits; (3) development of continuous processes of preparation.

The gas-phase method, together with the reduction of metal oxides, is now undergoing very vigorous development. Most studies of these classes of compounds have been devoted to oxides, with very close attention paid to the production of pigment titanium oxide (Refs. 327–338 and many others).

The possibility of obtaining single crystals and finished articles (with the prospect of articles from monocrystalline deposits) of borides, carbides, nitrides, silicides, and oxides makes this method one of the most promising

Table 6. Gas-phase preparation.

Compounds	Gas mixture or decomposable cpds.*	Ref.	Synthetic reaction	Ref.	Conditions of preparation				Ref.
					t, °C	time	rate of deposition	v.p. of mixture components	
Borides	$MHal_n(M) + BHal_3(B) + H_2$	277—279	$MCl_n(M)+BCl_3+H_2\rightarrow MB+$ $+HCl$	279	900—2700	a few min to a few h depending on thickness of deposited layer	7.5-65 $\mu m\ min^{-1}$	total = 1 atm provided that v.p. MHal > NmEl (El)	278, 279
Carbides	$MHal_n(M, M(CO)_n)+$ $+C_xH_y(CHal_4, CO, C)+$ $+H_2+(N_2)$	218, 278—282	$MCl_n(M)+C_xH_y+H_2\rightarrow$ $\rightarrow MC+HCl+(CH)$	279					
			$M(CO)_n+H_2\rightarrow MC+$ $+(C, H, O)$	279	450—2900	as with borides			278, 279
Silicides	$M(MHal_n) + SiHal_4(Si) + H_2$	279, 283, 284	$M(MCl_n)+SiCl_4+H_2\rightarrow$ $\rightarrow MSi+HCl$	279	1100—1800	ditto			278, 279
Nitrides	$MHal_n(M)+N_2(NH_3)+H_2$	278, 279, 281, 285	$MCl_n(M)+N_2+H_2\rightarrow MN+$ $+HCl$	279	1000—2700	ditto			278, 279
Oxides	$MHal_n(M)+CO_2+H_2$; CO_2+ $+[C_6H_7O_2]_nM([C_xH_yO_z]_nM)$ $M(OH)$; $M(OH)El$; $MOCl$	279	$MCl_n+CO_2+H_2\rightarrow MO+$ $+CO+HCl$	279					
		286—288	$[C_5H_7O_2]_3Cr+CO_2\rightarrow$ $\rightarrow Cr_2O_3+(C, H, O)$	279	800—1000	ditto			278, 279

*Hal usually Cl, more rarely Br; El = element.

for use in industry, especially when pyrolysis and synthesis are conducted in plasma systems. The main problems involved in developing this method will consist in working out very precise conditions for the deposition of individual refractory compounds, their various modifications, solid solutions, and mixtures.

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Comparison of the above methods for the production of refractory compounds shows that synthesis from solutions in melts, electrolysis, and the metallothermic reduction of oxides are the least developed. Nevertheless, they show considerable promise. Thus the metallothermic reduction of oxides is the most rapid method, not only requiring no external supply of energy but even evolving considerable amounts of energy, which can be utilised technically to produce large quantities of refractory compounds by this method. Preparation from solutions in melts at ultrahigh pressures may reveal several new modifications of such compounds, possessing valuable new properties. The electrolysis of melts and solutions in melts enables pure products to be obtained from greatly contaminated starting materials. These last two methods, together with the gas-phase method, can be used for continuous preparation (with a cyclic process). Furthermore, they enable uniform protective coatings to be applied to articles of complicated shape made of metals and various materials, for which purpose direct synthesis from the elements is considerably less suitable. Finally, these methods—especially formation from molten solutions and in the gas phase—are promising for growing single crystals of refractory compounds, being irreplaceable, as already mentioned, when the latter melt incongruently. Apart from this, single crystals grown by these methods may differ considerably in their physicochemical properties from similar single crystals pulled from the melt: the former possess faces of natural (spontaneous) growth, whereas the faces of the latter are formed under the influence of various seeds and other factors. The fine point still remains to be settled of how greatly such processes influence the difference in surface and bulk physicochemical properties of single crystals of the compounds. The small size of the crystals when grown from solutions in melts may also be significant here: the tendency to miniaturisation in instrumentation and technology makes the use of such single crystals considerably more advantageous and convenient than larger crystals obtained from their own melts, which require appropriate machining [339].

From the above considerations we may conclude that at the present time the main lines of development of methods for the production of refractory compounds are the following.

1. Further investigation of metal–non-metal systems [340-347] in order to complete the development of one [276] or a combination of several already known processes and methods [165,166,228].

2. A considerable expansion of research on preparation from solutions in melts [117,134,139,140,348] and the electrolysis of solutions in melts [148-150,162,163].

3. Preparation by the thermal decomposition of chemical compounds, including organoelementary compounds [258,259,265,349-351].

4. The development of fundamentally new processes [352,353] and the production of new forms and modifications of the compounds [100,150,260,354,355].

5. Direct production from ores [90-92,275,356] and initial components of technical purity [88,179,357], and the development of continuous processes [350] with the aim of intensifying and cheapening production.

6. Vigorous development of work on production in plasma installations having high output and offering great opportunities for the development and application of synthetic processes [104,105,357-367].

7. Broad and intense research on the production of single crystals [127,317,319,321,368-377].

In conclusion it should be noted that several major problems—such as the production of compounds of high purity throughout their ranges of homogeneity, and also the growth of especially pure and alloyed single crystals—remain to be solved in the preparation of refractory compounds of transition metals.

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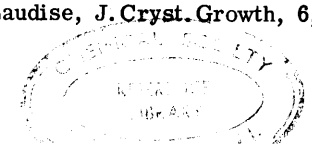

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The Principle of Hard and Soft Acids and Bases and the Problem of Competitive Coordination in Complex Compounds

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A systematic and general account is given of data on the location of the coordinate bond in systems with several potential electron-donating centres (competitive coordination). The problem is examined from the standpoint of the principle of hard and soft acids and bases.
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I. INTRODUCTION

The principle of hard and soft acids and bases (HSAB), put forward by Pearson[1] in 1963 has been recently widely adopted in chemistry not only as a result of the author's own efforts[2-6] but also due to the publication of monographs[5,7-9], reviews[10-16], and original papers[17-25] in which certain problems of inorganic, organic, and coordination chemistry as well as the chemistry of organic derivatives of the elements have been discussed from the standpoint of hard and soft acids and bases.

The HSAB principle is based on three fundamental postulates: (I) the majority of chemical reactions may be regarded as of the acid–base type[1-6] and compounds can be treated as complexes of Lewis acids and bases[4]; (2) all acids (A) and bases (B) can be classified as hard (H), soft (S), and intermediate (I);[1-6,11] (3) acid–base reactions take place in such a way that hard acids (HA) are preferentially coordinated to hard bases (HB) and soft acids (SA) are preferentially coordinated to soft bases (SB).[1,4,5] The reactivities of the intermediate acids (IA) and bases (IB) require a specific consideration.

The above postulates, combined in the HSAB principle, are not new to chemists, since (1) the possibility of assigning chemical reactions to the acid–base category follows directly from the Usanovich theory[26], as rightly pointed out by Yatsimirskii[13], Day and Selbin[27], Evans[18], and Denes[28]; (2) the classification of acids which follows from the HSAB principle is identical with the classification of metal ions into classes A and B (Schwarzenbach[29]) or a and b (Ahrland, Chatt, and Davies[30]), as was emphasised by Pearson himself[4,5] and also in monographs[31,32] and reviews[10,33]; an approach to the estimation of softness and hardness of bases was suggested by Schwarzenbach[34,35]; (3) the preferential coordination of hard acids to hard bases and of soft acids to soft bases has long been known to chemists as the postulate of the predominance of electrostatic or covalent interaction in individual acid–base reactions (including donor–acceptor reactions[13]). This fact, which follows from classical polarisation concepts of coordination chemistry, has been pointed out in monographs[36-38] and original papers[13,39]. Here it is interesting to note that in his paper published in 1962, Hudson[40] states directly that polarisable ions tend to react at polarising centres, while non-polarisable ions react at charged non-polarising centres".

Nevertheless, these postulates, which are familiar and comprehensible to chemists and which have been tested on numerous examples[1-25,30-38,41], have been frequently disregarded and have not yet been considered in the discussion of many general and specific problems of organic, inorganic, and coordination chemistry as well as in the chemistry of organometallic compounds.

In this connection the undoubted usefulness of the HSAB principle in individual correlations and the general correlation of a large number of experimental facts concerning primarily the stability and reactivity of inorganic, organic, and coordination compounds and organometallic compounds must be recognised. This is confirmed by the finding that the formulation of the HSAB principle[1,2] and its vigorous propagation[3-7] stimulated the consideration of problems of the stability of coordination[5-7,13] and organic[4,6,14-16] compounds and their reactivity[4,8,14,17,24], the problem of electronegativity[18,19], and also the consideration of the nature of the attacking agent in quantum-chemical estimations of reactivity[20].

In the present review an attempt is made to apply the HSAB principle in the discussion of the problem of the location of the coordinate bond in the chemistry of coordination compounds. The enormous amount of experimental data accumulated on this problem has already been the subject of some discussion[7,12,24,25,33,42], but this has been unduly narrow[12,42] or insufficiently objective[33].

Among the very large amount of data published on this question, we have considered mainly those of the last five years.

II. THE FUNDAMENTAL CONCEPTS OF THE PRINCIPLE OF HARD AND SOFT ACIDS AND BASES

Using the criteria of hardness and softness, Pearson compiled Tables classifying acids and bases[1-6]. Despite the wide range of acids and bases covered and the satisfactory treatment of the preferred paths for reactions, Pearson's classification is in many ways arbitrary and in many cases cannot be used to account for the reactivity of coordination and organic compounds as well as organic derivatives of the elements.

The stability series of complexes with electron-donating atoms found on the basis of the existing classifications[4,29,30]:

$$\text{hard}\begin{cases}N \gg P > As > Sb\\ O \gg S > Se > Te\\ F \gg Cl > Br > I\end{cases}\qquad \text{and soft}\begin{cases}N \ll P < As < Sb\\ O \ll S \sim Se \sim Te\\ F < Cl < Br < I\end{cases}$$

are valid only when one disregards electronic and steric factors in molecules[14], which may alter significantly the "softness" and "hardness" of both an acid and a base. This has been frequently pointed out[7,10,31,32] in the assessment of the stability series of complexes using the classification of Ahrland, Chatt, and Davies[30]; these remarks are undoubtedly valid also for Pearson's classification Tables. When estimating "hardness" and "softness" of acids and bases, it is particularly important to take into account electronic and symbiotic effects[4,7,43], which may result in the "transfer" of an acid or base, particularly those of intermediate types, from one category to another (SA–IA–HA or SB–IB–AB). Numerous data useful in understanding the arbitrary nature of this type of classification in organic chemistry are given in a paper by Nesmeyanov and Kabachnik[41], in the reviews of Gompper[44] and Shevelev[14], and in Sokolov's papers[24,45] or organic derivatives of the elements.

In estimations of "hardness" and "softness", an important role must be attributed to specific reaction conditions and the effect of the solvent[4,14,40]. We believe that in this respect the "hardness" of the proton and "softness" of the methyl cation (CH_3^+) are particularly instructive. The entire data quoted by Pearson[4] appear to be consistent with his conclusion that the methyl cation is "softer" than the proton. However, data on the affinities of the proton and the methyl cation for various bases in the gas phase suggest that they are equally "hard".[13]

Thus Pearson's classification as well as earlier classifications (Chatt, Schwarzenbach)[29,30] are very approximate and should be used with a certain amount of caution.

Classifications of acids and bases according to Yatsimirskii[13].

No.	Groups	Acids	Bases
1	Ionic	Cs^+, Rb^+, NH_4^+	BR_4^-
2	σ-Acceptor acids, σ-donor bases	H^+, CH_3^+, CR_3^+, BR_3	H^-, CH_3^-, NR_3, NH_3
3	Strong σ-acceptors and donors; weak π-acceptors and donors	Li^+, Be^{2+}, Mg^{2+}, Al^{3+} Sc^{3+}, Zr^{4+}, Hf^{4+}	OH^-, H_2O, OR^- $RCOO^-$, XO_n^{2-}, F^-
4	Strong σ, π-acceptors; strong σ, π-donors	Tl^+, Pb^{2+}, Sn^{2+}, Bi^{3+} Ga^{3+}, In^{3+}, Tl^{3+}	Cl^-, Br^-, S^{2-} RS^-, R_2S
5	π-Acceptors; π-donors	Fe^{n+}, Co^{n+}, Ni^{2+}, Cu^{n+} Ag^+, Cd^{2+}, Pt^{II}, Pd^{2+}	—
6	π-Donors; π-acceptors	—	CO, CN^-, $C_5H_5^-$ CNS^-, R_3P

In this connection Yatsimirskii's classification, based on the assignment of acids and bases to different categories on the basis of the types of bonds formed by them, appears to be more correct[13].

Not being in a position to characterise in detail each of the groups quoted in the Table, we shall point out that groups 2 and 3 are hard (group 1 belongs to the category of acid–base reactions with electrostatic interaction[13,26]) and groups 4–6 combine soft acids and bases.

We see the advantages of Yatsimirskii's classification not only because of a more rigorous approach to the nature of acid–base interaction in its derivation but also because of the more correct distribution of cations and anions among different classes which follows from it. These considerations concern primarily the H^+, CH_3^+, and CR_3^+ hard cations which belong to one group, and the separate assignment of Al^{3+} and Sc^{3+} to hard cations (group 3) and of Ga^{3+} and In^{3+} to soft cations (group 4). It is shown below that in most cases the classification of all the cations included in group 5 as soft is justified. At the same time the assignment of quadrivalent zirconium and hafnium to hard cations (group 3) is not always justified and in this case account must be taken of the symbiotic effects of anions[4,7,43].

A quantum-chemical basis has been obtained for the HSAB principle[5,46,47] using the mathematical apparatus of the simple perturbation theory[48]. This approach is unduly narrow and suffers from many disadvantages[20,49]. However, such discussion is outside the scope of the present review.

III. THE LOCATION OF THE COORDINATE BOND IN SYSTEMS WITH SEVERAL ELECTRON-DONATING CENTRES: COMPETITIVE COORDINATION

In the discussion of the problem of competitive coordination, one must distinguish non-conjugated and conjugated systems. The first type includes saturated compounds (or compounds with isolated multiple bonds) where the reaction centres are separated from one another by at least one atom with a saturated valence. In compounds of the second type, the electron-donating centres are linked in a single mesomeric system (ambident compounds[50])†. From the theoretical standpoint, such division is based on the important difference between localised and delocalised orbitals.

1. Experimental Methods for Solving the Problem of Competitive Coordination

X-Ray diffraction analysis constitutes a direct and reliable method for the determination of the site where the coordinate bond is located and the complete elucidation of the structure of complexes. It has been frequently used to unravel molecular structures with different potential electron-donating centres: complexes of pseudohalides (NCX; X = O, S or Se),[12,51,52] urea,[33,53] thiourea,[54–56] dimethyl sulphoxide[57], morpholine[58], thiocarbazide[59,60], thioacetamide[61], and many other complexes[10,33]. However, the scope of X-ray diffraction analysis is limited owing to the amount of labour involved.

Most studies in this field have used spectroscopic methods, among which vibration spectroscopy has the greatest importance[62–74]. Its scope in coordination chemistry has been quite fully discussed in well known monographs[9,38,42,68,69] and therefore does not require special consideration. We shall only mention that, when infrared spectroscopy is employed, one must use considerable caution in those cases where the displacements of

†In their review, Norbury and Sinha[33] did not always consider the necessity for the conjugation of reaction centres in the definition of ambident ligands. Therefore, among the ambident compounds they consider, there are also non-conjugated systems, for example 1,4-oxathiane.

many ligand vibration frequencies during coordination interaction are used to draw conclusions as to the location of the bonds. The most accurate of such information has been obtained from calculations of molecular infrared spectroscopic data [69,70]. We believe that low-frequency infrared spectroscopy [71-74], whereby it is possible to determine directly the type of M–X bonds (X is an electron-donating atom), is promising in the study of the type of coordination [73].

Among other methods, mention should be made of electronic spectroscopy. Comparison of the theoretically predicted behaviour of a ligand in coordination to different electron-donating atoms with the experimental spectrum yields reliable evidence on the location of the bond. An instructive series of such studies have been carried out [75-79]. Other methods for using electronic spectroscopic data in the solution of the problem of competitive coordination are also known [33,78].

On further development of NMR spectroscopy, this method too will find wide application in this field of coordination chemistry. However, so far its use is limited (see for example, Refs. 17, 62, 63, 71).

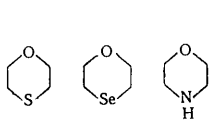
Modern quantum-chemical methods yield definite quantitative values for the electron distribution in molecules and therefore may be used to predict the direction of attack in systems with several electron-donating centres. Although so far few studies involving quantum-chemical calculations have been made in this field [12,52,80-84], they suggest that the coordinate bond is usually located at the electron-donating atom with the highest negative π-electron density.

In conclusion we may note that best results may be obtained by employing a combination of methods‡, including synthetic methods [75,80].

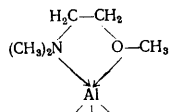
2. Non-conjugated Systems

The available literature data show that the location of the coordinate bond in non-conjugated systems in general obeys the requirements of the HSAB principle when account is taken of the hybrid state of the electron-donating atoms and of steric factors.

1,4-Oxathiane (I) and its selenium analogue (II) are perhaps the most successful models for the consideration of competitive coordination from the standpoint of the HSAB principle:



(I) (II) (III)



(IV)

Compounds (I) and (II) contain atoms, isolated from one another, belonging to the same group of the Periodic System, so that, according to the HSAB principle, in their interaction with hard acids, the coordinate bond should be preferentially located at the oxygen atom (hard centre) and in the interaction with soft acids, at the sulphur [compound (I)] or selenium [compound (II)] atom (soft electron-donating atoms). Experiments have confirmed these considerations.

‡The application of Mössbauer spectroscopy in this field is also promising [64,85].

The possibility of different sites of location of the coordinate bond (at oxygen or sulphur atoms) involving oxathiane was first formulated by Hendra and Powell [86], who established that in complexes with $CuCl_2$, $HgCl_2$, and $PtCl_2$, 1,4-oxathiane behaves as a monodentate ligand (only one of the electron-donating atoms is involved in coordination interaction). Subsequently it was shown in a series of studies [17,87-93] that the hard acids AlX_3 (X = Cl or Br)§ and BF_3 combine with the hard nucleophilic centre (oxygen) while the softer transition metal halides in the highest state of oxidation¶ combine with the soft sulphur and selenium atoms.

Platinum, palladium, rhodium [93], and mercury [92,94] salts also combine with the sulphur atom of compound (I). The above studies were carried out mainly by infrared and NMR spectroscopic methods [62,87-93] and the reliability of the conclusions may be open to certain objections because the vibration frequencies of the C–X–C linkages (X = O, S, or Se), on whose behaviour in coordination interactions the principle conclusions are based, are relatively non-characteristic. The work of McEwen and Sinn [94], where the coordination of mercury and sulphur atoms was demonstrated by an X-ray diffraction study of the $HgCl_2.I_2$ complex, is superior in this respect.

Morpholine (III) contains identically hybridised oxygen and nitrogen atoms, the first of which, being more electronegative [95], is therefore harder than amino-nitrogen. In this case too the location of the coordinate bond agrees with conclusions based on the HSAB theory: soft (AgI) [58] and intermediate (salts of many bivalent [96,97] and tervalent [98] metals) acids combine with the nitrogen atom. Only in the case of $Al(CH_3)_3$ is it possible to obtain a complex with the composition $2Al(CH_3)_3$.(III) where both centres are involved in the coordination interaction [99]. Probably the coordinate bond involves the oxygen atom also in the platinum complexes of morpholine [100]. Identically hybridised oxygen and nitrogen atoms are present also in α-dimethylamino-β-methoxyethane which forms a cyclic structure (IV) with $Al(CH_3)_3$. [101] However, in this case it is difficult to assess the competitive interaction of oxygen and nitrogen atoms owing to both the limited selection of acceptors and to the energy gain usually observed on formation of cyclic structures of type (IV). The latter factor must be always considered in the study of the competitive coordination of ligands the electron donating centres of which may be involved in the formation of metal-containing rings.

This approach appears to be particularly useful in studies of the possibility of the coordination of acids and their esters. These compounds are convenient models for a comparison of the coordination capacities of the sp^3-hybridised nitrogen atom (amino-group) and the oxygen atom (amino-group) and the oxygen atom in the sp^2-hybrid state (the carbonyl group). On the basis of the foregoing considerations, amino-nitrogen may be regarded as a softer electron-donating centre than the carbonyl oxygen.

§In the review of Norbury and Sinha [33], the halides AlX_3 are erroneously included in the group of acids combining with the sulphur atom of oxathiane.

¶The softness of cations of this kind is associated not only with the highest degree of oxidation of the metal but also with the symbiotic effect of the X anion. In particular $TiCl_4$ forms more stable complexes with dialkyl sulphides than with ethers [88], i.e. is a soft acid according to the HSAB classification.

This idea is confirmed by the finding that in complexes of α- and γ-amino-acids (AH) of the type $[(AH)_2Pt(NH_3)_2]Cl_2$ as well as in the glycine complexes $(GlH)-Pt(GlH)_2Cl_2$, the soft acid $PtCl_2$ is linked to the amino-nitrogen [102,103]. Similarly α-aminoacid esters may react with salts of comparatively soft bivalent metals as monodentate ligands with preferential formation of an M–N bond (only with methyl-L-tryptophan is coordination involving the C=O group observed) [104]. However, in most cases [105–107] amino-acids behave as bidentate ligands and form cyclic chelate compounds.

Similar cyclic structures arise in the coordination interaction of thio- and seleno-semicarbazides [108,109] with metal salts, although there is evidence that comparatively soft acids combine preferentially with the softer sulphur and selenium atoms [110,111]†.

Aminonitriles with the general formula $R_2N(CH_2)_nCN$ have two electron-donating centres: sp^3- and sp-hybridised nitrogen atoms. If one bears in mind that the electronegativity, which in many ways determines the hardness of nucleophilic agents [4], increases with the amount of s-character in the hybrid orbitals of the nitrogen atoms [95,112], one must assume that the nitrogen atom of the nitrile group is a harder donor than the amino-nitrogen. Therefore, in agreement with the HSAB principle, only may assume that hard acids will combine preferentially with the hard nitrile nitrogen and soft acids with the amino-nitrogen. Experimental data agree with these considerations. In the case of hard BCl_3, an increase of the vibration frequencies of the nitrile group in the aminonitrile with $R = C_2H_5$ and $n = 1$ is observed [113], showing that the coordinate bond involves the nitrile nitrogen [114–116]. The comparatively soft MX_4 (M = Sn, Ti, or Zr; X = Cl or Br) form complexes without involving the nitrile group [113]. However, with $n = 2$ or 3, the MX_4 also form cyclic structures and both electron-donating nitrogen atoms of the aminonitrile are involved in the coordination interaction [112].

Not only individual atoms but also the π bonds of unsaturated hydrocarbons can behave as soft electron-donating centres. Electron-donating systems of this kind include allylamines [117–120] and aminoallene and aminoacetylene hydrocarbons [121].

Depending on the reaction conditions, allylamine can behave as a monodentate or a bidentate ligand. As expected, in the first case $PtCl_2$ combines with the π bond of the ethylene group [119], which is a softer centre, and in the second case it combines with both electron-donating centres, forming dimeric bridge structures [117,118] or monomeric cyclic structures [119,120]. The latter are characteristic also of complexes of bivalent nickel, cobalt, manganese, copper, iron, zinc, and cadmium and tervalent iron, chromium, cerium, and praseodymium with aminoallene, aminoethylene, and aminoacetylene ligands [121].

3. Systems with Conjugated Bonds (Ambident Ligands)

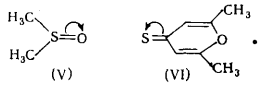
Examination of competitive coordination in compounds with conjugated electron-donating centres is very important not only because of the great range (mentioned above) of the reactivities of ambident systems but also because it deals with the salt [122] or structural [123] isomerism, which is extremely important for coordination symmetry‡.

From the standpoint of the HSAB principle, the problem of the location of the coordinate bond in conjugated systems with several electron-donating centres is of special interest, since nucleophilic atoms in ambident compounds become harder or softer, mainly under the influence of electronic effects, than in the isolated ligands or in the non-conjugated systems discussed above.

a. Ambident Ligands with Electron-donating Atoms of Elements in the Same Periodic Group

Oxygen and sulphur (selenium) atoms. In conjugated systems containing the hard oxygen atoms and the soft sulphur and selenium atoms, the position of the coordinate bond is generally consistent with the requirements of the HSAB concept: typical [1,25] soft acids (Pt, Pd, Rh, Hg) form a bond with the sulphur and selenium atoms, while harder acids (Al, Th) combine with the oxygen atom [10,33]. However, with intermediate acids (salts of bivalent metals, metal carbonyls), the oxygen atom is preferentially involved in the formation of the coordinate bond [33], although a bond with the sulphur atom is also observed. Thus not only iridium [126,127], palladium [128], platinum [129], and rhodium [130], but also cobalt [28,131] forms bonds with the sulphur atom of the sulphite anion. A bond with the sulphur atom is formed by the majority of metals [33,132,133] and their carbonyls [134] in complexes with sulphur dioxide and also sulphones and sulphonyl chlorides [33]. On the other hand, the hard $AlCl_3$ forms with the ligands of the last type complexes involving Al–O bonds [135].

There is a particularly large amount of data concerning the location of the coordinate bond in sulphoxide complexes. Intermediate and hard cations [10,28,136–143], organometallic derivatives [144–147], and even metal carbonyls [148] combine with the oxygen atom of dimethyl sulphoxide (DMSO) (V). However, in accordance with the HSAB principle, soft acids are coordinated via the sulphur atom [33,149–156]. The conclusions reached concerning the mode of coordination of DMSO give rise to no doubts not only owing to the reliability of the assignment of the S=O frequencies [68] but also because the conclusions were in many cases based on X-ray diffraction data [144,157–159]. Complexes with M–O bonds only have been described for dimethyl selenoxide [10,33]:



(V) (VI)

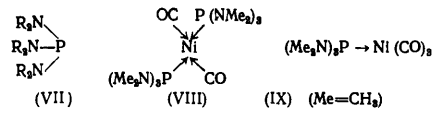
The different coordination behaviour of sulphoxides (compared with oxathiane and oxaselenane discussed in the preceding section) can probably be accounted for by a mesomeric effect which increases the "softness" of the oxygen atom. A similar effect may be observed for the sulphur atom in 2,6-dimethyl-4-thiopyrone (VI), for which M–S bonds have been described [160].

Nitrogen and phosphorus atoms. Tri-(*NN*-dialkylamino)phosphines (VII)—ambident systems containing tervalent electron-donating nitrogen and phosphorus

†It was stated in this study that the mode of coordination of thiosemicarbazide depends on the assignment of the metals to the Chatt classes a and b.

‡Recently this type of isomerism has been referred to as linkage isomerism in non-Soviet literature [5,124]; in Soviet coordination chemistry this concept is given a different significance [125].

atoms—are extremely sensitive to the "hardness" and "softness" of acids:



(VII) (VIII) (IX) (Me=CH_3)

The soft HgI_2, CdI_2,[161] and BH_3 [162,163] form adducts with aminophosphines which involve an M–P bond, while the harder BR_3, BCl_3, BF_3,[163] and PCl_3 [164] attack the nitrogen atom and dissociate the P–N bond:

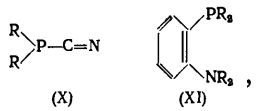
$$(NMe_2)_3P \rightarrow BH_3 \xleftarrow{(BH_3)_2} P(NMe_2)_3 \xrightarrow{BX_3(X=F,Cl)} Me_2NBX_2 + PX_3 .$$

Molecular complexes involving the "soft" phosphorus atom are also formed[161] when aminophosphines react with $Ni(CO_4)$ (VIII, IX). The soft diborane also adds to the phosphorus atom in *N*-diphenylphosphinotriphenylphosphazenes[165]:

$$(C_6H_5)_3P{=}N{-}P(C_6H_5)_2 + (BH_3)_2 \rightarrow (C_6H_5)_3P{=}N{-}\overset{\overset{C_6H_5}{|}}{P}{:}BH_3 + BH_3 .$$
$$\underset{C_6H_5}{|}$$

The coordination interaction of AlX_3 (X = H, Cl, or Br) with phosphorus(III) cyanides (X) probably involves the phosphorus atom[166].

Dialkyl-(*o*-dialkylphosphinophenyl)amines (XI) are interesting ambident systems[167]:



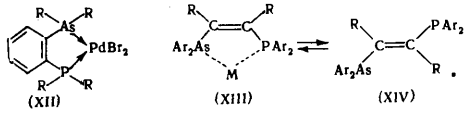
(X) (XI)

where R = alkyl or aryl. However, the formation of complexes by ligands of this type has not so far been investigated.

Here we may mention the exceptionally high electron-donating activity shown by tervalent phosphorus in ambident systems containing phosphorus and nitrogen atoms when interacting with halogens[165,168] oxygen, sulphur, selenium, tellurium[165], and other substances[165,170,171].

Quinquevalent phosphorus has almost no electron-donating properties and its derivatives are fairly active electron-acceptors[169,172]. Thus PF_5 is a stronger Lewis acid than BF_3—one of the hardest acids[173]. In agreement with this finding, ambident systems containing quinquevalent phosphorus and nitrogen behave as monodentate ligands, which form on coordination interaction complexes with exclusively M–N bonds. The complexes of phosphazenes are similar coordination compounds[174].

Phosphorus and arsenic atoms. Dialkyl-(*o*-dialkylphosphinophenyl)arsines are ambident systems containing electron-donating phosphorus and arsenic atoms, which form cyclic structures (XII) with the soft $PdBr_2$:[175]



(XII) (XIII) (XIV)

Probably metal-containing rings of this kind should be characteristic also of the *cis*-isomers of ethylene derivatives (XIII),[176] but, when the electron-donating centres in the ambident system (XIV) are in the *trans*-positions and for the *meta*- and *para*-substituted derivatives of compound (XII), it is very likely that the reaction will take place separately at the phosphorus and arsenic atoms[177]. Preferential coordination should be even more characteristic of analogous derivatives with nitrogen and phosphorus atoms and particularly of those with nitrogen and arsenic atoms[177].

b. Conjugated Systems with Electron-donating Atoms (of Group V and VI Elements)

Nitrogen and oxygen (sulphur, selenium) atoms. The simplest ambident systems containing nitrogen and oxygen systems are NO and NO_2 groups.

Nitrosyl complexes involve exclusively bonds with the nitrogen atom[33,38]. This conclusion was initially based mainly on infrared spectroscopic data and was recently confirmed for a series of complexes by X-ray diffraction studies[33,178].

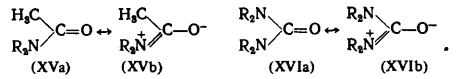
For the nitrite ion, in the study of the complexes of which salt isomerism[33,36,180] was discovered[179], two types of complexes are known: nitro-complexes in which the metal is linked to the nitrogen atom and nitrito-complexes in which a bond with the oxygen atom is formed (in the latter case cyclic structures are also possible)[33]. The majority of hard and soft metals form nitro-complexes and only a few very unusual compounds $[Ni(NO_2)_2L_X]_2$, $K_3Cu(NO_2)_5$, $K_4Ni(NO_2)_6$, etc. involve the formation of nitrito-complexes[28]. For both ions considered, the site of the coordinate bond is independent of the "hardness" or "softness" of the cations, being determined to a large extent by the ligand environment. Thus compounds of the type $ML_X(NO_2)_2$ (L = ammonia, ethylenediamine, pyridine, and its 2-amino-derivatives) are typical nitro-complexes, while 1,2-diphenylene-ethylenediamine is known to form also nitrito-complexes[33].

A similar situation arises also for cyanato-complexes[33,52]. It has been shown[52] that all the known cyanate complexes may be divided into four groups in terms of the mode of coordination of the NCO^- anion: in the first group NCO^- is coordinated via the nitrogen atom (isocyanates), in the second group via the oxygen atom (cyanates), the third group includes compounds with isocyanate bridges of the type $M\diagdown\!\!\diagup NCO$, and the fourth group includes compounds in which the NCO groups play the role of outer-sphere ions. The M–NCO structure has been observed for manganese(II), iron(II), cobalt(II), nickel(II), copper(II), zinc(II), cadmium(II), silver(I), lead(II), and indium(III) in compounds of the type $M(NCO)_n mL$ (L = pyridine, 2-aminopyridine, 2,2′- or 4,4′-dipyridyl, 1,10-phenanthroline, or urotropine). The same structure is characteristic of the typical soft platinum(II) and palladium(II) cations. The NCO group interacts via the nitrogen atom also with the "soft" mercury, silver, cadmium, and copper, but in this case bridge structures are formed (the third group).

The second group of compounds, involving the M–O bond includes only a few complexes with mercury(II), molybdenum(III), rhenium(IV), and rhenium(V). Preferential coordination via the nitrogen atom, which has been frequently demonstrated by systematic infrared spectroscopic[52,69,74] and X-ray diffraction[52] studies, agrees with the high π-electronic charge at the nitrogen atom of the cyanate anion[181–183].

A different picture is observed for the amides of monocarboxylic acids (XV), which behave mainly as

monodentate ligands with the coordinate bond located at the oxygen atom[33]:

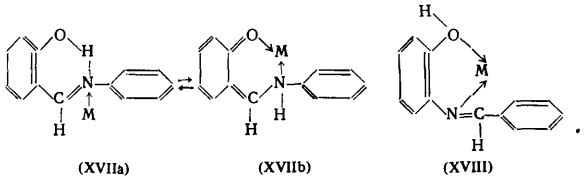


(XVa) (XVb) (XVIa) (XVIb)

Such coordination, which can be explained[184] by the enhanced electron density at the oxygen atom associated with the mesomeric effect of conjugation in (XVb), is characteristic of salts of Group I[185,186] and III–V[9,33,184,187-193] metals, the UO_2 cation[194-197], certain bivalent metals[198-203], and the soft platinum(II) and palladium(II)[33]. This type of coordination has been fairly convincingly demonstrated on the basis of infrared spectra (decrease of the stretching vibration frequencies of the amide bands[204]) and follows also from X-ray diffraction data[12,52] and NMR spectra[184]. The coordination interaction of MX_n with aminoacetophenone[205] and *NN*-dimethylamino-derivatives of unsaturated aromatic ketones[206] takes place similarly. At the same time in a few studies it has been suggested that complexes may be formed via the nitrogen atom[207], the N–M–O bridge linkage[33], and even via the hydrogen atom attached to the carbonyl carbon atom of dimethylformamide[208,209]. The above hypotheses and particularly the last one appear to be unlikely.

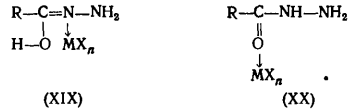
The possibility that the nitrogen and oxygen atoms of urea and its *N*-derivatives are involved in coordination interaction has been more rigorously demonstrated. It has become generally accepted[38,42,68] that, on coordination via the nitrogen atom, urea has the structure (XVIa) and the coordination via the oxygen atom is due to the mesomeric conjugation effect in (XVIb). It ought to be possible to apply successfully the HSAB principle to this compound in order to account for the location of the coordinate bond at the nitrogen atom in the complexes with the "soft" palladium and platinum[33] and at the oxygen atom in the complexes of "hard" acids[33,38,42,203,210-223]. However, the finding[224] that the "hard" BF_3 is coordinated at the nitrogen atom of *N*-alkyl(aryl)-substituted urea shows that in this case the HSAB concept should be employed with much caution§.

Among other ligands containing nitrogen and oxygen atoms, mention should be made of *p*-hydroxyazomethines (XVII, XVIII):



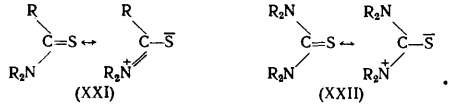
(XVIIa) (XVIIb) (XVIII)

For the complexes (XVIIa–XVIII) with MX_X (M = M^I, M^{II}, M^{III}, M^{IV}, or M^V; X = Cl, Br, or I), the formation of the quinonoid configuration (XVIIb), where the metal is linked to the oxygen and nitrogen atoms[235,236], is quite likely to occur, as well as structures in which the metal is bound to the nitrogen atom (XVIIa, XVIII).[225-234] The data obtained in the study of the structures of the complexes of transition metal, cadmium, and zinc halides with acetyl and benzoyl hydrazides are also consistent with the above considerations[237]. However, the "imidol" structure (XIX), rather than the hydrazide structure (XX), attributed in this case to the complexes requires additional proof:



(XIX) (XX)

In contrast to nitrogen- and oxygen-containing ligands, ambident systems with nitrogen and oxygen atoms enter into coordination interactions mainly in accordance with the HSAB principle. The behaviour of the thiocyanate anion is particularly instructive in this respect. The interaction of soft metals (platinum, palladium, silver, gold, and mercury) with this anion always results in the formation of a bond via the sulphur atom[5,12,33,52,68], while hard metals are linked to the hard nucleophilic centre—the nitrogen[12,33,52,238-242]. Such preferential coordination¶ via the nitrogen or sulphur atom in the thiocyanate ion has been rigorously demonstrated by infrared spectroscopic[12,28,69,243-245] and X-ray diffraction studies[12,33,52] and has been frequently discussed as a classical example of competitive coordination[12,33]. At the same time it is regarded as proven that, regardless of their "hardness" or "softness", metals react with thioamides[33,246,247] and thiourea[248-270] to form preferentially complexes with an M–S bond. Probably, as for amides and urea, the formation of structures with strongly polarised C=S bonds (XXI–XXII) leads to a reduced electrondensity at the nitrogen atom and makes it relatively inaccessible to coordination interaction:



(XXI) (XXII)

However, it has been suggested that "soft" acids [platinum(II) and palladium(II)] are linked to the nitrogen atom in *N*-methylthiourea[271] and intermediate acids ($TiCl_4$) are linked to the nitrogen atom in thiourea itself[272]. The possible involvement of the sulphur atom in thiourea in coordination interaction with the soft Ag^+ cation follows also from a potentiostatic study of complexes of the type $Ag^+[(NH_2)_2CS]_n$.[273] One cannot rule out the possibility that thiourea forms with soft metals (palladium, mercury) bridge structures in which nitrogen and sulphur atoms are simultaneously involved in coordination[274,275].

The site of the coordinate bond containing nitrogen and selenium atoms is also consistent with the HSAB principles: metals of class a (hard cations) prefer the hard nitrogen atom and those of class b (soft cations) prefer the soft electron-donating centre—the selenium atom[12,33,51,52,276].

As a result of many years of systematic study by Soviet chemists[12,51,52,276], the most complete data on the competitive coordination of nitrogen and selenium atoms have been obtained for the selenocyanate ion $NCSe^-$. The results yielded by infrared spectroscopic[52,69,276] and X-ray diffraction[12,52] methods make it possible to divide[276] selenocyanate complexes into three groups: ionic selenocyanates and complexes in which the metal is linked to the nitrogen or selenium atom. Ionic selenocyanates are formed by alkali metals, strontium, barium, and thallium:

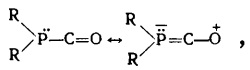
§The authors themselves[224] believe that the coordination of BF_3 at the nitrogen atom can be justified from the standpoint of the HSAB principle by its greater rigidity compared with the oxygen atom. However, this explanation conflicts with the coordination of the "soft" platinum(II) and palladium(II) via the nitrogen atom in urea[33].

¶One cannot exclude also the possibility of forming bridge structures in which the thiocyanate ion is linked to transition metal atoms via both electron-donating atoms[12,33].

complexes involving the selenium atom are characteristic of the soft cations of silver, gold, mercury, and the platinum metals [33,276]. The remaining metals form complexes via the nitrogen atom [12,33,276-283]. Cadmium, lead, and tervalent cobalt, which are capable of forming complexes both via the nitrogen and selenium atoms, may be regarded as an intermediate group of metals [74,276,281]. There is also a group of two-metal complexes in which the $NCSe^-$ anion behaves as a bridge [274,276]. The structure of these compounds also fits into the framework of the HSAB principle. Soft metals form a bond with selenium and hard and intermediate metals with the nitrogen atom. Thus in the complex $CoHg(SeCN)_4$ cobalt is linked to the nitrogen atom and mercury to selenium: the analogous lead derivative evidently has the same structure [276].

As was in fact to be expected, in complexes of selenourea and its *NN*-derivatives with soft metals, a linkage between the metal and selenium atom is formed [10,284,285]. This structure occurs also in mixed complexes of tervalent cobalt of the type $[Co(DM)_2Seu_2]X$ and $[Co(DM)_2(Seu)ThiO]X$, where DM = dimethylglyoxime, Seu = selenourea, ThiO = thiourea, and X = acid residue [221,286].

Phosphorus and oxygen (sulphur, selenium) atoms. As in the systems containing phosphorus and oxygen atoms, tervalent phosphorus exhibits a more pronounced electron-donating capacity than does the oxygen atom [170,171,287]. Thus the study of the infrared spectra of complexes of metal halides with the phosphides of monocarboxylic acids (XXIII) shows that, regardless of the "hardness" or "softness" of the acids, the coordinate bond involves the phosphorus atom (the stretching vibration frequencies of the C=O group increase) [287]:



(XXIII)

where R = alkyl, aryl, or arylalkyl.

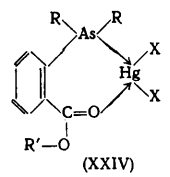
This result, which conflicts with the HSAB principle† might be explained by the conjugation of the carbonyl group with the *d* orbitals of phosphorus, which leads to the appearance of a negative charge at the phosphorus atom and a positive charge at the oxygen atom together with a decrease in the order of the C=O bond [288,289]. However, there are serious objections to such an explanation associated with the absence or an insignificant degree of p,π conjugation in systems with tervalent phosphorus [171].

In contrast to tervalent phosphorus, quinquevalent phosphorus has almost no electron-donating properties and in systems with $\rangle P{=}X$ (X = O, S, or Se) groups, the donor–acceptor interaction involves exclusively the X atoms. There are numerous literature data concerning the coordination interactions of metals with $POCl_3$, $PSCl_3$, and $R_3P = O$ which are quoted by Webster [172] and by Bridgland and McGregor [290] and for similar interactions involving $R_3P = Se$ by Nicpon and Meck [291].

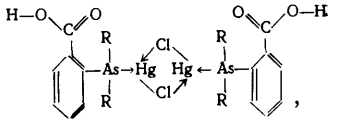
†Preferential coordination via the oxygen atom and not the phosphorus atom would be expected [1,4,16].

Arsenic and oxygen (sulphur) atoms. There are comparatively few data available for the discussion of the site of the coordinate bond in ambident systems containing tervalent arsenic and Group VI elements as electron-donating centres.

It has been shown that, in complexes of HgX_2 (X = Cl, Br, or I) with dialkyl(aryl)-2-carboxyphenylarsine and its derivatives, mercury is linked to the arsenic atom and the carbonyl oxygen [compound (XXIV)]: [292]



(XXIV)



(XXV)

where R = CH_3, C_6H_5, or C_7H_7 and R′ = H or CH_3 in compound (XXIV) and R = C_6H_5 in compound (XXV).

It has been suggested that 2-carboxyphenyldiphenylarsine forms a dimeric bridge structure in which the soft $HgCl_2$ is linked only to the soft electron-donating centre—the arsenic atom is (XXV). [292]

Like quinquevalent phosphorus, quinquevalent arsenic has no electron-donating properties and therefore in ligands of the type $R_3As = X$ (R = alkyl or aryl; X = O or S), the coordination interaction involves exclusively the X electron-donating atom [290,293-295]. This conclusion has been confirmed by studies on the complexes $R_3As{=}X \rightarrow MYn$ in the far infrared (the vibrations of the M–X bonds have been detected in the range 270 to 450 cm^{-1}). [296,297]

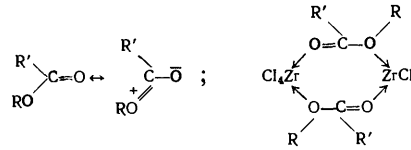
c. Ambident Systems with Identical Electron-donating Atoms

Analysis of the literature data shows that even for electron-donating atoms which are identical but subjected to different electronic and steric influences in the molecule, one may formulate the problem of competitive coordination. For such nucleophilic centres, the concepts of "hardness" and "softness" can probably retain their significance in the sense of a greater or smaller accessibility to coordination attack by electrophilic agents.

The postulate of an increased electron-donating capacity by nucleophilic atoms with increasing *p* character of the hybrid orbitals [298-300], which follows from Paulings' theory, would appear to predict an increase of preferential coordination in the following sequence of electron-donating atoms with different types of hybridisation: $sp < sp^2 < sp^3$. However, this postulate is probably valid only for isolated or non-conjugated systems. On the other hand, in ambident compounds the direction of coordination attack depends significantly on the distribution of electron density (the π-electronic densities at the nucleophilic centres), the degree of localisation of electrons at the electron-donating atoms, and steric factors.

Oxygen atoms. Numerous studies designed to establish the site of the coordinate bond in complexes of organic acids and esters with Lewis acids have shown that the oxygen of the carbonyl group is the electron-donating atom [9,16,38,42,68]. Regardless of the "hardness" or "softness" of the acids and the bulk and the electronic effect of the substituents (R and R′), the infrared spectra of the complexes (XXVI) always show a decrease of the stretching vibration frequency of the carbonyl group [301-309], which is

fairly convincing evidence [33,37] in favour of the reaction involving the carbonyl oxygen‡:

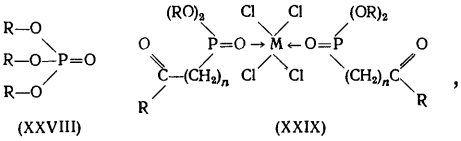


(XXVI)
R = alkyl or aryl;
R' = H, alkyl or aryl

(XXVII)
R=C_2H_5; R'=CH_3

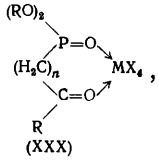
This direction of coordination attack (which contradicts Pauling's theory [311] can probably be accounted for by σ, π conjugation in compounds (XXVI), which leads to an increase in electron density at the carbonyl oxygen in esters compared with aldehydes or ketones and to a decreased capacity of the alkoxy-oxygen (the alcoholic oxygen) for participation in coordination interaction (compared with alcohols and ethers).

At the same time there is reason to suppose that not only carbonyl but also alkoxy-oxygen (alcoholic oxygen) of esters and organic acids may be involved in coordination interaction. In this case the non-planar dimers (XXVII) are formed in solution [312]. Evidently one cannot rule out the possibility of the formation in the condensed phase of coordination polymers involving the alkoxy- and carbonyl oxygen. Therefore, the conclusions concerning the site of the coordinate bond based solely on infrared spectroscopic data must be treated with caution. Dipole moments may prove very useful in solving this problem [313].



(XXVIII) (XXIX)

where M = Sn or Ti;



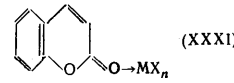
(XXX)

where M = Ti or Sn and X = Cl, Br, or I.

In alkyl phosphate complexes the coordinate bond is located solely at the oxygen of the phosphoryl group [compound (XXVIII)], [314-317] the electron-donating activity of which surpasses even that of the carbonyl group, since in complexes of α-ketophosphinic acids [318] and β-phosphonocarbonyl compounds [319] with the composition $MX_4.2L$ the coordination involves only the phosphoryl oxygen [compound (XXIX)]. On the other hand, in complexes with the composition $MX_4.L$, cyclic structures (XXX) are formed, the coordination interaction in which involves the carbonyl and phosphoryl but not the alkoxy-oxygen atoms, in agreement with the foregoing considerations [318,319].

‡In this connection one can hardly agree with the view of Pilipenko and Savranskii [301] that the carbonyl oxygen has a lower coordination capacity compared with the hydroxyl oxygen in the conjugated systems which they considered.

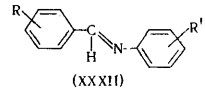
The formation of the complexes by the halides of Group III–V elements with the keto-derivatives (XXXI) involves the carbonyl oxygen [320]:



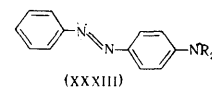
(XXXI)

where M = Ti, Sn, Zr, In, Ga, or Nb, X = Cl, Br, or I, and n = 3–5.

Nitrogen atoms. The azomethines (XXXII) and the azo-compounds (XXXIII) containing an amino- or a dimethylamino-group in the aromatic ring are suitable examples for discussing the problem of the site of the coordinate bond in ambident systems with sp^3- and sp^2-hybridised nitrogen atoms:



(XXXII)
a. R = p-$N(CH_3)_2$; R' = H
b. R = m-$N(CH_3)_2$; R' = H
c. R = H; R' = m-$N(CH_3)_2$
d. R = H; R' = p-$N(CH_3)_2$
e. R = R' = p-$N(CH_3)_2$

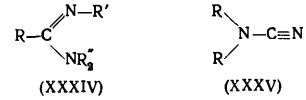


(XXXIII)
a. R = H
b. R = CH_3

It was established on the basis of infrared and ultraviolet spectra and quantum-chemical calculations that the formation of complexes by compound (XXXII) with the chlorides of Group IV and V elements involves the nitrogen atom of the azomethine group, which has the maximum π-electron density [80].

Only in compound (XXXIIc) is the electron-donating centre the amino-nitrogen [80], which forms also quaternary salts [75]. In view of the small difference between the ultraviolet spectra of the adducts of $CuCl_2$, $CoCl_2$, and $HgCl_2$ with 4-aminoazobenzene (XXXIII, R = H) and the spectrum of the initial azo-compound, one must assume that the coordinate bond in such compounds is located at the amino-nitrogen [67,76,77]. At the same time, BF_3, $SnCl_4$, and $SbCl_5$ form bonds preferentially with the nitrogen atom of the azo-group [77-79].

It has recently been shown that in the amidines (XXXIV) with sp^2- and sp^3-hybridised nitrogen atoms the coordinate bonds formed on interaction with $SnCl_4$ [321] and $B(n\text{-}C_3H_7)_3$ [322] is located at the nitrogen atom of the azomethine group:



(XXXIV) (XXXV)

where R = H, alkyl, or aryl and R' = R'' = aryl for compounds (XXXIV) and R = H or alkyl for compounds (XXXV).

Cyanamide and its *NN*-dialkylderivatives (XXXV) are the simplest ambident systems with sp^3- and sp-hybridised nitrogen atoms. On interaction with MX_4 (M = Sn, Ti, or Zn and X = Cl or Br), cyanamide itself behaves as a bidentate ligand, while its dialkyl derivatives are coordinated via the harder nitrogen atom of the nitrile group [323]. Probably in the case of sp^3- and sp-hybridised nitrogen atoms the direction of coordination attack is determined mainly by the negative π-electron densities§, although one

§The sp-hybridised nitrile nitrogen has a much higher negative π-electron charge density (−0.279) than that of the amino-nitrogen (−0.064). [324]

canot rule out the possibility that the bulky ethyl substituents prevent the location of the bond at the amino-nitrogen[325].

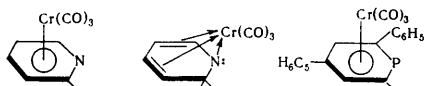
Thus the principal factor determining the mode of addition of electrophilic agents (acids) in ambident systems with several competing but identical electron-donating atoms is the magnitude of the negative π-electron charge density. This conclusion is directly related to the HSAB principal and the familiar postulate that the most nucleophilic centre in the molecule is the electron-donating atom with the highest negative potential.

d. Specific Ambident Systems

Heteroaromatic compounds. In five-membered heterocycles with a single heteroatom (furan, thiophen, selenophen, and pyrrole), which have two potential electron-donating centres (the heteroatom and the π-electron system), coordination interaction involves mainly¶ π electrons[9,327-334].

There is at present no doubt about the validity of this conclusion: (1) metal carbonyl π complexes of pyrrole[331,334], thiophen[335,336], and selenophen[336] have been synthesised; (2) azoferrocene has been obtained on the basis of the π-electron system of pyrrole[332,333]; (3) measurements of the dipole moments and studies on the infrared spectra of thiophen and furan complexes of $SnCl_4$ indicate the occurrence of π-electron coordination interaction[9,327-329].

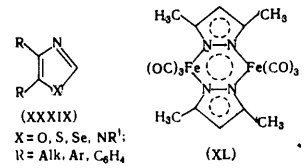
In contrast to five-membered heterocycles, six-membered heterocyclic nitrogen-containing systems (pyridine, quinoline, and many of their derivatives) react with metal salts exclusively via the nitrogen atom[337,338]. The reported synthesis of a chromium tricarbonyl π complex of pyridine (XXXVI)[339] was disproved by the same investigators[340]†, who showed that the π complex[339] is in fact a π,σ derivative of the hydrogenated pyridine ring[340] and the amino-olefinic system (XXXVII) is involved in coordination interaction. It is interesting to note that a similar π,σ bond has been attributed to the magnanese tricarbonyl derivative of pyrrole[342]. At the same time 2,4,6-triphenylphosphorine (phosphabenzene—L) forms both σ complexes with the compositions $L(CO)_5$ and $L(CO)_4$ and the π complex $L(CO)_3$ with the structure (XXXVIII):[343]



(XXXVI) (XXXVII) (XXXVIII)

The azoles (XXXIX)[334,345]—five-membered heterocycles with two heteroatoms one of which is nitrogen—and their aromatic analogues behave in coordination interaction like the six-membered heteroaromatic systems (pyridine) and not like the thiophen (furan, pyrrole) systems.

Azole-containing systems form mainly σ complexes via the nitrogen atom of the azole ring with Group II,[346-349] III,[350-353] IV,[354-359] and V[357-358] metal salts, Group III metal derivatives[359,360], and Group VI metal carbonyls[361-363]



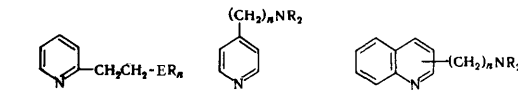
(XXXIX) X = O, S, Se, NR^1; R = Alk, Ar, C_6H_4 (XL)

However, objections have been made against the involvement in the coordination interaction of the π-electron system of the azole ring[364] and the electron pair of the X heteroatom[365] and therefore we believe that additional tests are required. The properties of the 3,5-dimethylpyrazole complex of iron carbonyl can be accounted for not only from the standpoint of π complex formation but also by the formation of the dimeric structure (XL), resembling that of the complexes of pyrazole with BF_3[366] and AlR_3.[359,360]

The hypothesis concerning the possible coordination via the X heteroatoms conflicts with the familiar postulate that sp^3-hybridised O, S, Se atoms and NR groups of azoles have no electron-donating properties[344,367]. Moreover, the negative π-electronic charge density is almost wholly localised at the nitrogen atom (the X atom is positively charged), which, was shown above to constitute the principal factor responsible for the location of the coordinate bond at the competing heteroatoms of the ambident system‡.

Thus, according to published data, heteroaromatic systems behave predominantly as monodentate ligands: five-membered systems (pyrrole, thiophen, furan, and selenophen) are π-electron donors and six-membered nitrogen containing systems and azoles are σ-electron donors.

Derivatives of heteroaromatic systems. The non-conjugated systems (XLI–XLIV) form several classes of complexes[368-374]:



(XLI-XLII) (XLI): E = P, As, N: R = Alk. Ar; $n = 2$ (XLII): E = O, S: R = H, Alk; $n = 1$ (XLIII) R = H, Alk, Ar. $n = 1, 2$ (XLIV) R = H, Alk; $n = 1, 2$

Nickel(II), cobalt(II), and zinc(II) salts form cyclic structures with 2-(β-diphenylphosphinoethyl)pyridine (XLI, E = P) involving the nitrogen and phosphorus atoms[368]. On the other hand, when there is a considerable difference in hardness, for example between the nitrogen and arsenic atoms, the above salts interact only with the nitrogen atom, while the soft copper(I) halides interact with the "soft" arsenic atom[369].

¶There is some evidence for the possibility of the quaternisation of the sulphur atom of thiophen[326]. The hydrogenated five-membered systems readily form σ-complexes via the heteroatom[9,327-330].

†Unfortunately this erroneous study was employed by Candlin et al. in their monograph[341] as an example of a π complex of a heterocyclic ring.

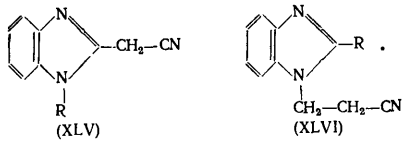
‡The high negative π-electron charge density at the oxygen atom of oxazole[367] suggests that the coordination interaction with "hard" cations (BF_3, AlX_3) may take place via this atom.

In a study of complex formation in a series of 2-[β-hydroxy(mercapto)ethyl]pyridines (XLII), it was noted[370] that the coordinate bond with relatively soft MX_2 is located at the nitrogen of the pyridine ring and not at the harder oxygen and sulphur atoms.

It is believed that α-substituted aminoethylpyridines (XLI, E = N) can form complexes of three types: (1) cyclic compounds with transition metals involving both electron-donating centres[371-374]; (2) complexes with NiI_2 involving only the amino-nitrogen[371]; (3) complexes of Group IV metal (tin and titanium; n = 2) tetrachlorides[375] and niobium oxide trichloride[376] involving the nitrogen atom of the pyridine ring.

γ-Derivatives of pyridine (quinoline) also form complexes of MX_4 and $NbOCl_3$ via the nitrogen atom of the pyridine (quinoline) ring[357,375,376]. These results in general agree with the greater hardness of MX_4 and $NbOCl_3$ compared with NiI_2 (in addition to the greater softness of the metal itself[13], the symbiotic effect[4,14] of the soft iodide anion probably operates in this case). However, it is noteworthy that Uhlig and Maeser[371] did not study the infrared spectroscopic behaviour of the pyridine ring and therefore their results should be treated with some caution.

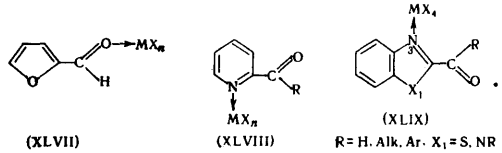
In complexes of $SnCl_4$ and $TiCl_4$ with cyano-derivatives of the benzazole series (XLV, XLVI), coordination interaction probably involves the softer nitrogen atom of the azole ring[377]:



(XLV) (XLVI)

MX_n forms complexes via the oxygen atom with carbonyl derivatives of five-membered heteroaromatic system having one heteroatom. Stable neutral complexes of furfural with MX_4 have been isolated[378,379], their infrared spectra showing a considerable decrease in the frequency of the carbonyl stretching vibrations indicating that the coordinate bond involves the carbonyl oxygen [compound (XLVII)].[37,68]

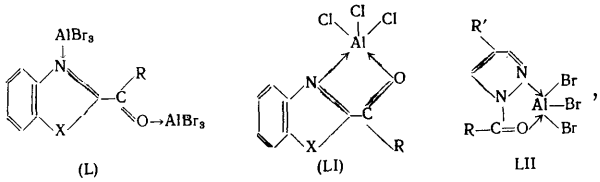
On the other hand, the formation of complexes via the nitrogen atom is characteristic of pyridyl ketones (XLVIII)[380] and carbonylazoles (XLIX)[353,377,381] containing electron-donating nitrogen and oxygen atoms:



(XLVII) (XLVIII) (XLIX)

R = H, Alk, Ar. X_1 = S, NR

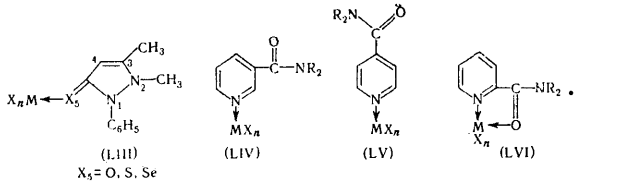
Only with AlX_3 (X = Cl or Br) and carbonylazoles can coordination interaction involve both electron-donating centres with the formation of complexes (L) having the composition $2AlBr_3$.(L) or, under favourable steric conditions, of cyclic compounds of types (LI) and (LII)[83,353,356,381]



(L) (LI) LII

where X = S or NCH_3 and R = H or CH_3.

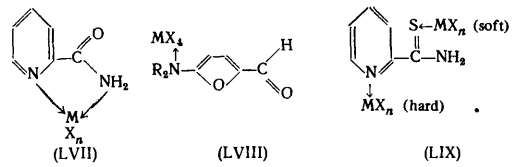
Antipyrine (LIII) and its derivatives should seemingly be included among nitrogen- and oxygen-containing ambident systems. However, the localisation of a high negative π-electron charge at the oxygen atom[81,382-384] renders antipyrine a monodentate ligand in which coordination interaction involves exclusively the exocyclic oxygen atom regardless of the type of MX_n.[81,384-391] Thio- and seleno-antipyrines behave similarly[81,389]:



(LIII) (LIV) (LV) (LVI)

X_5 = O, S, Se

The coordination interactions of MX_n with pyridine-carboxylic acid amides and thioamides is unusual. Nicotinamide (LIV) and isonicotinamide (LV) form complexes with the coordinate bond involving preferentially the nitrogen atom of the heterocyclic ring[380,392,393]. On the other hand, depending on the composition of the complexes and the properties of MX_n, picolinamide forms cyclic structures in which complex formation involves the pyridine nitrogen and the carbonyl oxygen [compound (LVI)][394] or the amino-nitrogen [compound (LVII)][395-397].



(LVII) (LVIII) (LIX)

The coordinate bond in the complexes of the tetrachlorides of Group IV elements with 5-(*N*-dialkylamino)-furfurals (LVIII) involves mainly the amino-nitrogen and not the carbonyl oxygen[399]. Whereas the direction of coordination attack in ambident systems containing nitrogen and oxygen atoms is difficult to predict§, in pyridine-carboxylic acid thioamides soft acids (Au, Ru, Os, Ag, and Rh) attack the "soft" sulphur atom and the harder transition metal salts attack the nitrogen atom [compound (LIX)], in agreement with the HSAB principle[400].

In the series of amino-,[82,348,353,401,402] azomethine[80,82], azo-,[348,403-405] and cyano-derivatives[406-407] of pyridine and azoles, the coordinate bond is preferentially¶ located at the electron-donating centre with the highest negative π-electronic charge[80,82], as for the aliphatic and aromatic ambident systems with nitrogen atoms hybridised in different ways.

Metal chelate ambident systems. It has been shown[409-411] that metal chelates may be used as ligands in complex formation ("complexes as ligands",[411-412] "complexes of complexes"[413,414]). The problem of the location of the coordinate bond in such dinulcear complexes arose at once[409-419]. It is believed[409,411-415,417] that coordination interaction involves the oxygen atoms of

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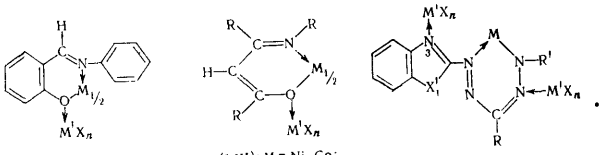
§In pyridine-2-acetamide, which has non-conjugated electron-donating centres, the coordinate bond is located in accordance with the HSAB principle: PdX_2 (X = Cl or Br) enters into coordination interaction with the soft nitrogen atom, while the harder MX_2 interact with the nitrogen and oxygen atoms[398].

¶It is believed that the formation of complexes with 2-amino-1,3,4-oxadiazole involves the amino-group[408].

the metal chelate unit of the inner-complex compounds of the Schiff bases (LX) and β-aminovinyl ketones (LXI). However, the investigators[410,416,418,419] concluded that the interaction of $SnCl_4$ and $TiCl_4$ with salicylideneanilinato-complexes leads to the rupture of the metal-containing ring and the location of the bond at the nitrogen atom of the azomethine group:



(LX): M = Ni, Cu; M' = Ni, Cu, Ti, Sn

(LXI): M = Ni, Co; M' = Sn, Ti

(LXII): M = Ni, Cu; M' = Sn, Ti; X = Cl, Br; X_1 = O, S, NR^1

In the metal chelates of the formazans of the benzazole series, the centres for the formation of a donor–acceptor bond with MCl_4 (M = Sn or Ti) are probably not only the nitrogen atom of the heterocyclic ring but also the nitrogen atoms of the formazan ring [compound (LXII)].[420]

The problem of competitive intramolecular coordination in metal chelates (the building up of square-planar and tetrahedral structures to octahedral structures) is probably directly related to these data. However, its discussion is outside the scope of the present review.

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The HSAB principle is a simple and convenient formulation of a number of postulates relating to acid–base interaction and not a new law or theory. The main postulates of the HSAB principle are extremely useful for a systematic arrangement and explanation of experimental data accumulated on the problem of the location of the coordinate bond in systems with several electron-donating centres. A general description of data on competitive coordination in non-conjugated systems from the standpoint of the HSAB principle is particularly desirable (unfortunately fewest studies have been made precisely in this field).

For conjugated (ambident) systems, the concepts of the "hardness" and "softness" of the electron-donating atoms are extremely arbitrary: the nitrogen and oxygen atoms, which have been assigned by Pearson to the same class of hard bases, can function as soft nucleophilic centres, while the "soft" sulphur can become hard (thiourea, thioamides, thioantipyrine). Similarly in many cases the terminological concepts of "hardness" and "softness" lose their significance in the case of cations. Probably, in a consideration of the problem of competitive coordination in ambident systems, one cannot in general relate the concepts of the "hardness" and "softness" of nucleophilic atoms to the Schwarzenbach, Chatt, and Pearson classifications. In estimating the "softness" and "hardness" of electron-donating centres, it is more correct to take into account the properties characterising the "soft" and "hard" nucleophilic agents as defined by Pearson†. In the same connection, one should evidently assume that in any polyfunctional system it is possible to isolate centres for the preferential formation of a donor–acceptor bond. As shown above, the position of such a centre coincides in general with that of the electron-donating atom bearing the highest negative π-electron charge density.

†Regardless of its position in the Periodic System, any atom can evidently exhibit Pearson's "hard" or "soft" properties.

The experimental data discussed in the present review indicate the unusually pronounced interest in the problem of competitive coordination among both Soviet and foreign investigators. At the same time there have been still too few systematic and comprehensive discussions of the causes of a particular mode of coordination in polyfunctional ligands‡. In many cases the experimental data are insufficient for this purpose (a narrow selection of "acids" and "bases"), while in others (these include the majority of investigations) the aim of the study was to discover the location of the bond at a particular electron-donating atom.

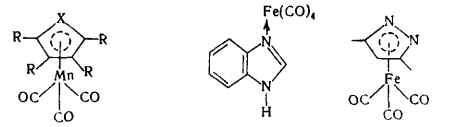
The tasks of the immediate future are probably specific synthesis of polydentate ligands with electron-donating centres of different types and specific selection of acids (both "hard" and "soft") for the solution and a comprehensive examination of the problem of competitive coordination. Such attempt designed to synthesise ligands are already being made[177,421] and they must be prosecuted in all possible ways. Naturally, the successful solution of the problem depends on the reliability of the experimental methods employed for this purpose.

A general description of data on competitive coordination in the chemistry of complex compounds may prove extremely useful in determinations of the mode of reactions in polyfunctional systems and for other branches of chemistry. We believe that the study of the problem of the location of the hydrogen bond and of the site of protonation of organic compounds with several electron-donating centres is particularly promising; the data which have accumulated[422–437] show that, in agreement with the HSAB principle, this process involves the hardest atom in non-conjugated and ambident systems. The question of the quaternisation of polyfunctional systems, primarily the amino-, azomethine, and azo-derivatives of nitrogen-containing heterocycles, is apparently closely related to this problem.

ADDENDUM

(to Section III, subsection 3d)

π-Complexes of manganese tricarbonyl with tetraphenylphosphole (LXIII) and tetraphenylarsenole (LXIV) have been synthesised[438]:



(LXIII): X = P; R = C_6H_5
(LXIV): R = C_6H_5; X = As

(LXV)

(LXVI): R = H, CH_3

Complexes (LXV) in which the ligand behaves as a monodentate base and is coordinated to the metal via the "pyridine" nitrogen atom have been described. Complexes (XL)[439,440] and (LXVI)[430] have been synthesised and the structure of a π-complex has been suggested for the latter[439].

Direct proof of the location of the coordinate bond at the "pyridine" nitrogen atom in benzazoles has been obtained in a study of ^{14}N NMR spectra of metal carbonyl complexes of azoles[441].

‡We believe that this problem has been most satisfactorily solved for pseudohalide ions[12,258,276].

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The Synthesis and Properties of New Complex-forming Thiophen Derivatives

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The review deals with the methods of synthesis and properties of new heterocyclic ligands-mercaptoaldimine derivatives of thiophen, thienothiophen, and thionaphthene. Data on the preparation and certain reactions of metal chelate complexes of mercaptoaldimines are presented. The tautomerism and the ^{1}H NMR spectra of mercaptoaldimine derivatives of thiophen are discussed.
The bibliography includes 100 references.

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I. INTRODUCTION

In recent years there has been a fresh spurt in the development of the chemistry of complex compounds. New experimental techniques, in particular infrared, ^{1}H NMR, and ESR spectroscopy, and especially the exceptional importance which complex formation has acquired as a special method of activating simple molecules acting as ligands, have undoubtedly played a significant role in stimulating interest in the field of complex compounds. Complex formation also makes it possible to transfer a metal from one part of a biological substrate to another or to remove from the organism a metal with toxic properties [1]. A new branch of organic chemistry, based on the modification of the organic molecule by coordination with a metal, has been developing at an increasing rate and attention has been concentrated on the organic part of the complex, while previously interest was directed almost exclusively to the study of the properties of the coordinated metal ions. Many relevant problems have been discussed in reviews and monographs [2-7].

Chelate compounds, the chemical and physical properties of which vary within extremely wide limits as a function of the coordinating centres of the ligands and the nature, valence state, and the coordination number of the central atom, are of special interest. In Collman's extensive studies [8], this has been demonstrated for a large number of metal acetylacetonates. Functional groups, in particular nitro-, acyl, and chloromethyl, and other groups, can be introduced into some of these compounds by electrophilic substitution reactions, the properties of the group becoming sharply altered as a result of the bond formed with the chelate ring. For example, the aldehyde group loses its capacity to form oxides, hydrazones, etc. and does not react with methylmagnesium iodide; the sulphide group is not oxidised by hydrogen peroxide. In view of the chemical behaviour of acetylacetonates, some investigators refer to their properties as pseudoaromatic. In this connection one can mention the recent work of Japanese investigators [9], who, wishing to compare the aromatic properties of the furan and chelate rings, studied the nitration and bromination of chromium(III) and cobalt(III) trisfuroylacetonates and obtained only the chelate ring substitution products.

Chelates the ligand component of which is a bifunctional derivative of a heteroaromatic compound constitute a group which has so far been little investigated. New possibilities have arisen in practice and in research not only as a result of the ability to vary the ring heteroatom but also owing to its capacity for involvement in complex formation together with atoms outside the ring. This branch of the chemistry of complex compounds has attracted the attention of the authors of the present review.

II. SYNTHESIS AND PROPERTIES OF SULPHIDE DERIVATIVES OF THIOPHEN

Thiophen is a heterocyclic compound with pronounced aromatic properties. During the decades elapsed since its discovery (1883) by Victor Meyer, the chemistry of thiophen has been treated in terms of the concept of its complete analogy with benzene. This approach, which is in many respects justified and is to some extent in keeping with the present general concept of aromaticity, suffers from the disadvantage that certain specific features of the chemical behaviour of thiophen remained undiscovered or were ignored. However, with the development of new theoretical views in organic chemistry and the adoption of modern physical methods for the investigation of organic molecules, differences between the properties of the thiophen and benzene systems were discovered; these are due, in particular, to differences between their geometry or the influence of the heteroatom as a unit different from the other units in the closed chain of the heterocycle.

In the light of these data, it is of considerable interest to investigate analogous bifunctional benzene and thiophen (or furan, etc.) derivatives as regards their capacity to form chelates and the chemical behaviour of the latter. One of the types of ligands for this purpose may be analogues of salicylaldehyde and its Schiff bases containing the mercapto-group instead of the hydroxy group [structures (I) and (II)].

It is noteworthy that in recent years there has been an increasing interest in complexes where one of the coordinating centres is a sulphur atom [10]:

(I) (II)

It appeared useful to employ 2-alkyl-5-mercaptothiophens for the synthesis of compounds of type (I). [11] However, it is known that in the analogous thiophenol system a second functional group cannot be introduced into the ring because, under the influence of both electrophilic and nucleophilic agents, the mercapto-group is the first to be altered. For example, under nitration and bromination conditions, thiophenol is converted into a disulphide [12,13] and in the Friedel–Crafts acetylation it yields phenyl thioacetate, which does not react further even at 150°C. [14] Individual cases of the ring alkylation of aromatic thiols in the presence of boron trifluoride have been described but under these conditions too the intermediate products are complexes of the thiol and the catalyst in which the mercapto-group is blocked [15].

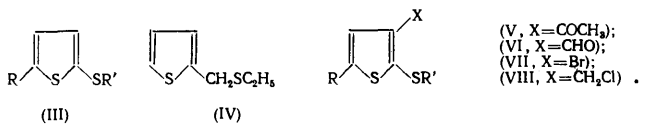
Thus, it is evident that, in order to introduce a second functional group into the molecule of an aromatic mercaptan, it is necessary to protect the mercapto-group by substituents which can be readily eliminated in the final stage. However, the use for this purpose of the corresponding mercaptals, disulphides or *S*-acylated mercaptothiophens did not yield satisfactory results [14,16,17]. On the other hand, alkyl aryl sulphides readily undergo electrophilic substitution but the dealkylation necessary for the above purpose has been rarely employed [18].

Ring-substituted thiophenols have been synthesised from sulphides formed by the reaction of thiophenols with 3-nitrobenzylideneacetophenone [16]. The use of this method for the synthesis of 3-substituted mercaptothiophens proved relatively inaffective. Thus the reaction of *N*-methylformanilide and phosphoryl chloride did not result in the introduction of the formyl group into the thiophen ring of β-[(5-ethyl-2-thienylmercapto)-β-(3-nitrophenyl)]propiophenone and the acetylation of this sulphide led to the formation of its cyclodehydration products [11].

The required result was achieved only when alkyl thienyl sulphides were employed as the starting materials. In this case the problem reduced to the introduction of the corresponding functional group into the 3-position of the thiophen ring and the subsequent dealkylation of the alkylthio-group in such a way that the resulting mercapto-group remained linked to the ring. Since alkyl thienyl sulphides are key compounds in this process, it is desirable to examine initially the methods of their synthesis and some of their properties.

Alkyl 2-thienyl sulphides are formed in high yields when thiophen and its homologues with at least one substituted α-position are treated in succession with butyl-lithium, elemental sulphur, and an alkyl halide [19,20]. Other methods of synthesis of similar sulphides, which also do not require a preliminary halogenation of the thiophen, are based on the use of thiyl radicals [21,22] or thiocyanatothiophens [23].

When 2-alkyl-5-alkylthiothiophens (III) were acetylated with acetyl chloride in the presence of $SnCl_4$ or with acetic anhydride and phosphoric acid [19], formulated by the Wilsmeyer method† [24], and brominated, the corresponding derivatives (V), (VI), and (VII) containing a new substituent in the 3-position were isolated:



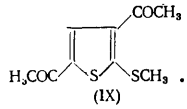
(III) (IV) (V, X=$COCH_3$); (VI, X=CHO); (VII, X=Br); (VIII, X=CH_2Cl).

where R and R′ = alkyl.

This is evidence that alkylthio-groups have a more powerful activating effect than alkyl groups. It is interesting to note that, on competitive acylation of a mixture of thiophen and 2-methylthiothiophen with acetyl chloride [26], 2-acetothienone and 5-methylthio-2-acetothienone were isolated in yields of 15 and 48% respectively.

On chloromethylation of type (III) sulphides, a 3,4-di-(chloromethyl)-substituted derivatives was isolated together with the monochloromethyl-substituted derivative (VIII). [27]

When 2-methylthiothiophen was acetylated, a small amount of a diacetyl derivative, probably with structure (IX), was detected in addition to 5-methylthio-2-acetothienone:



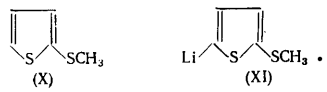
(IX)

Kinetic data for hydrogen exchange between an acid and 2- and 3-methylthiothiophens deuterated in specified positions may serve as a measure of the activating effect of the alkylthio-group in electrophilic substitution reactions of methylthiothiophens [28]. The results obtained show that in 2-methylthiothiophen the second α-position is strongly activated and the 3-position less so. The methylthio-group in the 3-position increases the rate of exchange in the 2-position by two powers of 10 more than in the 4-position. The rates of exchange of β-atoms in 2-ethylthio-5-methylthiophen also differ by approximately two powers of 10. The data quoted above for the site of acetylation, formylation, and bromination of 2-alkyl-5-alkylthiothiophens are also at least qualitatively consistent with these findings.

As already mentioned, the capacity of thiophen and certain types of its alkyl- or aryl-substituted derivatives for metallation, for example when treated with lithium alkyl, is important for synthetic purposes in the thiophen series. According to hypotheses put forward at one time [29,30], the first stage in this reaction is coordination of the metallating agent to the heteroatom with a lone electron pair; this determines the site where the metal is introduced and limits or excludes the effect of substituents [31]. Therefore the problem of the site of metallation of alkyl thienyl sulphides, the molecules of which contain two formally bivalent sulphur atoms, cannot be solved unambiguously *a priori*, particularly since their benzene analogue (thioanisole) yields on metallation exclusively the product of substitution in the side chain [32,33].

† Sulphides of type (IV) have an interesting property: when acted upon by *NN*-dimethylformamide or phosphoryl chloride, they do not yield the corresponding aldehydes but are cleaved with the formation of thienyl chloride and amidomercaptals [25].

In contrast to methyl phenyl sulphide, methyl 2-thienyl sulphide (X) readily gives the lithio-derivative (XI) when acted upon by butyl-lithium. Similar results were obtained also for the sulphide (IV) [34] although the possibility of substitution in the thiophen ring appeared unlikely in this case:



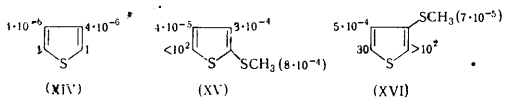
(X) (XI)

In a similar reaction involving protophilic substitution the alkylthio-group also has an activating effect. This is evident, for example, from the finding that, in an experiment involving the metallation of an equimolar mixture of thiophen and the sulphide (X) with a deficiency of butyl-lithium followed by carboxylation, it is possible to isolate only the acid (XII): [20]

(XII) (XIII)

The β-hyrodgen atoms in the thiophen group are not substituted at all under the influence of butyl-lithium, as in the case of 2,5-dimethylthiophen, or are substituted only with difficulty. The acid (XIII) could be obtained in only 27% yield from 2-methyl-5-methylthiothiophen [20].

All these observations are consistent with measurements of the rate of hydrogen–deuterium exchange between bases and methylthiothiophens containing a deuterium atom in a specified position in the molecule [35]. The formulae quoted below characterise the relative mobilities of the hydrogen atoms in all the C–H bonds in thiophen and isomeric methylthiothiophens:



(XIV) (XV) (XVI)

The rate constant for the exchange of the deuterium atom in the 2-position of unsubstituted thiophen with dimethyl sulphoxide catalysed by an alkali metal t-butoxide was adopted as a unit in formulae (XIV), (XV), and (XVI). Attention should be drawn to data concerning the mobility of hydrogen atoms in the methylthio-groups themselves. Evidently the rate of exchange involving these groups is smaller by several powers of ten than the rate of exchange of the ring α-hydrogen atom. In the case of thioanisole the opposite relations are obtained [36].

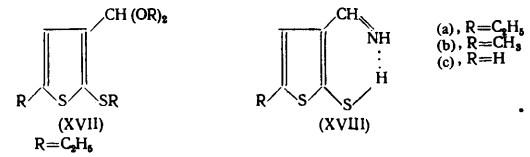
III. MERCAPTOALDIMINE DERIVATIVES OF THIOPHEN

1. Effect of Sodium in Liquid Ammonia on the Diethylacetals of 5-Alkyl-2-Alkylthiothiophen-3-aldehydes

As mentioned above, in order to obtain substituted mercaptothiophens of types (I) and (II) from β-substituted sulphides of type (VI), it is necessary to have an effective means of dealkylating the alkylthio-groups without affecting the bond between the exocyclic sulphur atom ahd the thiophen ring.

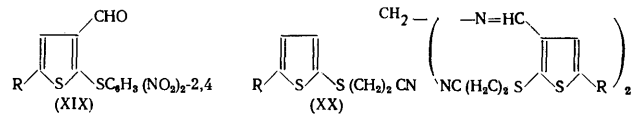
In the search for such a method, the discovery of the capacity of alkyl thienyl sulphides for dealkylation under the influence of sodium in liquid ammonia (Na/NH_3) with formation of the corresponding mercaptans in yields of 50–80% [37] (depending on the nature of the alkyl group) has played an important role. In order to "protect" the aldehyde group under the dealkylation conditions, compound (VI) was converted into the acetal (XVII), since it is known that aliphatic acetals do not react with aqueous and liquid ammonia and with aliphatic amines up to 130°C and are stable also in relation to sodium in liquid ammonia [38,39].

When two equivalents of sodium in liquid ammonia were allowed to react with the acetal (XVII) and the resulting aqueous alkaline solution was treated with HCl, a high yield was obtained of a nitrogen-containing crystalline compound—the mercaptoaldimine (XVIIIa)‡—instead of the expected mercaptoacetal (or aldehyde). [40] Its homologues (XVIIIb) [41] and (XVIIIc) [42] were obtained similarly:



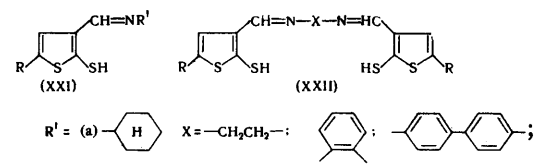
(XVII) (XVIII) (a), R=C2H5 (b), R=CH3 (c), R=H

When the mercaptoaldimine (XVIIIa) is treated with acid or alkali, ammonia is split off, which is consistent with its structure; in an acid medium, the product is a coloured polymer without nitrogen, which retains the capacity to form derivatives via the mercapto- and aldehyde groups, identical with the analogous derivatives obtained directly from (XVIIIa). On reduction with lithium aluminium hydride, (XVIIIa) is converted in high yields into 5-ethyl-2-mercapto-3-thenylamine [43]. One of the typical properties of compound (XVIIIa), reflecting the characteristics of its structure, is its instability under conditions where the hydrogen atoms of the mercapto-group are substituted under the influence of any reagent. For example, the reaction with 1-chloro-2,4-dinitrobenzene in an alkaline medium results in the formation of the formylsulphide (XIX) and the reaction with acrylonitrile gives the hydramide (XX): [40]



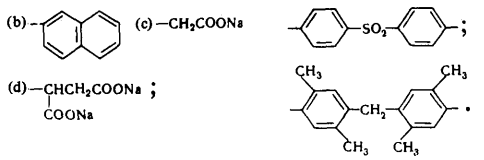
(XIX) (XX)

The formation of hydramides is known to be characteristic of extremely unstable aromatic imines [44] and is observed also when ammonia acta on thiophen-2-aldehyde and furfural [45]. On the other hand, reaction of compound (XVIIIa) with primary amines results in the formation, with evolution of ammonia, of stable di- and tetra-functional *N*-substituted mercaptoaldimines of types (XXI) and (XXII)—the thiophen analogues of the Schiff bases of thiosalicylaldehyde [40,41]. In the light of the above data, it becomes evident that the very existence and stability of compounds of type (XVIII) may be attributed to the formation of an intramolecular hydrogen bond stabilising the molecule (see Section III, 2):



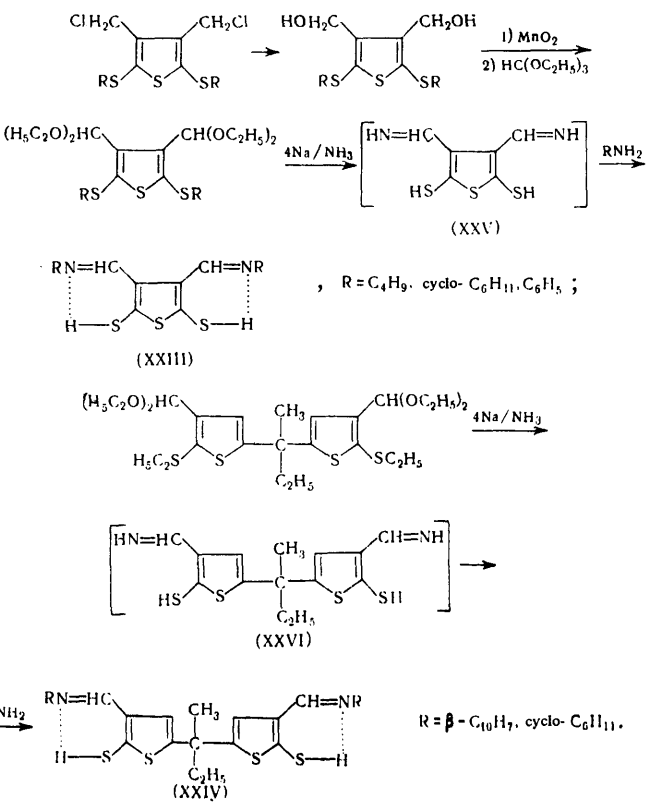
(XXI) (XXII)

‡ For brevity, here and henceforth compounds of type (XVIII) are called mercaptoaldimines although it has been shown [61] that they exist predominantly in another tautomeric form.



Compounds (XXIc) and (XXId), obtained from sodium glycinate and aspartate [41], are readily soluble in water, which in some cases may be an important condition for the applicability of a complex-forming agent.

Apart from the mercaptoaldimines described above, the derivatives (XXIII) and (XXIV) with analogous structure and four coordinating centres in one or in two thiophen rings separated by a methylene bridge have been obtained [46,47]. Such tetrafunctional compounds may be of interest in the synthesis of coordination polymers. The pathways in their synthesis are illustrated below:



It is noteworthy that satisfactory analyses have not been obtained for the bismercaptoaldimines (XXV) and (XXVI), since they are infusible powdery substance, probably with an oligomeric structure, and are difficult to purify. However, their capacity to evolve ammonia under the influence of alkalis and amines with formation in the latter case of readily crystallisable Schiff bases (XXIII) and (XXIV) may serve as confirmation of the structure attributed to them. One can therefore postulate that, when Na/NH_3 is allowed to act on compounds containing two acetal and two sulphide groups, reactions similar to those observed for the acetal (XVII) take place.

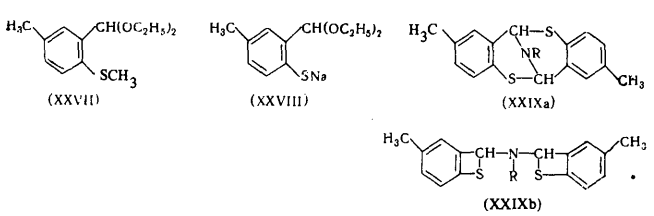
The problem of the mechanism of the formation of mercaptoaldimines of type (XVIII) cannot yet be regarded as finally elucidated. Nevertheless the available data [48] permit certain conclusions concerning the process.

1. When two equivalents of sodium in liquid ammonia are allowed to act on the alkylthioacetal (XVII), the acetal group is unchanged and only the dealkylation of the alkylthio-group with formation of the corresponding mercaptide takes place. (The mercaptoacetal was isolated as mercury mercaptide.)

2. The mercaptoaldimine (XVIII) is a product of the conversion of the mercaptide in the presence of an acid and ammonia.

3. The stability of mercaptoaldimines is due to the specific relative positions of the mercapto- and aldimine groups, which make possible the formation of a hydrogen bond or an inner salt. For other relative positions of the groups in the initial alkylthioacetal, for example, in the acetal of 5-ethylthiothiophen-2-aldehyde, a mercaptoaldimine is not formed. In this case the reaction reaches completion only after the addition of six equivalents of sodium, since sodium is consumed in the dissociation of the C–S bonds and in the reduction of the acetal group to a methyl group. Examples of similar reduction reactions have been described for certain aromatic ketals [49,50].

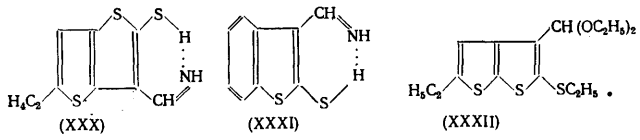
In the light of the foregoing facts, the results obtained in the study of the effect of sodium in liquid ammonia on benzene analogues of the alkylthioacetals (XVII) are of interest. When two equivalents of sodium in liquid ammonia are allowed to act on the acetal (XXVII), the product is, as for the thiophen acetal (XVII), the mercaptide (XXVIII) (obtained in quantitative yield), which reacts with ammonia and amines to give compounds (XXIXa) or (XXIXb). [51] Compound (XXIX, R = H) is formed also when Na/NH_3 is allowed to act on 3-methyl-6-methylthiobenzaldehyde [52]. Therefore in such cases the final product is not a benzene analogue of mercaptoaldimines of type (XVIII):



This may be due to differences between the geometries of the thiophen and benzene rings. Indeed, when a hydrogen atom in the benzene ring is substituted by a sulphur atom, a molecular model analogous to that of compound (XVIIIa), in which the nitrogen and sulphur atoms are linked by a hydrogen bond§, cannot be constructed. In thiophen, such a possibility exists, since its external valence angles are larger. An indirect confirmation of this interpretation comes from the fact that furan, the geometry of which is similar to that of thiophen, forms stable mercaptoaldimines as a result of the reactions described above [57].

§ Here one must again emphasise that these considerations apply only to mercaptoaldimines unsubstituted at the nitrogen atom. The synthesis, infrared spectra, and certain metal chelates of Schiff bases of *o*-mercaptobenzaldehyde were described recently [55,56].

Using the above method for the synthesis of mercaptothenylideneamines (XVIII), the mercaptoaldimines (XXX) and (XXXI), derived from 2-ethylthieno[3,2-*b*]thiophen and thionaphthene respectively, were obtained[58]:



(XXX) (XXXI) (XXXII)

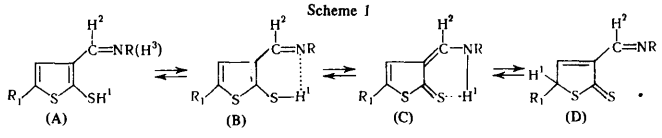
They are coloured crystalline compounds and, like (XVIIIa), form Schiff bases with β-naphthylamine and the corresponding chelates with zinc and nickel salts.

The attempt to synthesise the mercaptoaldimine from the acetal (XXXII) obtained from 2-ethylthieno[2,3-*b*]thiophen was unsuccessful[59].

2. Tautomerism of Mercaptoaldimine Derivatives of Thiophen

In a discussion of problems concerning the structure and chemical behaviour of mercaptoaldimines, one cannot exclude from consideration the possibility of a tautomeric equilibrium (see Scheme 1).

Scheme 1



(A) (B) (C) (D)

Together with the tautomeric forms A, C, and D, there is also a form B, which differs from A only by the presence of a hydrogen bond. Its inclusion in the scheme appears to be valid, since it can be regarded as intermediate between forms A and C.

The tautomerism of mercaptoaldimines in solution has been investigated by proton magnetic resonance (^{1}H NMR).[60,61] The signal from the ^{1}H proton has a chemical shift of 12–14 p.p.m., which indicates the presence of a strong intramolecular bond between H^1 and N or S. The formation of a chelate ring (structures B and C) is also confirmed by data for compounds in which R = H. In the spectra of these compounds both protons linked to the nitrogen atom have different shifts. The H^1 proton, the signal of which is at a lower field (by 2–2.5 p.p.m.), is rigidly fixed, while the other proton is involved in intermolecular exchange, since, on replacement of the ^{14}N isotope by ^{15}N, the H^1 signal becomes a well resolved quartet, while the H^3 signal remains broad.

The values of δH^1 leads to the conclusion that there are no appreciable amounts of the tautomer A and the fine structure of the signal due to the thiophen ring protons and the substituent R_1 shows that there are no appreciable amounts of the tautomer D.

The problem of the location of the H^1 proton within the limits of the chelate ring is of considerable interest. Namely whether it is linked by a covalent bond to the sulphur atom and hence by a hydrogen bond to the nitrogen atom or conversely, i.e. whether we are dealing with structure B or C. Experimental data confirmed the second hypothesis. The fact that the H^1 proton is located predominantly at the nitrogen atom is confirmed by the following observations.

a. In the spectra recorded at frequencies of 60 and 100 MHz, the distance between the signal lines corresponding to the H^1 and H^2 protons remained unchanged, which indicates the occurrence of spin–spin coupling between them (J_{H^1,H^2} = 13–15 Hz).

b. The study of the ^{1}H NMR of the products of the substitution of H^1 by a methyl group or deuterium leads to the same conclusion. Such substitution results in the merging of the components of the H^2 doublet into a singlet in addition to the disappearance of the H^1 signal.

c. When the ^{14}N isotope is replaced by ^{15}N, a constant $J_{^{15}N,H^1}$ = 85–87 Hz is observed for the spectrum. Consequently, even if there is an equilibrium at room temperature (see Scheme 1), it is appreciably displaced towards the tautomer C. This equilibrium may be shifted somewhat towards A or B by increasing the temperature.

Thus the compounds initially assigned to the class of mercaptoaldimines can be more correctly regarded as substituted 4-thiolen-2-thiones.

It is noteworthy that a change of solvent hardly affects the parameters of the spectra of these compounds.

The H^1 chemical shifts depend appreciably on the nature of the substituent at the nitrogen atom. The highest value of δH^1 and probably the longest hydrogen bonds are observed for aromatic substituents[61]. δH^1 increases in the sequence

$$H < n\text{-}C_4H_9 < \text{cyclo-}C_6H_{11} < C_6H_5 < \beta\text{-naphthyl.}$$

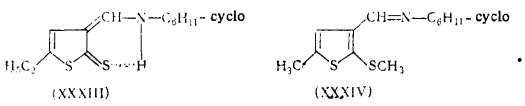
A significant change in the spectra of mercaptoaldimines is observed when they are heated above room temperature: the fine structures of the H^1 and H^2 signals disappear, the H^1 signal broadens so much that it vanishes altogether, and the H^2 signal is converted from a doublet into a broad signal, which is converted into a narrow singlet as the temperature is raised. These findings may be accounted for on the hypothesis that an increase of temperature entails a change in the contents of different forms in the equilibrium mixture.

The study of the H^1 NMR spectra of mercaptoaldimines of the furan series[62] showed that, as in the analogous thiophen derivatives, they have a strong intermolecular hydrogen bond C–S...HN. The H^1 proton (the numbering of the protons and the designation of the tautomeric forms is the same as for the thiophen derivatives) in the chelate ring is located predominantly at the nitrogen atom.

In general, when carbon tetrachloride and dioxan are employed as solvents, a situation similar to that for the analogous thiophen compounds is observed, but in polar solvents, for example in dimethyl sulphoxide (DMSO), the dipole moment of which is 4.3 D,[63] they exist in two forms. Under the influence of DMSO, the spectrum becomes "doubled". One can therefore postulate that, under the influence of this solvent, the intramolecular bond dissociates in some of the type C molecules, but the spin–spin coupling between the H^1 and H^2 protons persists. Thus the replacement of sulphur in the ring by oxygen leads to a weakening of the hydrogen bond in the chelate ring.

The characteristics of thiophen mercaptoaldimines as compounds with an intramolecular hydrogen bond are reflected in their polarographic behaviour. This has been shown for 5-ethyl-2-mercapto-3-thenylidenecyclohexylamine (5-ethyl-3-cyclohexylaminomethylene-1-thiolen-2-thione) and compound (XXXIII).[64] As a result of the protonation of the azomethine atom, it is reduced in

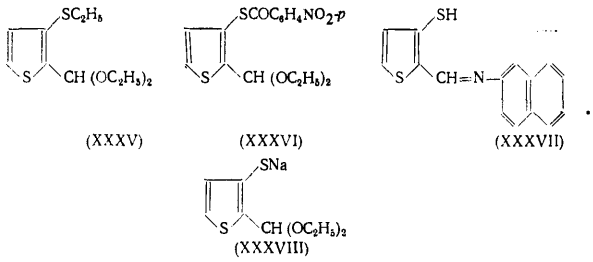
dimethylformamide (DMF) much more readily than compound (XXXIV), in which the hydrogen atom has been substituted and therefore the formation of an intermolecular hydrogen bond is ruled out:



(XXXIII) (XXXIV)

3. Effect of Sodium in Liquid Ammonia on the Diethylacetal of 3-Ethylthiothiophen-2-aldehyde

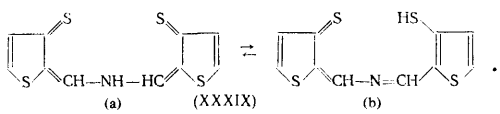
If the possibility of the occurrence of structures of types A–C (Scheme 1) depended ultimately only on the geometry of the ring, one might expect that the acetals of 3-alkylthiothiophen-2-aldehydes (XXXV) should be converted into the isomeric mercaptoaldimines (XVIII). However, the different relative positions of the functional groups in the thiophen ring might entail differences in reactivity. In contrast to the observations for the acetal (XVII), with the acetal (XXXV), the reaction reached completion after the addition of six equivalents of sodium and a high yield of 3-mercapto-2-methylthiophen was obtained[65]:



(XXXV) (XXXVI) (XXXVII) (XXXVIII)

If the amount of added sodium is restricted to two equivalents, it is possible to isolate from the resulting mixture 20–30% of the initial acetal and the dealkylation product in the form of the *p*-nitrobenzoyl derivative (XXXVI) or the Schiff base (XXXVII). Thus the processes involving two equivalents of sodium are in broad outline analogous for the acetals (XVII) and (XXXV) and lead to identical products, but they differ as regards quantitative relations.

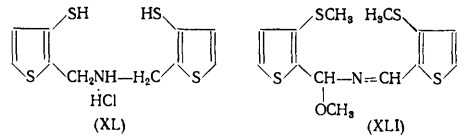
A different situation is observed when an acid is allowed to act on an alkaline solution of the mercaptide (XXXVIII) in the presence of ammonia. At pH ~ 8, under conditions analogous to those in the formation of compound (XVIII), a substance with the composition $C_{10}H_7NS_4$ is isolated and not the mercaptoaldimine. The structure of this compound can be best represented by the formulae (XXXIXa) and (XXXIXb), which reflect its tautomeric nature[66]:



(a) (XXXIX) (b)

This representation is supported by the following data. The molecule of compound (XXXIX) is found to have one active hydrogen atom; its infrared spectrum contains absorption bands in the region 1135–1157 cm^{-1}, which are characteristic of the –C=C–C=S group[67] and a band in the region of 3300 cm^{-1}, which may be assigned to the stretching vibrations of the secondary amino-group. The ^1H NMR spectrum of compound (XXXIX) in dimethyl sulphoxide corresponds better to structure (XXXIXa) than to structure (XXXIXb).

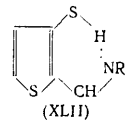
When compound (XXXIX) was treated with lithium aluminium hydride, an amine was obtained, isolated as the hydrochloride (XL). Compound (XXXIX) also yields an acetyl derivative, the reductive desulphuration of which with Raney nickel yields *NN*-dipentylacetamide. All these findings are consistent with formula (XXXIXa), although, as already mentioned, one cannot rule out a tautomeric equilibrium (see above):



(XL) (XLI)

An interesting reaction, confirming the presence in the molecule of (XXXIX) of an $\alpha\beta$-unsaturated thione group, occurs with methyl iodide in a methanol solution of potassium hydroxide. The resulting product probably has the structure (XLI), the formation of which can be accounted for by the 1,4-addition of methanol to the C=C–C=S molecular fragment.

On reaction with amines, compound (XXXIX) yields Schiff bases (XLII), one molecule of (XXXIX) giving two molecules of a new base. This process may be interpreted in different ways, in particular by regarding it as the aminolysis of (XXXIX) with a stage involving addition to the C= N bond[68] or it can be treated, by analogy with the reaction of (XXXIX) with methanol, as 1,4-addition:



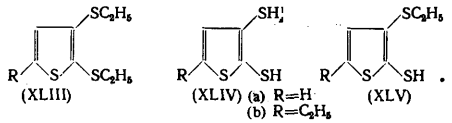
(XLII)

IV. SYNTHESIS OF DIMERCAPTOTHIOPHENS

An interesting type of complex, formed by α-dithiones or α-dithiols, which have unusual physical and chemical properties owing to their specific electronic structure, was discovered comparatively recently[69–75]. Compounds of this type, in particular the dimercapto-derivatives of benzene[76], can also be used as starting materials for further syntheses.

Of the four possible dimercaptothiophens, Gronowitz described 3,4-dimercaptothiophen[77]. His attempts to obtain the 2,4- and 2,3-isomers from the corresponding bromomercaptothiophens and also 2,5-dimercaptothiophen

from 2,5-dilithiothiophen or from magnesium bromide derivatives were unsuccessful[77,78]. The synthesis of 2,3-dimercaptothiophen derivatives was achieved by the dealkylation of di(alkylthio)-compounds of type (XLIII) with sodium in liquid ammonia[79]:



(XLIII) (XLIV) (a) R=H (b) R=C_2H_5 (XLV)

The reaction takes place smoothly and treatment with four equivalents of sodium per mole of the bis-sulphide resulted in the isolation of the corresponding dithiols (XLIVa) and (XLIVb) in a yield of 60–80%. These are viscous, coloured, liquids which vacuum-distil with decomposition. Since the bis-sulphides (XLIII) contain two identical functional groups in different positions in the thiophen ring, the problem arises whether they are dealkylated by sodium in liquid ammonia in any specific order.

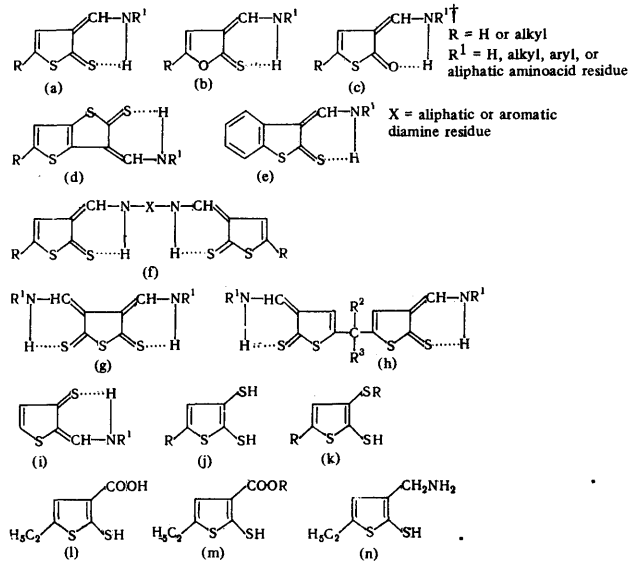
Comparatively recently it has been suggested[80,81] that the mode of cleavage of an organic sulphide by alkali metals depends to a considerably degree on the numerical values of the acidities of the mercaptide ions and carbanions formed. In the case of di(alkylthio)thiophens of type (XLIII), which have the same aliphatic group linked to the sulphur atom, the principal factor determining the order of dealkylation is probably the stabilities of the resulting thiophen-2-thiol or thiophen-3-thiol. Evidently the first is stabilised to a greater extent, since the delocalisation of the negative charge extends over the entire aromatic ring, while in the 3-isomer the delocalisation is restriced to the π-electron 1,3-system[82]:

In fact when 2,3-di(ethylthio)thiophen and 4,5-di(ethylthio)-2-ethylthiophen were treated with two equivalents of sodium in liquid ammonia, the corresponding mercaptosulphides (XLVa) and (XLVb) were isolated in a yield up to 80%.[83] That the latter are α-mercapto-derivatives of thiophen was confirmed by ^{1}H NMR data. It was found that the cleavage products (XLIIIa) and (XLIIIb) have chemical shifts and spectra identical with those of 3-ethylthio-2-mercaptothiophen and 2-ethyl-4-ethylthio-5-mercaptothiophen respectively, which were obtained by an independent method.

The delocalisation effect probably plays a decisive role in determining the mode of cleavage of bis-sulphide derivatives of thiophen with different alkylthio-substituents, for example 2-butylthio-3-ethylthiothiophen. If it is assumed that the ease of removal of the primary alkyl group as carbanions decreases in the sequence $CH_3 > C_2H_5 > C_4H_9$,[81] then the ethyl group should be preferentially eliminated from this bis-sulphide with formation of 2-butylthio-3-mercaptothiophen. However, the only product isolated in the reaction of this bis-sulphide with sodium in liquid ammonia was 3-ethylthio-2-mercaptothiophen.

V. TYPES OF LIGANDS AND CERTAIN CHELATE COMPOUNDS

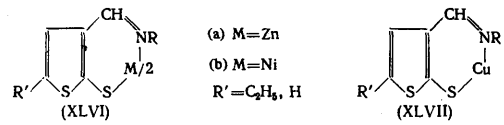
The formulae of the principal types of di- and tetrafunctional complex-forming compounds synthesised by the authors are given below¶:



5-Ethyl-2-mercaptothiophen-3-carboxylic acid (l)—the thiophen analogue of thiosalicylic acid—was obtained in 90% yield by the action of two equivalents of sodium in liquid ammonia on 5-ethyl-2-ethylthiothiophen-3-carboxylic acid[41]. The acid (l) forms a disulphide and in an alkaline medium is alkylated at the mercapto-group. Esterification in the presence of hydrogen chloride results in the formation of the corresponding esters (m).[85]

Some of the synthesised thiophen derivatives of types (a), (b), (c), (d), (e), (f), (i), (k), and (m) have been used to prepare chelate complexes with copper, zinc, and nickel ions. They were obtained by the reaction of the ligands in a suitable solvent with aqueous methanol solutions of the metal acetate or by the "method of nascent reagents"[86]. The data concerning the chelate complexes isolated are described in the literature[41,42,59].

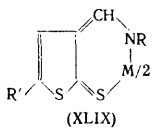
Compounds of the type (a) form with zinc and nickel ions the chelates (XLVIa) and (XLVIb) in which the ligand : metal ratio is 2 : 1, while in the copper complexes (XLVII) and in the complexes (XLVIII) of tetradentate ligands of type (f) the ratio is 1 : 1.

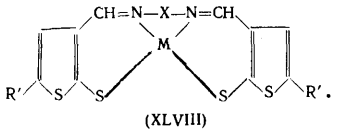


(XLVI) (a) M=Zn (b) M=Ni R′=C_2H_5, H (XLVII)

¶ For brevity only one of the possible tautomeric forms is quoted. For compounds (d), (e), and (h), the ^{1}H NMR spectra were not investigated and the thione structures are quoted by analogy.

† Compounds with the structure (c), which are oxygen analogues of mercaptoaldimine derivatives of thiophen, are formed when primary amines react with *NN*-disubstituted 5-alkyl-3-aminomethylene-4-thiolen-2-ones[84].

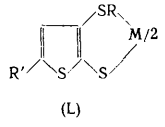

(XLIX)

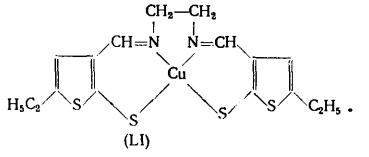

(XLVIII)

These are brightly coloured crystalline compounds fairly readily soluble in the usual organic solvents, for example in benzene and chloroform.

The infrared spectra of chelates of type (XLVI) contain stretching vibration bands in the region 1595–1610 cm^{-1}, which may be assigned to the vibrations of the coordinated C=N group[41] (cf. Trompson and Busch[87]). However, one should bear in mind that the structure of the metal chelates represented by formulae (XLVI), (XLVIII), etc. is not the only one possible, since the tautomerism characteristic of the corresponding ligands can also obtain in the chelate complexes formed by them. The problem of which form, (XLVI) or (XLIX), predominates under particular conditions must be regarded as open at the present time.

On interaction with nickel and copper acetates in methanol, dimercaptothiophen (j) forms black infusible powders insoluble in the usual solvents[79]. Probably they are polymeric (oligomeric) complexes analogous to the polymeric bisdithioglyoxalnickel complexes[69]. On the other hand, alkylthiomercaptothiophens (m) form with nickel acetate the chelate compounds (L) in which the metal : ligand ratio is 1 : 2. In contrast to the complexes formed by dimercaptothiophen (j), they have definite melting points:


(L)

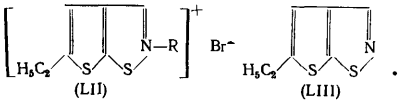

(LI)

Valuable information about the type of metal–ligand bond in complexes may be obtained from ESR spectra. This of course applies only to paramagnetic compounds incorporating a metal atom (ion) with one or several unpaired electrons. An example of such a compound is [bis-(5-ethyl-2-mercapto-3-thenylidene)ethylenediaminato]copper(II) (LI), in which the immediate environment of the central metal atom resembles that in copper(II) complexes with the Schiff bases of salicylaldehyde.

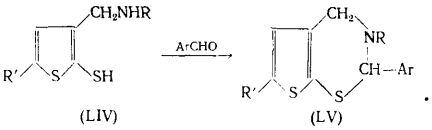
The ESR spectrum of this complex[88] contains, apart from the four lines generated as a result of the interaction of the unpaired electron spin with the spins of the copper nuclei[63,65], an additional hyperfine 11-line structure. Detailed analysis of the spectrum combined with a comparison with the literature data led to the conclusion that these 11 additional hyperfine structure lines are due to the pair interactions of the unpaired electron spin with the spins of the nuclei of ^{14}N and the CH protons.

VI. SOME REACTIONS OF THE MERCAPTOALDIMINES AND THEIR CHELATES

The presence in mercaptoaldimines of type (XVIII) of two highly reactive functional groups linked to adjacent carbon atoms of the thiophen ring creates interesting possibilities for the synthesis of new condensed bicyclic compounds. One of the ways in which such systems can be obtained consists in simple bromination of compound (XVIII) by an equimolar amount of bromine in chloroform. The reaction is accompanied by the evolution of hydrogen bromide and probably proceeds via a stage involving the formation of sulphene bromide, which undergoes ring closure to the bicyclic system (LII):[43]


(LII) (LIII)

As a result of hydrolysis, compound (LII, R = H) loses HBr, yielding 5-ethylthieno[3,2-*d*]isothiazole (LIII), which has also been obtained by the oxidation of 5-ethyl-2-mercapto-3-thenylamine (LIVa) with iodine. Mercaptothenylamines (LIVa) and (LIVb), formed in high yields when the corresponding mercaptoaldimines are reduced with lithium aluminium hydride[43], are also capable of entering into reactions leading to the formation of condensed systems. Thus they react with aldehydes to form derivatives belonging to the class of 3,4-dihydrothieno-1,3-thiazines (LV):[89]


(LIV) (LV)

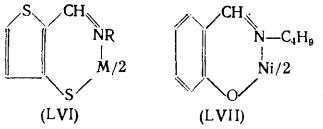
(a) R = H
(b) R = cyclo-C_6H_{11}; R′ = C_2H_5.

The above examples do not of course exhaust the possibilities of the use of different types of thiophen derivatives in syntheses. They illustrate only one of the developments in the chemistry of these compounds.

At the same time, as noted in the introduction, the study of the reactivities of the coordinated ligands examined is of greatest interest. Here we may note that we are at present only at the beginning of the development of this field.

On the basis of studies related to this field, Jones[90–93] arrived at the following most general conclusion: coordination does not alter the orientation of the substitution in the organic part of the ligand, but, by influencing the nature of the transition state, can cause appreciable changes in the rate of reaction. For example, many electrophilic substitution reactions of bis-(8-hydroxyquinolinato)copper take place more readily than with the free ligand[93].

Chelates of type (XLVI) and (LVI) can be regarded as condensed systems, one of the rings of which includes a metal ion as a unit. The problem of the reactivity of such compounds, which are readily susceptible to the action of both electrophilic and nucleophilic agents since they incorporate the thiophen ring, is of considerable interest:

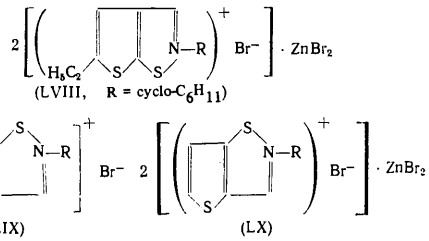

(LVI) (LVII)

(a) M = Zn; (b) M = Ni; R = cyclo-C_6H_{11}.

Treatment of bis-(salicylidenebutylaminato)nickel (LVII) with *N*-bromosuccinimide (NBS) is known to yield a dibromo-derivative[94,95], but the question of its structure remains open. It has been shown only recently[96] that initially bromine enters the 5-position of each ring and on subsequent bromination also the 3-position. The complex with cobalt(III) reacts similarly. Thus, when bromine is introduced by treatment by NBS, the chelate ring (LVII)

is not cleaved. A different behaviour is observed when the chelates (XLVI) and (LVI) are subjected to attack by bromine and NBS.[97] The nickel chelate (XLVIb, R = cyclo-C_6H_{11}, R′ = C_2H_5) reacts with two moles of bromine in chloroform to form 2-cyclohexyl-5-ethylthieno[3,2-*d*]-isothiazolium bromide, which is isolated from the mixture as the perbromide; as stated above, this compound is also obtained by the direct action of bromine on the corresponding ligand. The results are similar when NBS is employed as a brominating agent. When the zinc chelate (XLVIa, R = cyclo-C_6H_{11}, R′ = C_2H_5) is treated with bromine, a complex of thienoisothiazolium bromide with zinc bromide (LVIII) is formed.

In contrast to (XLVI), in the complexes (LVI) there are two hydrogen atoms in each thiophen ring potentially capable of being substituted by electrophilic agents. Consequently, one might expect here the formation of bromination products if the rate of substitution exceeded the rate of reaction of the electrophilic agent with the chelate ring. However, when the nickel chelate (LVIb) is treated with two moles of bromine or NBS in chloroform, the chelate ring is in fact also cleaved and 2-cyclohexylthieno[2,3-*d*]isothiazolium bromide (LIX) is formed in a mixture with its perbromide[97]:



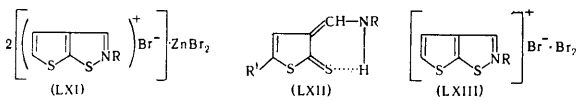
(LVIII, R = cyclo-C_6H_{11})

(LIX) (LX)

The zinc chelate (LVIa) reacts with bromine similarly to the nickel chelate, forming the complex (LX).

Summarising, one may say that the nickel and zinc chelates of both types (XLVIa and XLVIb, R = cyclo-C_6H_{11}, R′ = C_2H_5) and (LVI) are unstable under conditions corresponding to bromination with bromine and NBS.

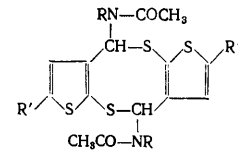
The study of the action of bromine in chloroform on the chelate (XLVIa, R = cyclo-C_6H_{11}, R′ = H)[42] showed that, as for the homologue substituted in the 5-position, the chelate ring is the primary site of attack, which ultimately leads to the formation of the complex (LXI) with zinc bromide. A similar bicyclic system is obtained also when the Schiff base (LXIIa) is brominated, the reaction product being isolated as the perbromide (LXIII). Consequently in both cases the α-hydrogen atom in the thiophen ring is not substituted:



(LXI) (LXII) (LXIII)

(a) R′ = H; (b) R′ = C_2H_5, R = cyclo-C_6H_{11}.

Together with bromination, the action of acetic anhydride in the presence of boron trifluoride-ether was investigated; this method has been successfully employed for the acetylation of metal acetylacetonates[98]. However, it proved impossible to introduce the acetyl group into the thiophen ring of the chelate (XLVIa, R = cyclo-C_6H_{11}, R′ = H) under these conditions. The final product isolated was a substance for which the structure of dithienodithiocine (LXIVa) was proposed on the basis of infrared spectra and data for reductive desulphuration; it is also formed when compound (LXIIa) is treated with acetic anhydride. A homologue of compound (LXIVa), compound (LXIVb), was obtained under the same conditions:

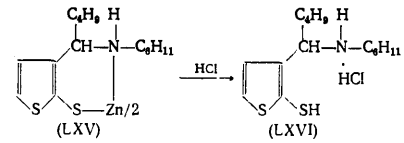


(LXIVa, R′ = H); (LXIVb, R′ = C_2H_5, R = cyclo-C_6H_{11})

Summarising, one can also say that the presence of an unsubstituted α-position in chelates of type (XLVI) does not entail a change in the direction of electrophilic attack compared with their substituted analogues. In such systems the process involving the chelate ring, which ultimately results in its decomposition, also predominates. The deactivation of the thiophen ring probably plays a significant role in this phenomenon, but one cannot rule out *a priori* an effect of the geometrical parameters of the condensed chelate ring, which may influence its stability.

It is quite evident that organometallic compounds behaving as nucleophilic agents can act also on other centres in the molecule of the type (XLVIa) complex. In principle, these chelates may be capable of coordination via the thiophen sulphur atom. As mentioned above, some investigators believe that such a process is a preliminary stage in the metallation of the thiophen ring by organometallic compounds, for example n-butyl-lithium.

By treating the chelate (XLVIa, R = cyclo-C_6H_{11}, R′ = H) with an excess of butyl-lithium, compound (LXV) was obtained[42], which on treatment with hydrogen chloride yields the hydrochloride (LXVI). The formation of compound (LXV) might have been regarded as an example of the addition of an organometallic compound to the azomethine bond, which is characteristic of aromatic and aliphatic aldimines[99] and pyridine bases[100]:



(LXV) (LXVI)

However, since the nitrogen atom in the initial chelate is coordinated, forming a unit of the chelate ring, compound (LXV) is probably formed by another mechanism. In order to determine whether butyl-lithium is coordinated to the ring sulphur atom at any stage, a study was made of the reaction of the chelate (XLVIa, R′ = H) with butyl-lithium and carbon dioxide but carboxylic acid was never detected.

Here one should note that, in an examination of the reactions of type (XLVI) chelates, one cannot rule out the possibility of their involvement in the reactions in the tautomeric form (XLIX).

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In undertaking this review, the authors wished to draw attention to the methods of preparation and certain properties of complex-forming compounds which in a certain sense may be regarded as new. The metal chelates mentioned in the review, the number of which is fairly limited have been treated mainly as derivatives indicating the complex-forming properties of the compounds synthesised. The problem of their steric structure and other physical properties as well as the synthesis of other chelate compounds of this series will be the subject of future investigations.

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Advances in the Chemistry of Aliphatic Diazoketones

A.L.Fridman, G.S.Ismagilova, V.S.Zalesov, and S.S.Novikov

The review deals with the methods of synthesis of aliphatic diazoketones and gives a systematic account of the extensive literature data on their chemistry. The work on the physical properties, structures, and ultraviolet, infrared, and NMR spectra of diazoketones is summarised in a separate section where problems of $p-\pi$ conjugation and rotational isomerism are also discussed. The concluding section deals with the hitherto few but interesting data on the biological activity of diazoketones.
The bibliography includes 295 references.

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INTRODUCTION

The remarkable part which aliphatic diazoketones have played in the development of organic chemistry is well known. Numerous original papers, reviews, and monographs have been devoted to these compounds[1-10].

The aim of the present review is to give a systematic account of the literature data for the methods of synthesis, spectra, structure, and chemical properties of diazoketones. Earlier such attempts were not made, although they merit special consideration in view of some of their characteristics.

The earlier reviews emphasise primarily the fact that aliphatic diazo-compounds have common properties. Therefore these reviews and the present review are not mutually exclusive but complement one another. The inevitable repetition may be justified in each case by the novelty of approach to the analysis of literature data and by the authors' wish to give a complete presentation of the available information.

In recent years interesting data were obtained on the structure of diazoketones, which, in contrast to diazoalkanes, have many structural characteristics and show an unusual chemical behaviour owing to the presence of the α-carbonyl group. $p-\pi$ conjugation, which involves a chain of five atoms in the $COCH_2N_2$ fragment, leads to the appearance of partial bonds. As a result, free rotation about the C–C bond is hindered and *cis–trans* conformers are produced. In the discussion of the structure of diazoketones, ultraviolet, infrared, and NMR spectroscopic data, dipole moments, and also calculations by the molecular orbital method are invoked.

The present review gives a brief account of the methods of synthesis of diazoketones. In order to demonstrate the large number and great variety of procedures, we have described both well known methods developed long ago as well as methods which have appeared recently. In the discussion of chemical reactions, certain reactions of diazoketones have been omitted. In particular the large series of studies on the addition of diazoketones to double bonds is not dealt with, since many excellent reviews have been devoted to this reaction[8,9]. On the other hand, we considered the reactions which have not as yet been developed adequately but have undoubted interest for the further development of the chemistry of diazo-compounds.

The last section of the review deals with data on the biological activity of diazocarbonyl compounds. The fact that certain diazoketones inhibit the growth of malignant tumours is noteworthy.

II. METHODS OF SYNTHESIS

The methods of preparation of diazoketones may be divided into seven principal groups: (1) *C*-acylation of aliphatic diazo-compounds; (2) reaction of organic azides with active methylene compounds; (3) oxidation of monohydrazones of α-aldehydoketones and α-diketones; (4) diazotisation of primary amines containing a carbonyl group; (5) diazotisation of ketoximes; (6) alkaline cleavage of *N*-acyl-*N*-nitrosamines; (7) alkaline cleavage of tosylhydrazones of α-carbonyl compounds. Within the limits of the scope of the present review, each of the above methods is discussed below.

1. *C*-Acylation of Aliphatic Diazo-compounds

The method consists of the direct acylation of diazo-derivatives by carboxylic acid halides and anhydrides. The nature of the product formed depends considerably on the reaction conditions and on the structure of the diazo-compounds and acylating agents. For example, acetyl chloride reacts with diazoacetic ester according to the mechanism[11]

$$ClCOCH_3 + N_2CHCOOC_2H_5 \longrightarrow C_2H_5COOCN_2COCH_3.$$

The reaction of carboxylic acid chlorides with diazo-compounds without an activated α-hydrogen atom takes place differently[11]:

$$R{-}COCl + N_2C(C_6H_5)_2 \rightarrow R{-}\overset{\overset{O}{\|}}{C}{-}\overset{\overset{Cl}{|}}{C}(C_6H_5)_2 + N_2 .$$

The reaction of aromatic acid chlorides with diazomethane at room temperature using equimolar amounts of the reactants leads to the formation of aryl chloromethyl ketones[12-15]:

$$C_6H_5COCl+CH_2N_2\longrightarrow C_6H_5COCH_2Cl+N_2\,.$$

C-Acylation of diazoalkanes takes place in the presence of an excess of the latter at a reduced temperature (0–5°C) and may be described by the following mechanism[16-19]:

$$R-COCl+2CH_2N_2\longrightarrow R-COCHN_2+HCl,$$
$$HCl+CH_2N_2\longrightarrow CH_3Cl+N_2\,.$$

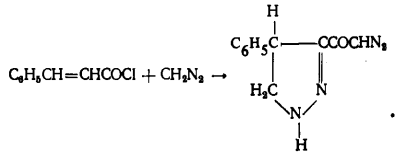
In the presence of a deficiency of diazoalkane, a side reaction leading to the formation of a chloromethyl ketone is possible:

$$HCl+R-COCHN_2\longrightarrow R-COCH_2Cl+N_2\,.$$

Triethylamine may be used to combine with hydrogen chloride[20]. An excess of diazoalkane promotes the formation of an azine[21,22].

The method of *C*-acylation of diazo-compounds (the Arndt–Eistert method) has been developed in fair detail and is widely used to synthesise not only primary but also secondary diazoketones[23]. It constitutes the basis of the synthesis of mono-, bis-, and tris-diazoketones[24,25]. Thus 1,3,5-tridiazoacetylbenzene has been obtained by treating trimesoyl chloride with an excess of diazomethane[25].

The reaction of diazomethane with unsaturated acid chlorides results in its 1,3-cycloaddition to the double bond simultaneously with *C*-acylation[26-28]:



Many different diazoketones, including derivatives with heterocyclic and perfluoroalkyl substituents[29-32] and also with heteroatoms in the chain, have been obtained by the Arndt–Eistert method[33,34]:

$$ClCOCH_2N(NO_2)CH_2COCl+CH_2N_2\rightarrow N_2CHCOCH_2N(NO_2)CH_2COCHN_2\,.$$

A systematic account of all past studies on the Arndt–Eistert reaction is given in a review by Bachmann and Struve[1].

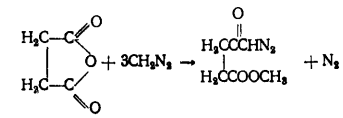
While *C*-acylation of diazo-compounds by carboxylic acid chlorides and bromides has been investigated in fair detail, acid fluorides are rarely used for this purpose. The synthesis of diazoacetaldehydes may serve as an example[35]:

$$HC(=O)F+CH_2N_2\rightarrow HC(=O)CHN_2\,.$$

There are also only a few examples of the *C*-acylation of diazo-compounds by carboxylic acid anhydrides[5,36-40]. Benzoic acid anhydride reacts with diazomethane to form diazoacetophenone[36]. Trifluorodiazoacetone is formed in the reaction between diazomethane and the mixed anhydride of acetic and trifluoroacetic acids[5]:

$$F_3CC(=O)-O-C(=O)CH_3+2CH_2N_2\rightarrow F_3CC(=O)CHN_2+CH_3COOCH_3+N_2\,.$$

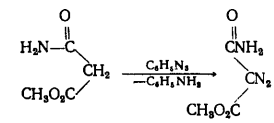
Anhydrides of dibasic acids are converted into monodiazoketones[37]:



The mechanism of the *C*-acylation of diazoalkanes has been frequently discussed in the literature and therefore we do not consider it here[2-4].

2. Reactions of Organic Azides with Active Methylene Compounds

The reaction involving the introduction of diazo-groups into an active methylene group with the aid of phenyl azide was discovered in 1910 by Dimroth[41]:



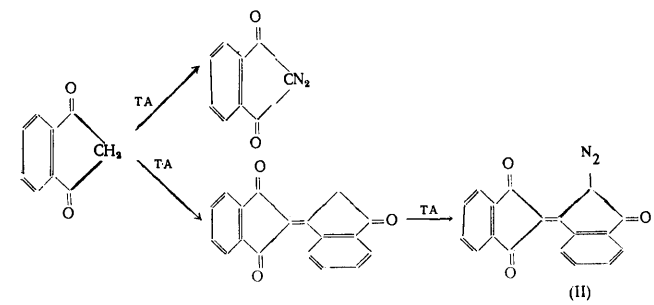
Later it was shown that *p*-tosyl azide can also be used to transfer the diazo-group[42]. However, at the time this interesting method of preparing diazo-compounds did not attract attention and its detailed development began as late as 1953[43-50]. The method proved to be suitable for the synthesis of cyclic diazo-compounds[44-48], including diazoketones[49,50]. The reaction is carried out in ethanol in the presence of potassium ethoxide, triethylamine[51,52], or potassium hydroxide[53] and also in methanol in the presence of sodium methoxide[54].

Diazoketones are not always obtained in a pure form owing to the formation of secondary reaction products. Thus, in the reaction of *p*-tosyl azide with benzoyl-(*p*-nitrobenzoyl)methane in methylene chloride in the presence of pyridine, the process does not stop at the stage involving the formation of product (I):

$$C_6H_5COCH_2C_6H_4NO_2\text{-}p\longrightarrow C_6H_5COCN_2C_6H_4NO_2\text{-}p\,.$$
(I)

The product is partly cleaved into benzoyl diazomethane and *p*-nitrobenzoyldiazomethane. The separation of the mixture of diazo-derivatives is difficult[55]. Pure diazoketone (I) may be obtained when the reaction is carried out in ethanol with added catalytic amounts of triethylamine[53,55].

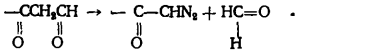
The formation of a mixture of diazo-compounds was also noted in the synthesis of 2-diazoindan-1,3-dione. The principal reaction product is 2-diazo-1′,3,3′-trioxo-1,2′-bisindanylidene (II), which arises as a result of the self-condensation of indan-1,3-dione under the influence of a base. The self-condensation product reacts further with tosyl azide (TA)[51]:



(II)

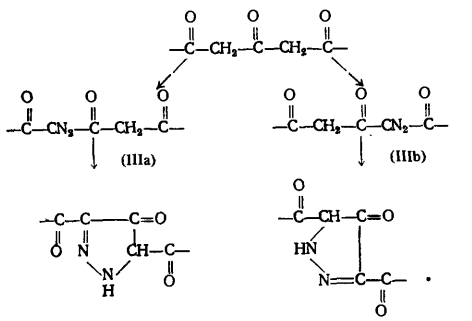
Carbonyl compounds of the type $-CH_2C(=O)-$ react with sulphonyl azides to form diazo-derivatives when the C–H group is sufficiently activated[56-61].

β-Oxoaldehydes are convenient acceptors of the diazo-group. Ketones, which are unsuitable for the direct introduction of the diazo-group, are converted by the Claisen condensation into β-oxocarbonyl compounds. The latter are smoothly converted into diazoketones, with elimination of the formyl group[62,63]:



α-Formylcycloalkanones are also readily converted into diazocycloalkanones[62-65]:

In the reaction of 1,3,5-triketones with tosyl azide, pyrazolones were isolated in high yields, instead of the expected bisdiazoketones. The formation of the pyrazolones is due to an intramolecular reaction of the intermediate diazoketone (IIIa,b)[66]:



However, when the reactants are mixed slowly, the reaction can be driven towards the formation of bisdiazoketones[67]:

$$C_6H_5COCH_2COCH_2COC_6H_5 + CH_3C_6H_4SO_2N_3 \rightarrow C_6H_5COCN_2COCN_2COC_6H_5 .$$

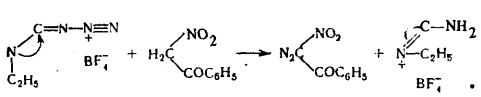
Diazoketones are formed in the reaction of enamines with arenesulphonyl azides[68,69]:

$$C_6H_5COCH{=}CHN(CH_3)C_6H_5 \xrightarrow{TA} C_6H_5COCHN_2 .$$

The method involving the transfer of the diazo-group to active methylene compounds has proved suitable for the synthesis of diazoaldehydes[68] and other diazo-compounds: diazosulphones[54,70], α-diazophosphinoketones, and α-diazophosphinoethers[71,72]. For example, diazoaldehydes are formed according to the mechanism:

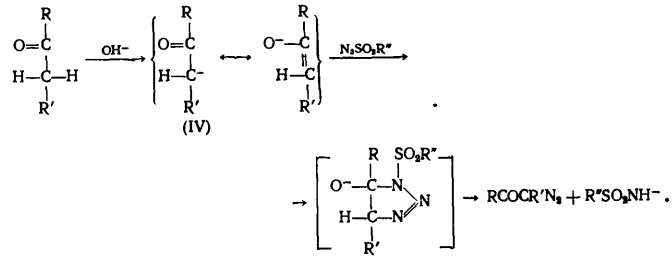
$$(H_3C)_2N{-}CH{=}\overset{R}{\overset{|}{C}}{-}CHO \xrightarrow{TA} RCN_2CHO .$$

Attempts to extend this method to the synthesis of nitrodiazoketones have been described. Azidinium salts were used as donors of the diazo-group. The reaction takes place in methanol at room temperature in the presence of sodium acetate[73]:



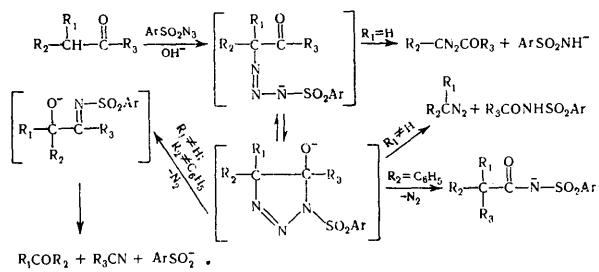
Various mechanisms for the reaction of organic azides with active methylene compounds have been proposed[56,58,74].

The cyclic mechanism is the most probable. In the first stage the diazo-group acceptor is converted under the influence of the base into a carbanion in which a double bond may be formed. The subsequent addition of the sulphonyl azide to the anion (IV) leads to the formation of a triazoline which dissociates into a diazo-compound and a sulphonamide[56,58]:



Some workers believe that the formation of a cyclic intermediate product is possible only when the activated methylene group contains one hydrogen atom[74].

A general mechanism has been proposed for the transfer of the diazo-group, which can explain the formation of diazoketones, amides, ketones, cyano-derivatives, and sulphonate salts[74]:



3. Oxidation of Monohydrazones of α-Aldehydoketones and α-Diketones

In 1889 Curtius obtained benzoylphenyldiazomethane by oxidising benzilhydrazone with yellow mercury(II) oxide in cold benzene solution[75]:

$$C_6H_5COC{=}N{-}NH_2 + HgO \rightarrow \underset{\displaystyle C_6H_5}{\overset{\displaystyle O}{\overset{\|}{C}}}{-}\overset{\displaystyle C_6H_5}{\overset{|}{C}}{-}CN_2 + Hg + H_2O .$$

Subsequently mercury(II) oxide was used for this purpose also by other investigators[76-86].

Other metal oxides are also widely used for the synthesis of diazoketones. The oxidation of diacetyl monohydrazone with silver oxide in the presence of anhydrous sodium sulphate has been described[87]:

$$\underset{\displaystyle O\ \ CH_3}{\overset{\displaystyle O}{\overset{\|}{C}}}{-}C{=}N{-}NH_2 + Ag_2O \xrightarrow{Na_2SO_4} \underset{\displaystyle O\ \ N_2}{\overset{\displaystyle O}{\overset{\|}{C}}}{-}CCH_3 + Ag + Na_2SO_4 \cdot H_2O .$$

As a rule, in the presence of drying agents such as sodium or magnesium sulphate silver oxide is used only in those cases where other oxidants (HgO, CuO, PbO) are ineffective[88].

A mixture of sodium hydroxide and calcium hypochlorite in aqueous methanol has been used to synthesise 3-diazo-D-camphor[89]. Recently activated manganese dioxide has been suggested as an oxidant. The reaction was carried

out in chloroform at room temperature, diazoketones being formed in quantitative yields[89-91]:

$$RCOCH=N-NH_2+MnO_2\longrightarrow RCOCHN_2 .$$

It is noteworthy that the oxidation of hydrazones by metal oxides is used mainly for the preparation of acyclic monodiazoketones and aryl-substituted diazomethanes[92].

4. Diazotisation of Primary Amines

This method has been used to synthesise diazoacetophenone[93]:

$$C_6H_5COCH_2NH_2\cdot HCl+NaNO_2\longrightarrow C_6H_5COCHN_2 .$$

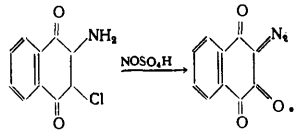
Later the method was employed to synthesise many cyclic diazoketones[93-97]. Diazotisation of an amino-group located between two carbonyl groups leads to the formation of the corresponding diazoketones[98-101]:

$$RC(=O)-CH(NH_2)-CR(=O)\rightarrow RC(=O)-CN_2-CR(=O) .$$

Intermediates obtained by the reduction of nitration, nitrosation, or azo-coupling products and not the pure amines are as a rule employed in the reaction[5]. The diazotisation takes place via a diazohydroxide, which, depending on the mobility of the α-atom, is converted either into a diazo-compound or an alcohol is formed with evolution of nitrogen[3]. In the case of α-aminoketones and α-aminoacid esters, an activated methylene group removes a proton with formation of diazoketones or diazoesters:

$$RCOCH_2NH_2\cdot HCl+NaNO_2\xrightarrow{H^+}RCOCH_2NH{-}NO\rightarrow RCON{=}NOH\rightarrow RCOCHN_2+H_2O .$$

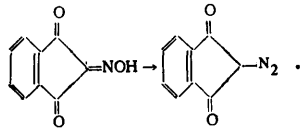
The use of nitrosylsulphuric acid as a nitrosating agent has been described[102,103]. The diazotisation of 2-amino-3-chloro-1,4-naphthoquinone with this reagent is accompanied by oxidation, which leads to the formation of 2-diazo-1,3,4-trioxotetralin[102]:



Similarly 2,5-diamino-3,6-dichlorobenzoquinone forms 1,4-bisdiazotetraoxocyclohexane[102].

5. Diazotisation of Oximes

Several examples of the conversion of cyclic ketoximes into α-diazoketones under the influence of chloramine via the familiar Forster reaction[104] have been described:



The reaction is carried out in a cooled alkaline medium. The method is used to synthesise a wide variety of cyclic diazoketones[105-108]. The synthesis of condensed polycyclic bisdiazoketones was described recently[109].

6. Alkaline Cleavage of *N*-Acyl-*N*-nitrosamines

Diazoketones with the structure $H_3CCOCN_2CH_2R$ may be obtained via the mechanism[110]

$$RCH(NH_2)COOCH_3 \xrightarrow[\text{pyridine}]{Ac_2O} RCH(COCH_3)-NH-COCH_3 \xrightarrow{N_2O_3} RCH(COCH_3)-N(NO)-COCH_3 \xrightarrow{NaOCH_3} RC(=N_2)-COCH_3 .$$

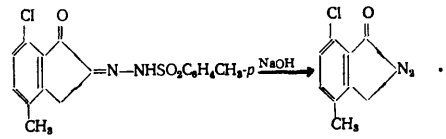
The conversion of aminoacids into *N*-acylaminoketones has been investigated in detail[111]. *N*-Nitroso-derivatives are formed in the nitrosation of *N*-acylaminoketones with N_2O_3 in glacial acetic acid. They are subsequently decomposed to diazoketones with sodium methoxide[110]. Benzoylphenyldiazomethane with a labelled carbonyl carbon atom was obtained by the above mechanism[111].

Alkaline cleavage of nitrosourethanes containing the sulphone group makes it possible to obtain diazosulphones[112]:

$$H_3CCOC_6H_4SO_2CH_2NHCOOC_2H_5 \xrightarrow{KOH} H_3CCOC_6H_4SO_2CHN_2 .$$

7. Alkaline Cleavage of Tosylhydrazones of α-Carbonyl Compounds

The method was first used to synthesise 7-chloro-2-diazo-4-methylindan-1-one[105]:



The reaction proved convenient for the synthesis of cyclic diazoketones. It takes place in pentane, ether, and methylene chloride at a low temperature in the presence of sodium hydroxide or basic alumina. A series of papers dealing with detailed studies of this reaction have been published[25,113-118].

Other methods of synthesising diazocarbonyl compounds are also known. For example, the synthesis of *N*-acetyldiazoacetamide by the reduction of *N*-acetyl-3-benzylsydnoneamine in methanol in the presence of palladised charcoal has been described[119].

In choosing the method of synthesis of diazoketones, it is of course necessary to take into account the specific features of the method and the characteristics of the structure of the diazo-derivatives. The Arndt–Eistert method and the reactions of organic azides with active methylene compounds are the most common and universal.

III. SPECTRA AND STRUCTURE

1. General Characteristics

The lowest representatives of the diazoketone series are liquids. For example, diazoacetone is a mobile pale-yellow liquid with b.p. 46–47°/13 mm and d_4^{20} = 1.0864.[120] 1-Diazo-2,3-dimethylbutan-2-one is a brick-red liquid with b.p. 69°/15 mm, d_4^{25} = 0.9630, and n_D^{25} = 1.4709.[121] The higher diazoketones are crystalline substances. Depending on the substituents, their colour

varies from lemon-yellow to white. As a rule, diazoketones are readily soluble in organic solvents. The accumulation of electronegative substituents in the diazoketone molecule, for example of carbonyl and nitro-groups, leads to an increase of the melting point, a "lightening" of the colour, and an increase of chemical stability.

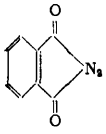
Certain diazoketones have a specific odour, for example diazoacetophenone and diazoacetone.

In contrast to diazoalkanes, diazoketones can be stored for a long time in the dark at 0–20°C; they decompose under the influence of sunlight. The liquid compounds may decompose on coming into contact with a rough surface. Special care is necessary in the distillation of diazoketones: rapid heating (at about 100°C) leads to explosion[5].

2. Spectra and Structure

The ultraviolet spectra of diazoketones have two absorption bands: in the range 240–270 nm and in the range 270–301 nm.[122–125] Table 1 shows the dependence of the electronic spectra on solvents. In protic solvents, the intensity of the first band diminishes relative to that of the second[126].

Table 1. Ultraviolet spectra of certain diazoketones[51,122].

Diazoketone	λ_{max}, nm		ϵ_{max}*, litre mole^{-1} cm^{-1}	Solvent
$N_2CHCO(CH_2)_4COCHN_2$	247		24 800	Dioxan
	248	273	21 200	Chloroform
	248	270	19 100	Ethanol
			16 700	
$(CH_2)_3COCHN_2$	251		6 840	Methylene chloride
	250	270	6 990	Ethanol
	247	275	6 600	Water
			4 600	
	244		4 550	Methanol

* $\epsilon max = (1/bc)\ lg_{10}(I_0/I)$.

The absorption spectra of 1,8-bisdiazo-octane-2,7-dione recorded in an acetonitrile–water solvent mixture intersect at an isosbestic point[122]. It would appear that this can be readily accounted for by iso–diazo (1) or diazoketo–diazoenol (2) tautomerism:

$$R{-}CO\overline{C}H{-}\overset{+}{\overline{N}}{\equiv}N \rightleftarrows R{-}CO{-}\overline{C}{=}\overset{+}{\overline{N}}{=}NH, \quad (1)$$

$$R{-}CO\overline{C}H{-}\overset{+}{\overline{N}}{\equiv}N \rightleftarrows R{-}C(OH){=}\overline{C}{=}\overset{+}{\overline{N}}{=}\overline{N}. \quad (2)$$

However, the ultraviolet spectra of benzoyldiazoacetic ester and dimethyl $\alpha\alpha'$-bisdiazo-$\beta\beta'$-dioxoadipate, which show no tendency towards tautomeric conversion, also have an isosbestic point[125]. Fahr rejected the possibility of an intramolecular rearrangement and explained the presence of the isosbestic point by the reaction of the diazocarbonyl compound with the hydroxyl-containing solvent[125].

Special studies on the ultraviolet spectra of diazoketones in hydroxyl-containing solvents showed that Fahr's hypothesis of an intermolecular reaction between the diazoketone and the solvent cannot account for the spectra. The shift of the absorption band from 250 to 300 nm cannot be explained solely by an intermolecular reaction between the diazoketone and the solvent, since the energy difference between the two bands is fairly large (11.0 kcal mole^{-1}). It is most probable that in this case the band splits owing to a conformational equilibrium[127].

The spectra of diazoacetone in hydroxyl-containing solvents also have an isosbestic point. It could be accounted for by the presence of the *cis*- and *trans*-isomers of the diazoketone owing to the different $\pi \rightarrow \pi^*$ transitions for each isomer. However, similar effects of the solvent were observed for 2-diazocyclohexanone, 3-diazonorcamphor, and 3-diazocamphor, for which the existence of *trans*-isomers is impossible. Consequently, the effect of the solvent on the spectra of acyclic diazoketones cannot be accounted for by the occurrence of conformational isomerism[128].

In a study of the ultraviolet spectra of *para*- and *meta*-substituted derivatives of diazoacetophenone, a linear relation was observed between the shift of the 250 nm band in hexane for different *para*-substituted (F, Cl, Br, CH_3, NO_2, CH_3O, and C_2H_5O) derivatives relative to the unsubstituted compound and the activity constant σ_S for the corresponding substituent[126].

Thus, in the interpretation of the ultraviolet spectra of diazoketones, it is necessary to bear in mind that they may be significantly influenced not only by the structure of the diazo-derivatives but also by the experimental conditions. At the present time there is no unique hypothesis which would account for the above characteristics of the ultraviolet spectra of diazocarbonyl compounds. Nevertheless, on the basis of data derived from electronic absorption spectra, one may conclude that, depending on the compound investigated, the absorption bands of diazoketones correspond either to $\pi \rightarrow \pi^*$ or $\pi \rightarrow \sigma^*$ transitions or to their combination. Since α-diazoketones exhibit *s*-isomerism, the absorption bands represent the sum of the superimposed spectra of the *s-cis*- and *s-trans*-isomers[128].

The study of the electronic spectrum of diazoacetone and quantum-mechanical calculations for this compound make it possible to illustrate the $\pi \rightarrow \pi^*$ and $\pi \rightarrow \sigma^*$ transitions with the aid of the orbital energy levels. The diazoacetone molecule may be excited by ultraviolet irradiation in four ways, two of which (Figs. 1 and 2) occur in the region observed.

Fig. 1 presents the principal spectroscopic orbital energy levels and transitions for *s-cis*-diazoacetone[128]. Fig. 2 shows the predicted transition energies for *s-cis*- and *s-trans*-diazoacetones. The low and high vertical lines represent respectively the allowed and the overlap forbidden transitions[128].

In α-diazoketones with different substituents, the number of ways in which the molecule may be excited increases and the electronic spectra are more complex.

The diazo-group gives rise to a distinct band in the infrared spectra of diazoketones in the region 2058–2170 cm^{-1}, which is characteristic of the stretching vibrations of the N–N bond[125,129]. This confirms the linear structure of the diazoketones, otherwise the N–N stretching vibration would give rise to absorption in the region of 1636 cm^{-1}.[129] Moreover, in the spectra of diazoketones and diazoesters an intense absorption is observed in the region 1429–1335 cm^{-1}.[130] This band was assigned to the symmetrical stretching vibrations of the diazo-group, which are markedly displaced owing to conjugation and interaction with skeletal vibrations.

The infrared spectra of diazoacetone, diazoacetophenone, and benzoylphenyldiazomethane have been investigated in carbon tetrachloride and butanol. A change of solvent almost does not affect the position of the maximum of the band due to the N–N bond in the infrared spectrum and has little effect on its integral intensity. However, the peak intensity of this band in butanol is much lower than in carbon tetrachloride and its half-width is greater in butanol. Since this effect is observed not only for diazoacetone and diazoacetophenone but also for benzoylphenyldiazomethane which has no mobile hydrogen, it cannot be due to tautomerism but must be caused by hydrogen bonding, dipole–dipole interaction, and rotational isomerism. The formation of hydrogen bonds between the above diazoketones on the one hand and phenol and pyrrole on the other has been observed on the basis of the shift of the OH and NH absorption bands. The appearance of new absorption bands due to the carbonyl group in the low-frequency region in the spectra of diazoketones in the presence of butanol or phenol is associated with the rotational isomerism of these compounds[127].

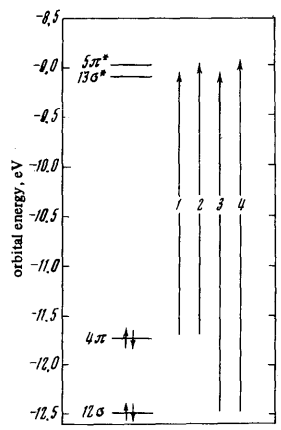


Figure 1.

Using the infrared spectroscopic data for the N–N stretching vibrations, it is possible to assess unambiguously the multiplicity of the bonds between the nitrogen atoms in the diazo-group. If the bond multiplicity is close to 3, the diazo-group absorbs at high frequencies but if the multiplicity is less than 3 the absorption shifts towards lower frequencies. This agrees well with calculations on the distribution of π-electron density in the C–N–N fragment in diazo-compounds (Table 2).

In diazomethane the π-electron cloud is appreciably displaced towards the extreme nitrogen atom and the multiplicity of the bond between the nitrogen atoms is a minimum. If the diazo-compound has substituents with –I and –C effects at the α-carbon atom, the p-electrons at this atom are delocalised over the orbitals of the atoms of the substituents, which leads to a shift of electron density from the orbital of the extreme nitrogen atom. The introduction of a carbonyl group into aliphatic diazo-compounds in the α-position relative to the diazo-group, causes a shift of the absorption bands of the diazo-group towards higher wave-numbers, on average by 40 cm^{-1}. For example, the diazo-group in diazomethane absorbs in the region of 2088 cm^{-1} and in acetyldiazomethane in the region of 2107 cm^{-1}. The introduction of a chlorine atom into the methyl group of diazoacetone promotes, owing to its inductive effect, an even greater shift of the absorption bands due to the diazo-group towards higher wave-numbers (2114 cm^{-1})[132]. The diazo-group in benzoylphenyldiazomethane absorbs in the region of 2072 cm^{-1}, which is evidence that the phenyl group at the carbon atom linked to the diazo-group behaves as an electron donor and reduces the multiplicity of the N–N bond[133]. The diazo-group in diazoacetophenone absorbs in the region of 2108 cm^{-1}.[134] The multiplicity of the bond between the nitrogen atoms increases. An example of the limiting shift of electron density in the diazo-fragment is provided by aromatic diazo-compounds.

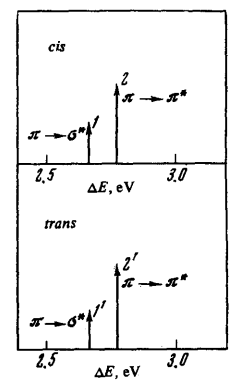


Figure 2.

Table 2. Distribution of π-electron density in the diazo-fragment[131,140].

Diazo-compound	Distribution of π-electron density in C–N–N diazo-fragment	Multiplicity of N–N bond (Ref.140)	Wave-number cm^{-1}
Diazomethane	–0.4995 +0.8418 –0.3423	2.7441	2088
Diazoacetone	–0.4214 +0.8679 –0.2095	2.8194	2103
Diazomalonic ester	–0.3869 +0.8779 –0.1486	2.8543	2188
Phenyldiazonium	+0.0062 +0.8800 +0.0772	2.9284	2304–2237

The introduction of a nitro-group in the α-position relative to the diazo-group has a considerable effect on the position of the band due to its stretching vibrations. Thus $\Delta\nu$ for diazomethane and its nitro-derivatives is 27 cm^{-1},[135] while for diazoacetophenone and its nitro-derivatives $\Delta\nu$ increases to 47 cm^{-1}.[73] A similar behaviour is observed also with N-nitraminodiazoketones[136].

The carbonyl group in diazoketones gives rise to two absorption bands in the region 1755–1620 cm^{-1}. The shift of the bands towards lower wave-numbers (1652–1620 cm^{-1}) is associated with a decrease of the multiplicity of the C=O bond[129,137], which is caused by a shift of electron density to the carbonyl oxygen atom.

The carbonyl absorption band in the spectra of diazoketones has undergone significant changes relative to the spectra of unsubstituted ketones. Thus in the spectrum of diazoacetone it is displaced towards lower wave-numbers by 60 cm^{-1}, which is due to the effect of the $p-\pi$ conjugation in the $COCHN_2$ fragment[137]. A similar shift is observed also in diazoacetophenone relative to acetophenone[134,138]. The phenyl group in diazoacetophenone increases the electron density at the oxygen atom in the carbonyl group owing to its conjugation with the ring and the carbonyl absorption band in the spectrum of diazoacetophenone is displaced towards lower wave-numbers by 26 cm^{-1} compared with diazoacetone. A negative inductive effect of substituents in diazoketones promotes a shift of the absorption bands of the carbonyl group towards higher wave-numbers. Thus, for diazoacetone and trichlorodiazoacetone, this shift is 20 cm^{-1}.[132]

The presence of two carbonyl absorption bands and several absorption bands of different intensities due to the diazo-group in the region of higher wave-numbers is due to the existence of the *s*-isomers in diazoketones[128,137].

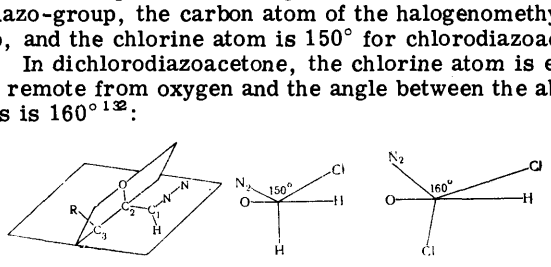
Important evidence in support of the *s*-isomerism of diazoketones was obtained in a study of NMR spectra. Kaplan and Meloy demonstrated that the NMR spectrum of diazoacetone varies with temperature, which indicates the existence of *cis*- and *trans*-isomers[139]. The NMR spectra of other diazocarbonyl compounds, recorded in the temperature range between 71° and −40°C, also confirmed the occurrence of conformational isomerism. In the temperature range investigated, the ratio of the *cis*- and *trans*-isomers of diazoacetaldehyde varied from 9 : 1 to 7 : 3.

The dipole moments of diazoketones agree with the rigid planar structure of the $COCHN_2$ fragment, where CO and CN_2 can be either in the *cis*- or the *trans*-configuration[132] (Table 3).

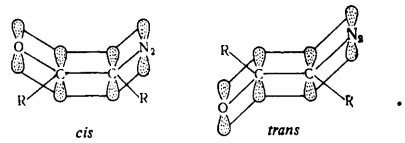
Table 3. Dipole moments of diazoketones[132].

Diazoketone	Dipole moment, debyes
CH_3COCHN_2	3.37
$ClCH_2COCHN_2$	2.80
$Cl_2CHCOCHN_2$	2.65
$Cl_3CCOCHN_2$	2.46

In diazoacetone an equilibrium is observed between the *cis*- and *trans*-conformers, while chloro-derivatives of diazoacetone are mainly in the *cis*-form. Free rotation of the halogenomethyl group about the R–CO bond is hindered by steric and electrostatic effects. The optimum angles between the planes in which the diazo-fragment is located and the plane containing the carbon atom joined to the diazo-group, the carbon atom of the halogenomethyl group, and the chlorine atom is 150° for chlorodiazoacetone. In dichlorodiazoacetone, the chlorine atom is even more remote from oxygen and the angle between the above planes is 160°[132]:



s-Isomerism in diazoketones is the result of the limited free rotation about the central carbon–carbon bond, which is caused by the interaction of the electron pair of the α-carbon with the π-electron-system of the carbonyl group:



cis *trans*

The barrier to free rotation in diazoketones about the carbon–carbon bonds is between 9 and 18 kcal $mole^{-1}$. For diazoacetone and diazopropanone, it amounts to 15.5 and 16.1 kcal $mole^{-1}$ respectively[35].

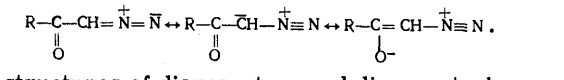
Table 4. Multiplicity of the bonds in the $COCHN_2$ fragment[132,149].

C–O	C–C	C–N	N–N
1.80	1.50	1.54	2.81
—	—	1.70	2.77

$p-\pi$ Conjugation in the $COCHN_2$ system leads to the appearance of fractional bond orders. Table 4 lists the calculated bond multiplicities in the $COCHN_2$ fragment.

Recently the molecular orbital method was used to demonstrate the occurrence of *cis–trans* isomerism in the diazoketone series. The calculations were made for diazoacetone and diazoacetophenone. The author succeeded in demonstrating convincingly the occurrence of rotational isomerism in these compounds. The geometrical configuration of diazoacetone used in the calculation is presented in Fig. 3†, which also gives the results of the calculation of the distribution of charges and dipole moments in the *s-cis* and *s-trans* diazoacetone isomers[128].

Studies in recent years have made it possible to describe the structure of diazoketones in the following way. The $COCHN_2$ ($OC^2-C^1-N^2-N^1$) fragment is coplanar, the C^1 atom is sp^2-hybridised, the C^1-N^2 bond is formed as a result of the withdrawal of the lone electron pair of the nitrogen atom to the sp^2 orbital of the carbon atom (singlet), and the lone electron pair in the p orbital of the C^1 carbon atom is conjugated with the π orbitals of the carbonyl and diazo-groups. This results in a conjugation chain involving five atoms. The above effect is illustrated in Fig. 2. It can also be described by the canonical structures‡



The structures of diazoacetone and diazoacetophenone have been discussed from the standpoint of the molecular

† The *Z* axis is not shown in Fig. 3; it is perpendicular to the plane and demonstrates the planarity of the molecule.

‡ Another interpretation of the bond types is possible. In particular, the C^1-N^2 bond is regarded as covalent and conjugation in the CNN fragment arises owing to the p electron of the carbon atom, the two p electrons of the middle nitrogen atom, and the p electron of the extreme nitrogen atom[132].

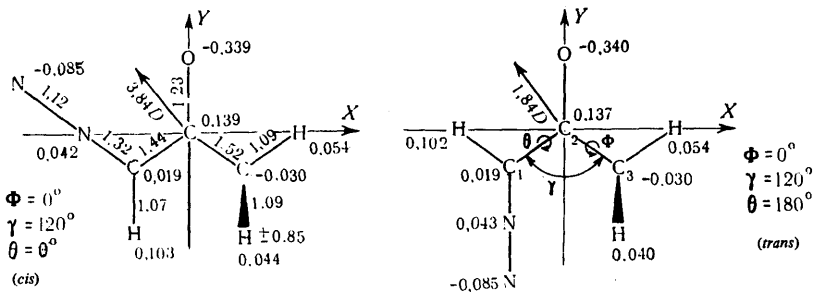


Figure 3.

orbital theory[128]. In the diazoacetone molecule there are 28 molecular orbitals: 21 of these are σ orbitals and 7 are π orbitals. Six π orbitals are formed from the $2p_Z$ orbitals of the nitrogen, carbon, and oxygen atoms. The seventh π orbital is formed from the orbitals linking in the methyl group the two hydrogen atoms located above and below the plane in which the diazoketone is located (the pseudo-π-orbital). Of the seven π orbitals, four are populated and three are vacant. The π orbital with the lowest energy (1π) embraces the π bond of the carbonyl group. A higher π orbital (2π) embraces the CNN fragment and has no vertical nodal plane between the three atoms. The third π orbital constitutes a pseudo-π-bond. The fourth π orbital has the highest energy, is also linked to the CNN bond, and has no nodal plane between the nitrogen atoms. The first antibonding π^* orbital (the $5\pi^*$ molecular orbital) embraces the entire diazoketone and has nodal planes between O and C, C and N, and N and N bonds. Of the 21 σ molecular orbitals, the first 12 are populated and the remaining 9 are vacant.

In the study of the mass spectra of diazoacetone, chlorodiazoacetone, trichlorodiazoacetone, and diazoacetophenone, the ionisation potentials of the compounds were determined as 9.40 ± 0.03, 9.92 ± 0.1, 9.95 ± 0.06, and 9.22 ± 0.04 eV respectively. From the ionisation potentials and the appearance potentials of the fragment ions, the bond dissociation energies in the above diazoketones were obtained: 3.3 eV for diazoacetone, 2.9 eV for chlorodiazoacetone, and 2.2 eV for trichlorodiazoacetone[141].

The above characteristics of the structure of diazoketones are responsible for their high chemical reactivity.

IV. CHEMICAL PROPERTIES

An intense investigation of the chemical reactions of diazoketones was begun in 1928, when Arndt and Amende discovered the reaction in which diazoalkanes are acylated by carboxylic acid halides[17]. Since then diazoketones have become readily available. They undergo reactions of the following characteristic types: (1) reactions with evolution of nitrogen; (2) reactions involving the nitrogen atoms of the diazo-group; (3) reactions in which the mobile α-hydrogen atom is substituted. Examples of these reactions are given below.

1. Reactions involving the Formation of Carbonium Ions

This group of reactions includes the reactions of diazoketone with water, alcohols, acids, halogens, *N*-halogeno-derivatives, and nitrogen oxides. Under the usual conditions, diazoketones are as a rule inert with respect to water. However, a few drops of acid (usually inorganic) are sufficient for the evolution of nitrogen to begin and an α-hydroxyketone to form. Sometimes the reaction takes place on heating. For example, an acetylmethanol may be obtained in this way from diazoacetone[94]. The hydrolysis of higher diazoketones with water is usually carried out in dioxan in the presence of catalytic amounts of inorganic acids.

Despite the fact that the decomposition of diazoketones in water has been known for a long time, the mechanism of this reaction remained controversial until recently. Wolff[94] and Bredig and Frankel[142] described the decomposition of diazoketones in an acid medium by the following process:

$$RCOCHN_2+H^++H_2O\longrightarrow RCOCH_2OH+N_2+H^+.$$

In other studies a different reaction mechanism was proposed by analogy with the hydrolysis of diazoalkanes, which has an A-SE2 mechanism[143–145]:

$$RCOCHN_2+H^+\longrightarrow RCOCH_2N_2^+, \quad (a)$$

$$RCOCH_2N_2^+ + H_2O \rightarrow RCOCH_2OH + H^+ + N_2. \quad (b)$$

The rate of hydrolysis is determined by stage (a). The role of catalytic amounts of acid reduces to the protonation of the diazoketone.

Ingold suggested a mechanism including the protonation of the diazoketone (c) in the pre-equilibrium stage[146] with a subsequent slow stage (d) involving its decomposition—an A – SE1 mechanism:

$$RCOCHN_2 + H^+ \rightleftharpoons RCOCH_2N_2^+, \quad (c)$$

$$RCOCH_2N_2^+ \rightleftharpoons RCOCH_2^+ + N_2, \quad (d)$$

$$RCOCH_2^+ + H_2O \rightarrow RCOCH_2OH + H^+. \quad (e)$$

However, he did not reject the possibility that diazoketones may be converted into hydroxyketones via the bimolecular mechanism involving reaction (a) and (b).

Whereas previously it was believed that the role of acid reduces to the protonation of the diazoketone, in recent studies it has been suggested that the catalyst protonates water[147,148]. The hydronium ion reacts with primary diazoketones via the mechanism

$$RCOCHN_2 + H_3O^+ \rightleftharpoons RCOCH_2N_2^+ + H_2O. \qquad (f)$$

Subsequently the diazonium ion is converted into a hydroxyketone via mechanism (b) (an $A - SE2$ mechanism)[149-152].

In contrast to primary diazoketones, secondary diazoketones are protonated irreversibly [stage (g)]. This stage is rate-determining. The hydroxyketone is formed from the diazonium ion via mechanisms (d) and (e):

$$RCOC(R)N_2 + H_3O^+ \rightarrow RCOCH(R)N_2^+ + H_2O. \qquad (g)$$

This reaction mechanism has been demonstrated for arylbenzoyldiazomethanes[153,154] and cyclic diazoketones[155,156].

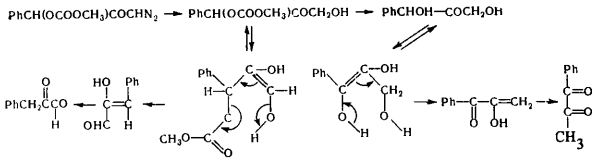
Acid hydrolysis of primary diazoketones does not result in the formation of α-hydroxymethylketones only. In the decomposition of 3-diazo-1-methoxycarbonyl-1-phenylpropan-2-one by dilute sulphuric acid, Bradley and Eaton isolated benzylglyoxal in 12% yield, the formation of which they believe may be due to an anionotropic migration of the phenyl group and the elimination of the second substituent[157]. Weygand et al. repeated this reaction with the diazoketone containing labelled carbon atoms and isolated benzylglyoxal in 6% yield[158]. On the basis of the measurements of the radioactivity of the products, they established that the phenyl residue does not migrate:

$$C_6H_5{}^{14}CH(OCOOCH_3)COCHN_2 \rightarrow C_6H_5{}^{14}CH_2COCHO.$$

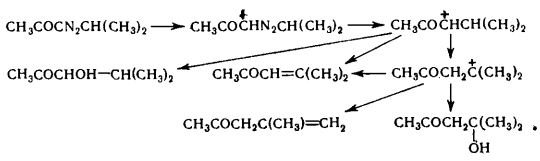
This reaction was investigated in greater detail by Dahn et al.,[159] who employed 10% phosphoric acid for the hydrolysis and obtained benzylglyoxal in 44% yield. In addition to the aldehyde, benzoylacetyl was also isolated. Hydrolysis of the diazoketones in which the carbon atom linked to the diazo-group was labelled confirmed that the phenyl group does not migrate from the first to the third atom, since the benzoic acid thus obtained is not radioactive:

$$\begin{matrix} C_6H_5 \\ | \\ CH{-}CO{-}{}^*CHN_2 \\ | \\ OCOOCH_3 \end{matrix} \rightarrow C_6H_5CH_2CO{-}{}^*CHO \rightarrow C_6H_5COOH + CO_2 + {}^*CO_2.$$

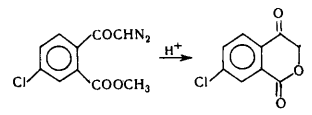
The authors explain the formation of benzylglyoxal and benzoylacetyl by the intermediate formation of a hydroxyketone and a diol:



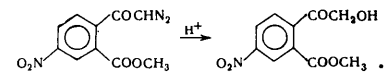
Unsaturated ketones were isolated in the acid hydrolysis of 3-diazo-1-methylpentan-2-one together with hydroxymethyl ketones[160]:



In the acid hydrolysis of diazoketones, the stabilisation of the carbonium ion depends both on the nature of the substituents and on their distribution relative to the diazo-group. For example, p-chloro-ω-diazo-o-methoxycarbonylacetophenone gives 7-chloro-1,4-dioxoisochroman on treatment with 3% sulphuric acid[161]:

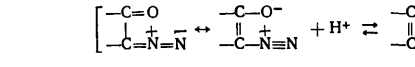


ω-Diazo-o-methoxycarbonylacetophenone undergoes a similar reaction[162]; under the hydrolysis conditions, ω-diazo-o-methoxycarbonyl-p-nitroacetophenone is converted into ω-hydroxy-o-methoxycarbonyl-p-nitroacetophenone[163]:



The acidity of alcohols is insufficient for the decomposition of diazoketones. Therefore the reaction with alcohols is as a rule carried out in the presence of catalysts. Inorganic acids, boron trifluoride, and metallic copper are employed for this purpose[153,164-166]. The reaction results in the formation of alkoxy-derivatives of α-hydroxyketones.

In contrast to diazoalkanes, diazoketones are more stable in relation to electrophilic agents. Many of them do not react with organic acids such as benzoic and cold acetic acids. Bisdiazoketones in which the diazo-group is between two carbonyl groups are not decomposed by concentrated nitric acid[137]. The authors explain this unusual behaviour of bisdiazoketones by the fact that the proton attacking the nucleophilic α-carbon atom is captured by the oxygen of the carbonyl group[137]:

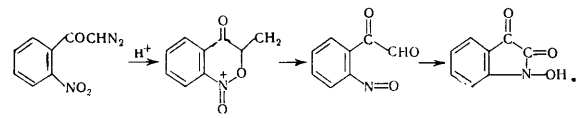


The inertness of diazoketones with respect to cold acetic acid makes it possible to carry out certain reactions in it[167].

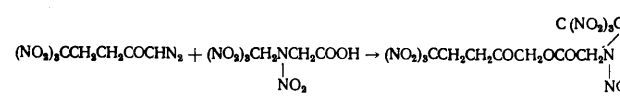
On heating with acetic acid, diazoketones form ketoesters[168-171]:

$$RCOCHN_2 + CH_3COOH \rightarrow RCOCH_2OCOCH_3.$$

An analogous synthesis was carried out using copper dioxide as a catalyst[172]. After refluxing 1-diazo-3-(o-nitrophenyl)acetone in glacial acetic acid, N-hydroxyisatin was isolated. The authors suggest that the initial reaction stage is cyclisation of the intermediate carbonium ion with formation of a six-membered ring followed by its deprotonation and cleavage to o-nitrosophenylglyoxal. Cyclisation of the latter leads to the formation of N-hydroxyisatin[173]:



Strong organic acids decompose diazoketones at room temperature[5]. ω-Nitrodiazoketones react with polynitrocarboxylic acids when the reactants are fused together[174]:



Platter and Heusser[175] achieved an interesting reaction of diazoketones. Starting with diazoketones and bromoacetic acid, they obtained butenolides:

$$RCOCHN_2+BrCH_2COOH\longrightarrow RCOCH_2OCOCH_2Br\longrightarrow \text{butenolides}\ .$$

Thiocarboxylic acids also decompose diazoketones with formation of the corresponding hydroxyketone esters[176].

The reaction of diazoketones with aliphatic and aromatic mono- and di-sulphonic acids led to the isolation of sulphonates derived from the α-hydroxyketones. The reaction is carried out in dioxan in the presence of a catalyst ($CuCl_2$) at 60–70°C[177] in polar solvents or acetic anhydride[34,178,179]. In the latter case the sulphonates are isolated after the hydrolysis of acetic anhydride with water. p-Toluenesulphonates derived from α-hydroxyketones are formed in high yield, readily crystallise, have distinct melting points, and may be used for the identification of diazoketones[178,179,180]:

$$RCOCHN_2+CH_3C_6H_4SO_2OH\longrightarrow RCOCH_2OSO_2C_6H_4CH_3+N_2\ .$$

Diazoketones undergo unusually interesting reactions with inorganic acids. However, only isolated examples of such reactions have been described. The reaction with nitric acid results in the formation of the corresponding nitric acid esters[34,138,167,181]:

$$RCOCHN_2+HNO_3\longrightarrow RCOCH_2ONO_2+N_2\ .$$

The reaction of diazoketones with sulphuric acid leading to the formation of sulphates derived from α-hydroxyketones has been described[34,153,182]:

$$2RCOCHN_2+H_2SO_4\longrightarrow (RCOCH_2O)_2SO_2+N_2\ .$$

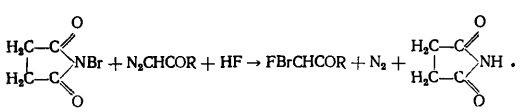
The reaction of diazoketones with phosphoric acid also yields the corresponding hydroxyketone esters[183].

In the reaction with inorganic acids, diazosulphones behave analogously to diazoketones. The synthesis of perchloric acid esters involving the mechanism

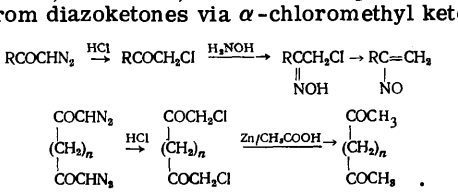
$$H_3CC_6H_4SO_2CHN_2+HClO_4\longrightarrow H_3CC_6H_4SO_2CH_2OClO_3+N_2$$

was described recently[184].

Hydrogen halides, except hydrogen fluoride, readily decompose diazoketones. Interesting experiments have been performed on the decomposition of diazoketones in hydrofluoric acid in the presence of N-bromosuccinimide[185]:



When diazoketones are treated with dry hydrogen chloride, α-chloromethyl ketones, which are starting materials for various syntheses, are obtained[5]. For example, nitroso-olefins, diketones, and other compounds have been obtained from diazoketones via α-chloromethyl ketones:



α-Bromomethyl ketones, formed in the reaction between diazoketones and hydrogen bromide, are also important starting materials for the synthesis of polyfunctional compounds[186]:

$$C_6H_5COCHN_2\xrightarrow{HBr}C_6H_5COCH_2Br\xrightarrow[CH_3CN]{AgNO_3}C_6H_5COCH_2ONO_2\rightarrow C_6H_5COCHO\ .$$

Hydriodic acid causes a far-reaching transformation of diazoketones leading to the formation of methyl ketones[187]. The conversion of the diazomethyl into the methyl group was first achieved by Wolfrom and Brown[187] for 1-diazoglucoheptulose[187]:

$$AcOCH_2(CHOAc)_4COCHN_2\xrightarrow{HI}AcOCH_2(CHOAc)_4COCH_3+N_2\ .$$

α-Iodomethyl ketones are formed according to the mechanism[138]

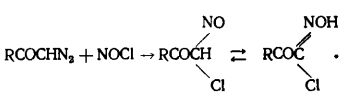
$$RCOCHN_2+HCl\rightarrow RCOCH_2Cl\xrightarrow{NaI}RCOCH_2I\ .$$

When diazoketones are decomposed in the presence of an excess thiocyanate, nitrate, and chloride anions in the reaction mixture, α-thiocyanato-, α-nitroxy-, and α-chloro-methyl ketones respectively are readily formed[138,188].

Treatment of diazoketones with chlorine, bromine, or iodine in inert solvents leads to the formation of $\alpha\alpha$-dihalogenomethyl ketones[187]. Iodobenzene dichloride may be employed as the chlorinating agent[189]:

$$ClCH=\underset{Cl}{C}COCHN_2+C_6H_5ICl_2\rightarrow ClCH=\underset{Cl}{C}COCHCl_2+C_6H_5I+N_2\ .$$

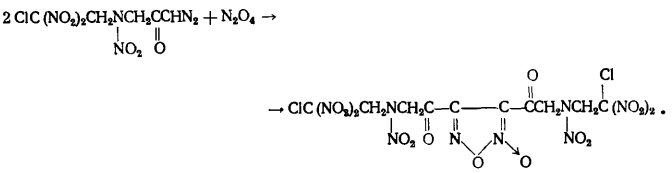
The reaction of a number of diazoketones with nitrosyl chloride has been investigated[190]. The resulting chloronitrosoketones are in tautomeric equilibrium with hydroxamic acid chlorides:



Benzoylphenyldiazomethane reacts with nitrogen tetroxide to form phenyldinitromethane[191]:

$$C_6H_5COCN_2C_6H_5+N_2O_4\longrightarrow HC(NO_2)_2C_6H_5\ .$$

It was established recently that ω-nitrodiazoketones are converted under the influence of nitrogen tetroxide into furoxans[192]:



In the series of diazoketones only a few examples of this interesting reaction have been carried out and it undoubtedly requires further study.

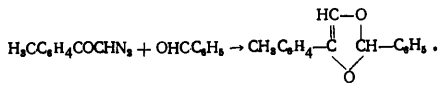
2. Reaction of Diazoketones with Carbonyl Compounds

This group of reactions includes those of diazoketones with aldehydes and ketones. The reaction of diazoketones with aldehydes was investigated for the first time by Diels and Ilberg[193]. On mixing 2-diazo-3-butanone with formaldehyde, they observed a vigorous evolution of nitrogen and heat. The reaction resulted in the isolation of o-hydroxy-2-methylbut-2-en-3-one:

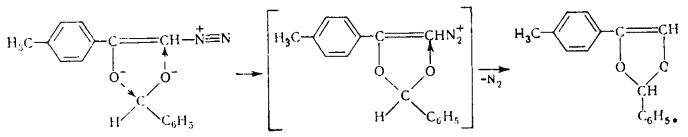
$$CH_3COCN_2CH_3+O=CH_2\rightarrow CH_3\underset{CH_3}{C}OC=CHOH+N_2\ .$$

The reaction of diazoketones with higher aldehydes occurs under more severe conditions. Thus on heating

with benzaldehyde in xylene for 18 h, *p*-methylbenzoyldiazomethane was converted in 39% yield into 2-phenyl-5-tolyl-1,3-dioxole[194]:

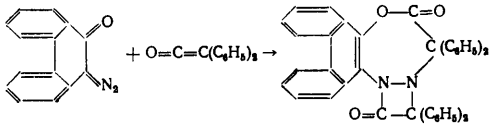


According to the authors, the condition governing the formation of dioxoles is the addition of the electrophilic carbon of the aldehyde group to the carbonyl oxygen of the diazoketone before the elimination of the diazo-group; otherwise the Wolff–Schroeter rearrangement is possible:

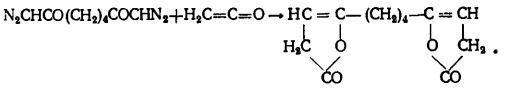


It is noteworthy that the reaction takes place smoothly only with *p*-methyl- and *p*-methoxy-benzoyldiazomethane. Benzoyldiazomethane having substituents with a +*C* effect either does not undergo the reaction or the reaction leads to the formation of diacylethylenes in high yields[194].

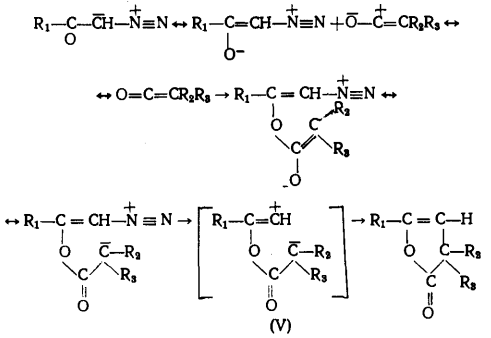
Diazoketones readily react with ketens. After allowing azibenzil to react with diphenylketen, Staudinger and Reber isolated a nitrogen-containing crystalline adduct[195]. Ried and Dietrich made a detailed study of the reaction of *o*-quinone diazides with ketens and showed that it results in the formation of polycyclic nitrogen-containing systems[196,197]:



Primary diazoketones react with ketens with evolution of nitrogen. This leads to the formation of $\beta\gamma$-butenolides, which split off a lactone and are converted into keto-acids[198]. The reaction of bisdiazoketones with ketens leads to the formation of bisbutenolides[198]:



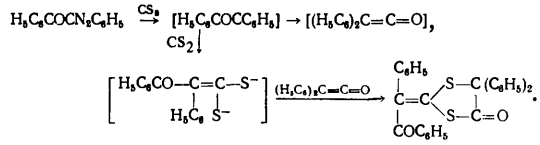
The reaction proceeds via the intermediate formation of a dipolar ion (V), which readily cyclises to a lactone[198]:



(V)

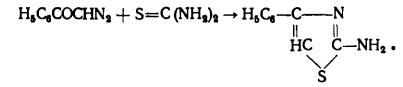
3. Reaction of Diazoketones with Sulphur-containing Compounds

In a study of the reaction of hydrogen sulphide with azibenzil, Meyer isolated 5-oxo-2-(2-oxo-1,2-diphenylethylidene)-4,4-diphenyl-1,3-dithiolane in 90% yield. Evidently, after the evolution of nitrogen, this reaction involves the formation of a carbene, part of which adds to the hydrogen sulphide and another part undergoes the Wolff–Schroeter rearrangement and adds to both sulphur atoms of the intermediate adduct[199]:

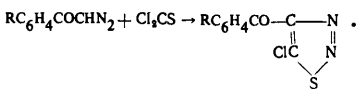


Analogous syntheses have been carried out by other investigators[200,201].

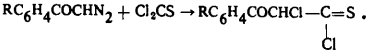
Benzoyldiazomethane reacts with thiourea to form a heterocyclic compound according to the mechanism[202]



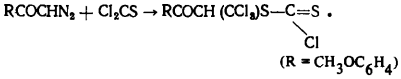
Depending on the position and nature of the substituent, ring-substituted benzoyldiazomethane derivatives can react with thiophosgene to form 1,2,3-thiadiazoles, substituted thiopropionic acid chlorides, and trichloroethanethiol derivatives. Thus *p*-nitro-, *p*-chloro-, and *p*-methyl-benzoyldiazomethane and *m*-nitrobenzoyldiazomethane react with thiophosgene to form 1,2,3-thiadiazoles[203]:



m-Methyl- and *m*-methoxy-benzoyldiazomethanes form β-aryl-α-chloro-β-oxothiopropionic acid chlorides:

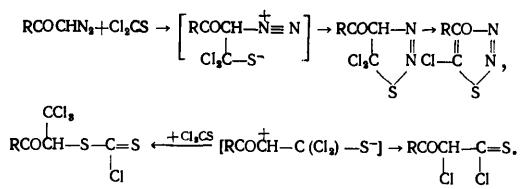


In the presence of an excess of thiophosgene, chlorothiocarbonic acid esters are formed:



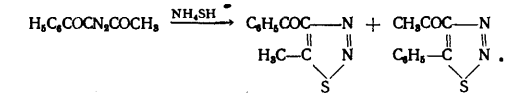
Azibenzil reacts with thiophosgene to form a thiafuran derivative via a thi-iran.

The authors suggest that the products enumerated above are obtained by the following mechanism:

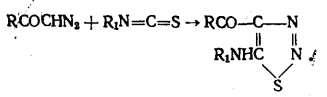


When secondary diazoketones react with hydrogen sulphide, thiadiazole derivatives are formed[92,204]. Thus treatment of azibenzil with hydrogen sulphide in ethanol in the presence of a small amount of ammonia leads to the

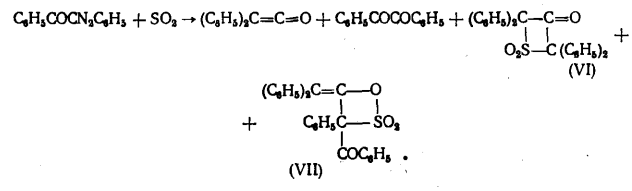
formation of 4,5-diphenyl-1,2,3-thiadiazole[205,206]. The reaction of asymetric 2-diazo-1,3-diketones with hydrogen sulphide in the presence of ammonia yields two isomeric 1,2,3-thiadiazolyl ketones: 4-benzoyl-5-methyl-1,2,3-thiadiazole and 4-acetyl-5-phenyl-1,2,3-thiadiazole[95]:



Ried and Beck obtained 1,2,3-thiadiazole by the reaction of primary diazoketones with mustard oils[207]:



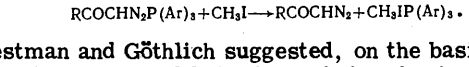
Thermolysis of azibenzil in benzene in the presence of sulphur dioxide yielded cyclic sulphones (VI, VII), benzil, and diphenylketen. Photolytic decomposition of azibenzil in the presence of sulphur dioxide at temperatures between −5° and −20°C leads to the formation of the above sulphones and benzil[208]:



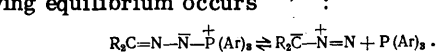
4. Reaction with Phosphines and Organophosphorus Compounds

The reaction of diazo-compounds with tertiary phosphines, in particular with triphenylphosphines, which was discovered by Staudinger, has been described in a number of publications[209-211]. It was investigated in detail by Bestman's school[143,212]. It results in the formation of triphenylphosphazines[212]. α-Ketoaldehydes[213], ketoesters[214], methyl ketones[212], and heterocyclic compounds[25,143,184,215,216] may be obtained via the phosphazines.

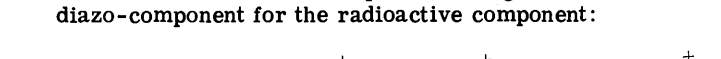
It is striking that very pure diazoketones may be obtained by the cleavage of phosphazines with methyl iodide[212,217]:



Bestman and Göthlich suggested, on the basis of the chemical and thermal behaviour of phosphazines, that the following equilibrium occurs[211,212]:

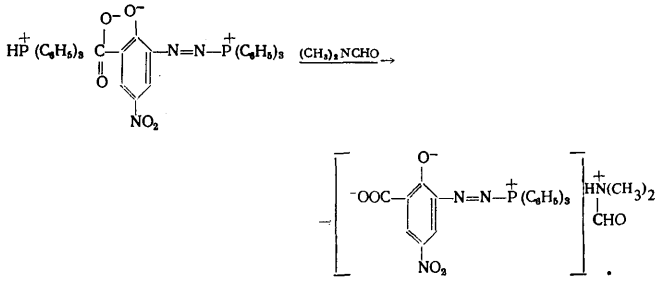


The accumulation of electronegative substituents in the diazoketone promotes a shift of the equilibrium to the right. To demonstrate the occurrence of the equilibrium, the authors carried out an exchange between the diazo-component of the phosphazine and a diazoketone containing a labelled carbon atom and isolated a radioactive phosphazine. This involved a complete exchange of the inactive diazo-component for the radioactive component:



Infrared spectroscopic data also confirmed this conclusion. The phosphazine spectra, recorded using potassium bromide discs, do not have absorption bands characteristic of the diazo-group, while in chloroform solution the band does appear[218].

Quinone diazides (*o*- and *p*-derivatives) react with triphenylphosphine to form the corresponding phosphazines[217,219]. *o*-Quinone diazides with electronegative substituents in the 4- and 6-positions of the ring behave anomalously[184,217]. In some cases it proved possible to isolate stable yellow adducts with the composition *o*-quinone diazide: $P(Ar)_3 = 1:2$. The diadducts are salt-like. This was confirmed by the finding that the triphenylphosphine molecule in the diadduct, which is linked by an anionic bond, is readily substituted by a dimethylformamide molecule:

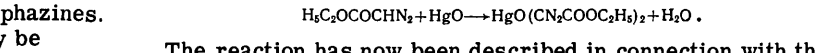


Apart from triphenylphosphine, the more nucleophilic triaminophosphines may be employed as the second component in the formation of phosphazines. In this case the reaction takes place instantaneously[220].

Phosphazines are synthesised in ether[211,212], acetonitrile[106], isopropyl ether[216], ethyl acetate[55], or in a mixture of benzene and ether[221]. Sometimes anhydrous zinc chloride is employed as a catalyst[213].

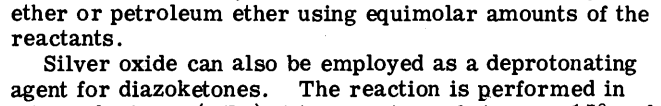
5. Electrophilic Substitution of α-Hydrogen in Diazoketones

Diazoketones are known to undergo a reaction in which electrophilic substitution of the hydrogen at the carbon atom linked to the diazo-group takes place. The reaction was first discovered by Buchner[221] when he allowed diazoacetic ester to react with yellow mercury(II) oxide:



The reaction has now been described in connection with the synthesis of mercury derivatives of 2,4,6-trimethylbenzoyldiazomethane, diazoacetone, and 4-methyldiazopentan-2-one[130,222]. The synthesis was carried out in anhydrous ether or petroleum ether using equimolar amounts of the reactants.

Silver oxide can also be employed as a deprotonating agent for diazoketones. The reaction is performed in tetrahydrofuran (THF) at temperatures between −15° and 0°C. Silver derivatives of diazoketones are excellent alkylating agents and serve as intermediates for the synthesis of unsaturated diazoketones[223]:



Organotin derivatives of diazoacetic ester, formed in the reaction of the latter with organotin derivatives of alkylamines, have been recently described[224].

An interesting example of this range of reactions of diazo-derivatives was recently discovered by Schollkopf and coworkers[225,226]. They succeeded in synthesising α-nitrodiazo-compounds. Thus nitrodiazoacetic ester was obtained by nitrating diazoacetic ester with nitrogen pentoxide[225]. Benzoyldiazomethane reacts with nitrogen

pentoxide in carbon tetrachloride at −30°C to form benzoylnitrodiazomethane[226]:

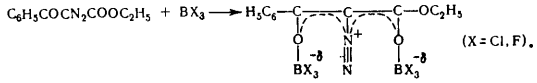
$$C_6H_5COCHN_2 + N_2O_5 \longrightarrow C_6H_5COC(NO_2)N_2 .$$

By nitrating nitrodiazomethane[135] with nitrogen pentoxide, it proved possible to isolate a most interesting α-nitrodiazoalkane: dinitrodiazomethane[227].

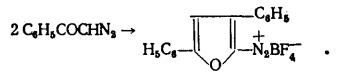
We believe that a more detailed study of the above reactions and subsequent transformations of the resulting products should lead to a further development of this interesting field in the chemistry of diazo-compounds.

6. The Complex-forming Capacity of Diazoketones

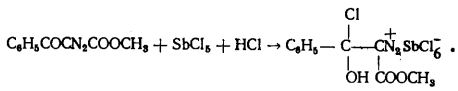
The synthesis of internal diazonium complexes of diazocarbonyl compounds was first reported by Fahr[228], who found that benzoyldiazoacetic ester reacts with boron trifluoride or trichloride to form colourless, stable, but moisture-sensitive compounds. The following structure was attributed to them:



Benzoyldiazomethane reacts with boron trifluoride-ether in toluene at 60–70°C with evolution of nitrogen and the formation of 2,4-diphenyl-furan-5-diazonium fluoroborate, the first example of compounds with a diazonium group at the furan ring[229–231]:



Benzoyldiazoacetic ester reacts with antimony pentachloride in methylene chloride in the presence of hydrogen chloride, forming a diazonium salt[232]:



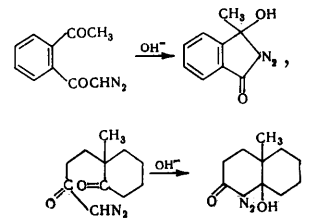
A complex of diazobarbituric acid with di(trinitromethyl)mercury was described recently. It is interesting that the reaction of 9-diazofluorene and diphenyldiazomethane with di(trinitrophenyl)mercury led to the isolation of 1-biphenylene-2,2-dinitroethylene and 2,2-dinitro-1,1-diphenylethylene[233].

7. Reactions of Diazoketones under the Influence of Bases

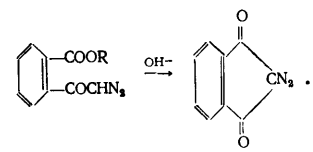
The reactions of diazoketones with bases have been inadequately investigated, evidently owing to their complexity. The reaction takes place unambiguously in the case of the amide of diazoacetic ester[234] and 2-diazo-3-pentanone[235]. In the first case the product is 5-oxo-1,2,3-triazole and in the second 1-(3,3-dimethyl-2-oxobutyl)-5-(2,2-dimethyl-1-oxopropyl)tetrazole. The reaction of ω-diazoacetophenone with sodium hydroxide or sodium methoxide in dioxan and ether leads to the formation of benzoic acid, 4-phenylbenzoylpyrazole, 3-benzoyl-5-hydroxy-4-phenylpyrazole, acetophenone, hydrogen cyanide and hydroxylamine. In concentrated sodium methoxide solutions the products are 3-benzoyl-4-hydroxy-5-phenylpyrazole and 5-benzoyltetrazole[236]. The reaction of diazoacetophenone with potassium t-butoxide yields a dimer of diazoacetophenone, 5-benzoyl-1-phenyltetrazole, and 5-benzoyl-2-phenylacyltetrazole. 1-Phenylacyltetrazole is obtained in ether in the presence of ammonium chloride[237].

On treatment with bases, diazodicarbonyl compounds decompose into diazomonocarbonyl derivatives[238]. No hypotheses have been put forward concerning the mechanism of the reaction of diazoketones with bases. A detailed study of the process is necessary in order to elucidate the causes of the formation of such a large number of reaction products.

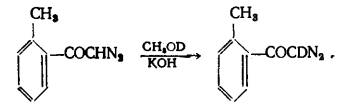
It was found recently that diazoketones undergo intramolecular condensation on treatment with alkalies[239]



Under the influence of bases, alkoxycarbonyldiazoketones undergo the Dieckmann condensation:



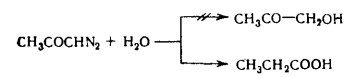
Diazoketones which are incapable of undergoing the above condensations, readily exchange their α-hydrogen atom for deuterium in an alkaline medium, which indicates an anionic mechanism of the above condensation[239]:



8. Reactions of Diazoketones via Ketocarbenes

A characteristic reaction of diazoketones is decomposition via ketocarbenes on irradiation and under the influence of heat and light. The intermediate species with an incomplete octet at the α-carbon atom, formed after the elimination of nitrogen, can be stabilised in different ways.

Wolff, who studied the reaction of diazoacetone and diazoacetophenone with water in the presence of silver oxide, isolated, instead of the expected α-hydroxyketones, propionic and phenylacetic acids[94,120].



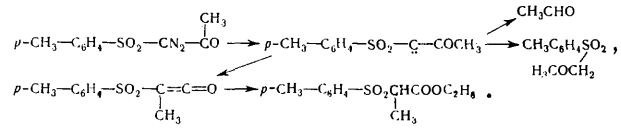
Somewhat later and independently of Wolff, Schroeter studied a similar reaction of phenylbenzoyldiazomethane and isolated diphenylacetic acid. By thermolysing azibenzil, he succeeded in obtaining diphenylketen—an intermediate in the formation of diphenylacetic acid[240,241]:

$$C_6H_5COCN_2C_6H_5 \rightarrow C_6H_5COC\ddot{C}C_6H_5 \rightarrow (C_6H_5)_2C{=}C{=}O .$$

Subsequently the conversion of α-diazoketones into acids or their derivatives, which takes place on heating under the influence of catalysts or on irradiation with

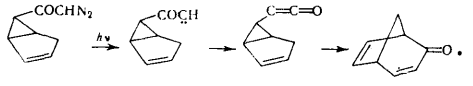
ultraviolet light in the presence of water, alcohols, ammonia, amines, etc. was called the Wolff–Schroeter rearrangement (more often this reaction is referred to as the Wolff rearrangement). Excellent reviews dealing with various reactions of diazo-compounds describe in detail both the theoretical and experimental aspects of this rearrangement[6,8,242–251]. A systematic account of work published recently is given below.

The catalysis of *p*-tosyl(acetyl)diazomethane in ethanol leads to the formation of ethyl α-methyl-α-tosylacetate, acetaldehyde, and tosylacetone[252]:



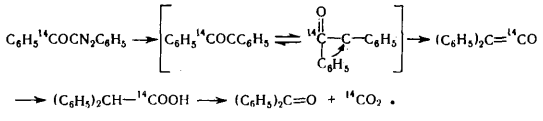
The reaction proceeds via the intermediate formation of a ketocarbene.

Recently the Wolff–Schroeter rearrangement has been intensively investigated for diazoketones with cyclic substituents[253–257]. The photolysis of *endo*-6-diazomethyl-oxobicyclo[3,2,0]hex-2-ene in tetrahydrofuran yielded bicyclo[3,2,1]octa-3,6-diene-2-one—the product of the intramolecular cyclisation of the keten formed as a result of the normal Wolff rearrangement[254]:

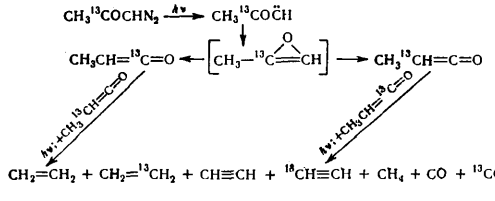


In contrast to the mechanism proposed previously for the Wolff–Schroeter rearrangement, where the formation of the intermediate keten was assumed to take place via a ketocarbene, it has been shown[258] that the ketocarbene is converted into the keten via acetylene oxide [oxiren].

Franzen achieved the photochemical decomposition of azibenzil containing a labelled carbon atom in the carbonyl group. The position of the labelled atom was established by the oxidative decarboxylation of the resulting diphenylacetic acid. Subsequently the radioactivity of the carbon dioxide formed was measured. The author concluded that the ketocarbene is stabilised as a result of the migration of the phenyl group with formation of diphenylketen[259]:

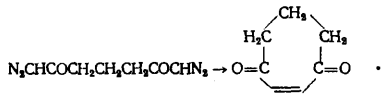


The results of this study agree with earlier data[260]. The gas-phase photolysis of diazoacetone and 2-diazo-3-butanone with a labelled carbon atom in the carbonyl group leads to the formation of a large number of products[258]: non-radioactive and radioactive unsaturated hydrocarbons, carbon monoxide, and methane. The appearance of these compounds can be accounted for by the intermediate formation of an oxiren according to the mechanism

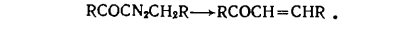


Evidently additional studies are necessary to prove unambiguously the validity of the above mechanism.

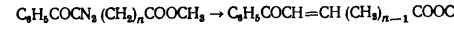
The rearrangement of a ketocarbene into ketens is not the only possible stabilisation pathway. For example, the decomposition of benzoyldiazomethane in the presence of copper(I) chloride in an inert solvent gives a 60% yield of 1,2-dibenzoylethylene[261], which is a valuable product for the synthesis of heterocyclic compounds[262,263]. Thermolysis of 1,7-bisdiazo-2,6-heptanedione in benzene in the presence of copper(II) oxide leads to the formation of 3,7-dioxocycloheptene[264]:



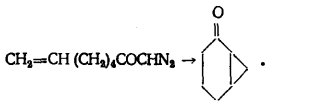
Under analogous conditions, cyclic diazoketones form polymeric products in addition to the dimers[265–267]. When diazoketones in which a CH group adjoins the diazo-group decompose under the influence of light or silver oxide, αβ-unsaturated ketones are formed as a rule[21]. The ketocarbene is stabilised as a result of the migration of the hydrogen atom:



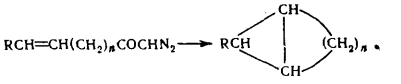
Recently a number of unsaturated ketoesters were synthesised in this way[268]:



If the decomposition of unsaturated diazoketones is carried out in inert solvents, the ketocarbene formed may be stabilised in yet another way, namely via intramolecular addition of the carbon atom with an incomplete octet to the double bond, resulting in the formation of a cyclic product. Thus, when 1-diazo-oct-7-en-2-one is refluxed in cyclohexane in the presence of copper bronze, bicyclo-[0,1,4]-2-heptanone is formed[299]:

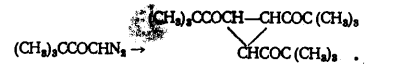


The intramolecular reaction of unsaturated diazoketones was investigated in greater detail by Fawzi and Gutsche[270], who note that substituents at the double bond do not have a significant influence on this reaction:



If the diazomethyl group is separated from the double bond by a benzene ring or the double bond is located in a ring, polycyclic systems are formed[271–274].

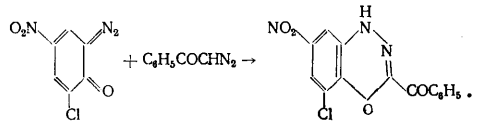
Low yields of cyclopropanes may be obtained by the thermal decomposition of diazoketones[275]. When the reaction is carried out in thioanisole in nitrogen and in the presence of copper bronze, the yield of the cyclic compound may be increased[276]:



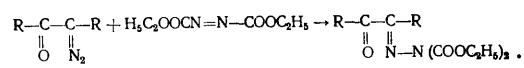
The decomposition of diazoketones in the presence of liazoalkanes leads to the formation of azines[259,277]:

The decomposition of *o*-quinone diazides in the presence of α-diazoketones and diazoacetic ester does not terminate at the stage involving the formation of azimes but leads to

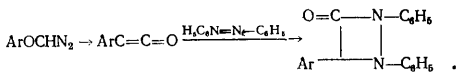
the formation of bicyclic products[278]. Thus, when 6-chloro-4-nitrobenzoquinone 2-diazide [6-chloro-2-diazo-4-nitro-1-oxobenzene?] was heated with diazoacetophenone, 2-benzoyl-8-chloro-6-nitro-4*H*-benzo-1,3,4-oxadiazine was isolated:



α-Diazoketones react with azodicarboxylic acid diesters on heating with formation of the monohydrazones of 1,2-dicarbonylcompounds[279,280]:



The reaction with azobenzene takes place under the influence of ultraviolet light. This involves the formation of ketens which are subsequently coupled to the azo-group with formation of heterocyclic compounds[281]:



2-Diazo-1,3-dicarbonyl compounds react similarly with azo-derivatives[282].

V. SOME ASPECTS OF PRACTICAL APPLICATIONS

In a discussion of the practical applications of diazoketones, one must emphasise in the first place their great preparative value for the synthesis of various classes of organic compounds: aliphatic, aromatic, heterocyclic, and heterochain compounds, and polymers. The possibilities of diazoketones in the synthesis of products which are difficult and sometimes impossible to obtain by other methods are unsurpassed. In this sense comparison of aliphatic diazocompounds with the "Genie of Aladdin's Lamp", made in one of Huisgen's studies, describes graphically and accurately their role in organic chemistry.

The biological activity of certain diazoketones has been investigated. 6-Diazo-5-oxonorleucine inhibits the metabolic process in photosynthesis in algae[283]. The same compound, diazotetronic acid, and *O*-diazoacetyl-L-serine inhibit the growth of malignant tumours[284-288]. The antileukaemic action of 1,2-bisdiazoacetylethane has been studied. The preparation exhibits a wide spectrum of antitumour activity, inhibits or completely suppresses the growth of many experimental tumours (sarcoma-45, Geren [spelling uncertain (Ed. of Translation)] carcinoma, Walker carcinosarcoma, carcinoma-755, sarcoma-180, and Ehrlich ascites tumour)[289]. It was noted recently that certain diazoketones exhibit antitumour activity against three ascites tumours in mice: ARE-G, S-180, Nkly, and haematocytoblastosis La in mice of strain C_{57}bl.[136]

1,8-Bisdiazo-octane-2,7-dione shows a powerful mutagenic activity over a wide spectrum of mutations[290-293].

It is interesting that 1,7-bisdiazo-4-nitro-4-azaheptane-2,6-dione exhibits a weak antibacterial activity, is relatively non-toxic, and does not show neurotropic, anticonvulsant, antitremor, analgesic, and soporific effects[294].

Unfortunately we were unable to find any publications dealing with systematic studies of the biological activity of diazoketones, although, as pointed out by Berlin and Yaguzhinskii[295], they are of undoubted interest in this respect.

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Application of Proton Magnetic Resonance to the Investigation of Organophosphorus Compounds

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Methods of analysing the p.m.r. spectra of organophosphorus compounds are examined, the chief features of the chemical shifts of protons and the proton-proton and proton-phosphorus spin-spin interaction constants are summarised, and the main lines of investigation of organophosphorus compounds by the p.m.r. method are discussed. A list of 167 references is included.

CONTENTS

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I. INTRODUCTION

The vigorous development of nuclear magnetic resonance (n.m.r.) spectroscopy, especially of proton magnetic resonance (p.m.r.) spectroscopy, is due to the wide possibilities for its application in chemistry both for structural and physicochemical investigations and for a more thorough understanding of the electronic structure of complicated organic molecules. The fundamental difference between n.m.r. and other widely used spectroscopic methods is the presence in the spectra of two groups of cross parameters—the chemical shifts of equivalent nuclei and the spin–spin coupling constants between magnetically non-equivalent nuclei—which leads to a significant enhancement of the reliability and the concreteness of the information obtainable. During the past decade the n.m.r. method has rightly occupied a leading position among spectroscopic methods for investigating organic compounds, and in fact now constitutes an independent branch of science.

The n.m.r. method is especially useful in the investigation of organophosphorus compounds because the stable phosphorus-31 isotope (natural content 100%) possesses a magnetic moment and a nuclear spin of $\frac{1}{2}$, which enables additional parameters—chemical shifts of phosphorus δP and spin–spin coupling constants of phosphorus with protons and other magnetic nuclei of the molecule—to be obtained. Interest in these parameters had already appeared in the first fundamental n.m.r. investigations[1,2]. The modern n.m.r. technique enables chemical shifts of phosphorus to be obtained both by direct resonance at ^{31}P nuclei (^{31}P n.m.r.) and by use of double nuclear resonance methods ($^{1}H-\{^{31}P\}$ and $^{19}F-\{^{31}P\}$ d.n.m.r.).[3-5] As a consequence of the accumulation of comprehensive experimental results on chemical shifts of phosphorus[2,4-11] combined with theoretical analysis[11-15], this parameter can be used widely with the various phosphorus compounds investigated.

At the same time the investigation of organophosphorus compounds by single resonance on protons (p.m.r.) retains its value, since proton resonance is accompanied with the simplest of apparatus, accessible to a wide circle of investigators, and will reveal most parameters of the spectrum. Besides the investigation of the effect of phosphorus-containing groups on the proton chemical shifts δ_H and the proton–proton interaction constants J_{HH}, the p.m.r. method will usually yield the spin–spin coupling constants of protons and phosphorus J_{HP}, and in isolated cases also the spin–spin coupling constants between the phosphorus nuclei J_{PP}. In his excellent reviews Mavel[16,17] has carefully collected the literature on this problem up to 1965 inclusive; the subsequent voluminous literature has described the application of p.m.r. both for the identification of organophosphorus compounds and to reveal the main features of the spectra. The chief purpose of the present Review is to summarise these regularities, and also to examine features of the analysis of p.m.r. spectra applied to those of organophosphorus compounds. For this reason the Review does not claim to cover exhaustively all papers on the proton magnetic resonance of organophosphorus compounds. However, it does consider the results of some of the most comprehensive investigations outside the scope of the actual p.m.r. of these compounds.

II. ANALYSIS OF COMPLEX p.m.r. SPECTRA OF ORGANOPHOSPHORUS COMPOUNDS

The relation between the position and intensity of lines and the parameters of the p.m.r. spectra of organophosphorus compounds conforms to the general rules of nuclear magnetic resonance[18]. The main difficulty in the analysis is that single resonance of protons leaves transitions in the resonance range of phosphorus outside the spectrum. Nevertheless, the use of special procedures enables most of the spectral parameters to be determined in individual cases when the molecules contain a small number of ^{31}P nuclei (one or two).

In the case of compounds containing one phosphorus atom the *method of subspectra* provides a such procedure. The complete proton spectrum of these compounds $(A_mB_nC_kX)$† can be regarded as the superimposition of two simpler subspectra $(A_mB_nC_k)'$ and $(A_mB_nC_k)''$,

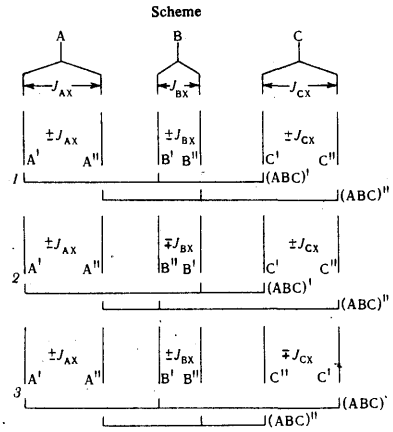
†The letters A–C denote protons, and X is a phosphorus nucleus. The symbol ν_K indicates the chemical shift (in c/s) of the K nucleus with respect to a reference point.

defined by the spin–spin coupling constants *only* between protons and the so called *effective shifts*, which are connected with the true proton chemical shifts and proton–phosphorus spin–spin coupling constants by the simple relations[19]

$$\nu'_A = \nu_A + \frac{1}{2}J_{AX};\ \nu'_B = \nu_B + \frac{1}{2}J_{BX};\ \nu'_C = \nu_C + \frac{1}{2}J_{CX}\ldots$$

$$\nu''_A = \nu_A - \frac{1}{2}J_{AX};\ \nu''_B = \nu_B - \frac{1}{2}J_{BX};\ \nu''_C = \nu_C - \frac{1}{2}J_{CX}\ldots$$

Subspectra provide a very graphic method of determining the relative signs of the constants J_{HP}. Indeed, the lines of the complete spectrum should be distributed between the subspectra according to the relative signs of J_{AX}, J_{BX}, and J_{CX}:.



where in (1) the three constants have the same sign, in (2) the constant J_{BX} is opposite in sign in sign to J_{AX}, and in (3) the constant J_{CX} is opposite to sign to J_{AX} and J_{BX}. If the experimental spectrum enables lines to be assigned unambiguously between subspectra, it is possible also to choose the relative signs of the spin–spin coupling constants.

Fig. 1 shows the experimental and theoretical spectra of the ethylenic protons in vinylphosphonic bisdimethylamide[20]. It is readily seen that the relative intensities agree well with the distribution among subspectra assumed to correspond to constants J_{AX}, J_{BX}, and J_{CX} having the same sign. The spectra of allenic derivatives having a three-coordinated (Fig. 2) or a four-coordinated (Fig. 3) phosphorus atom[21] clearly show how the line intensity ratio varies with the signs of the constants. Thus in the p.m.r. spectrum of propadienylphosphonous bisdimethylamide the constants have the same sign, whereas in the spectrum of propadienylphosphonic bisdimethylamide the signs are different. Most of the parameters in the spectra can be obtained by direct measurement.

If, however, the subspectrum is highly symmetrical (e.g. the AB subspectrum in ABX, or AA'BB' in AA'BB'X[21]), unambiguous distribution of lines among subspectra is impossible. Complete analysis of the spectrum then requires a change in the relation between chemical shifts and spin–spin coupling constants, which can be achieved by using a spectrometer having a different working frequency[23] or by the employment of specific solvents to change the chemical shifts of individual protons[24].

Subspectra can be analysed in various ways depending on their complexity—manually[23] and by the use of previously calculated standard data[25], e.g. Corio's tables[26] (also Ref. 27, p. 587) or tables taking into account the resolving power of the spectrometers[28], and also with the application of electronic computers and special programmes[20,24,29,30].

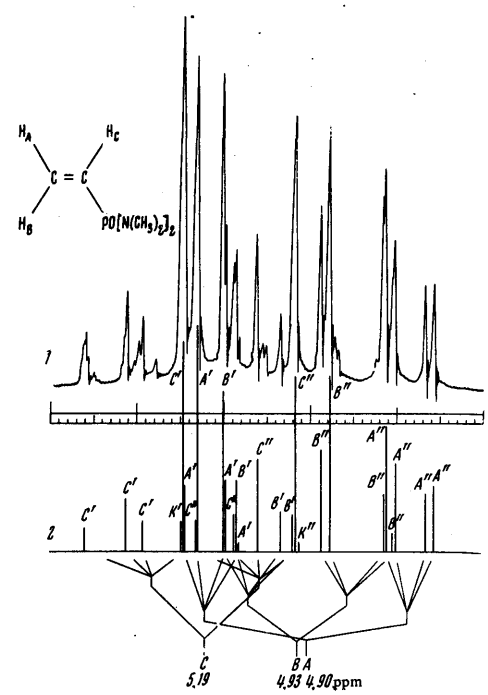


Figure 1. Proton magnetic resonance spectrum of ethylenic protons of vinylphosphonic bisdimethylamide (spectrum of type ABCX, with J_{CX} = 30.9, J_{BX} = 28.6, J_{AX} = 58.0, J_{AB} = 1.25, J_{BC} = 18.25, and J_{AC} = 12.35 c/s): 1) experimental spectrum at 100 Mc/s; 2) theoretical spectrum.

The presence of two phosphorus atoms in a molecule may produce considerable complication of the spectrum. Nevertheless, partial or complete analysis is possible in individual cases without the use of computers. Harris[31] used certain symmetry properties of the $A_nXX'A_h$ system to show that all parameters governing the form of such a spectrum can be obtained by direct measurement and simple calculation. If the spin–spin coupling constant between two groups of protons $J_{AA'} = 0$, the spectrum theoretically contains $2n + 1$ pairs of lines symmetrically arranged about $\nu_{A'}$, the chemical shift of $2n$ chemically equivalent protons. Since the nuclei are magnetically equivalent within each group of protons A and A', the spin–spin coupling constant between protons within a group does not affect the form of the spectrum, and therefore cannot be determined. The three remaining parameters of the spectrum J_{AX}, $J_{AX'}$, and J_X are elucidated by means of the relations

$$N = |J_{AX} + J_{AX'}|;\ L = |J_{AX} - J_{AX'}|\ .$$

The parameter N is easily determined from the distance between the pair of most intense lines in the spectrum (Fig. 4), representing half the total intensity. The remaining lines can be grouped into quartets, each corresponding to a definite value of the parameter χ, which assumes

integral values from 1 to n. The distance between the more intense inner lines of a quartet is connected with the parameters of the spectrum by the relation

$$S_{\text{inn}}(\chi) = (\chi^2 L^2 + J_X^2)^{1/2} - [(\chi - 1)^2 L^2 + J_X^2]^{1/2}.$$

The outer lines of the quartet are weak; the distance between them is determined by the similar expression

$$S_{\text{out}}(\chi) = (\chi^2 L^2 + J_X^2)^{1/2} + [(\chi - 1)^2 L^2 + J_X^2]^{1/2}.$$

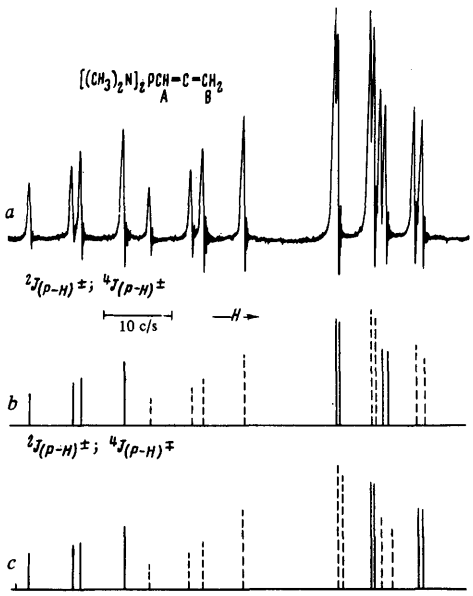


Figure 2. Proton magnetic resonance spectrum of allenic protons of propadienylphosphonous bisdimethylamide (spectrum of type AB_2X): *a*) experimental spectrum at 60 Mc/s; *b*) theoretical spectrum with the constants $^2J_{HP}$ and $^4J_{HP}$ having the same sign; *c*) theoretical spectrum with the constants having opposite signs.

The distance between the inner lines of the quartets increases with increase in χ, but does not exceed L, so that the latter can be determined roughly from the spectrum by finding the limit to which values of Sinn converge. At the same time the intensity of these lines drops rapidly. This applies also to the outer lines of the quartet, which diverge from the value $2L$. Since these lines are in general weak, in some cases only the first pair of lines ($\chi = 1$) can be observed. The constant $|J_X|$ is then determined by direct measurement from the distance between outer and inner lines of the first quartet ($\chi = 1$); from the results the parameter L is readily determined by means of the above formulae. If the outer lines cannot be observed, $|J_X|$ and L can be determined only from the inner lines of the first and second quartets, but the accuracy is considerably lower.

It is significant that, in spectra of this type, the form of the quartets depends only on the two parameters L and $|J_X|$, so that their appearance is completely determined by the ratio $L/|J_X|$. Fig. 4 shows the variation in the spectrum of $A_3XX'A_3'$ with change in this ratio. The general pattern is preserved in the spectra of compounds having a different number of protons [32].

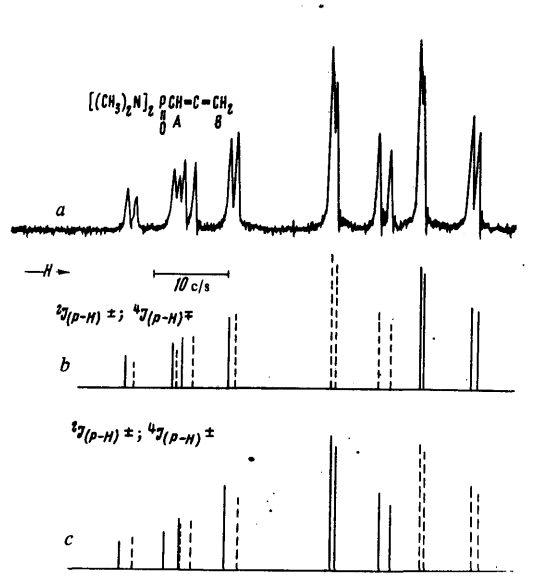


Figure 3. Proton magnetic resonance spectra of propadienylphosphonic bisdimethylamide.

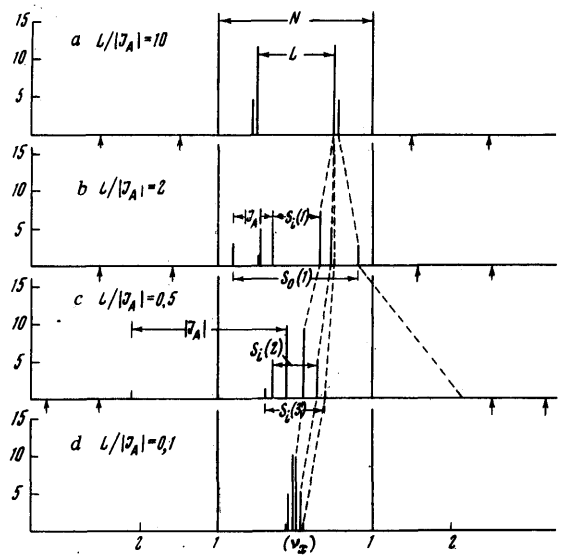


Figure 4. Theoretical spectra of the $A_3XX'A_3'$ system.

Complete analysis of the $A_nXX'A_n'$ spectrum enables only the absolute magnitude of the constant J_X to be determined. However, the relative signs of J_{AX} and $J_{AX'}$ can be ascertained: if any of the inner lines of the quartets lie outside the doublet N, these two constants are opposite

in sign; otherwise, they have the same sign. If the constant J_A is not zero, it is small, the general appearance of the spectrum is preserved, and each line in the quartets is split further; J_A can be evaluated from the magnitude of this splitting, although the calculation is fairly complicated[33]. A particular case is the simple AA'XX' spectrum: its complete analysis involves no theoretical difficulties, and all four spin–spin coupling constants can be determined without the use of tables or electronic computers[34].

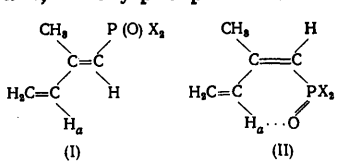
The present Section has considered ways of analysing the complicated p.m.r. spectra of organophosphorus compounds. It is noteworthy that in many cases the p.m.r. spectra are simple, first-order spectra not requiring special analysis. However, additional methods can be used for the analysis, in particular homonuclear and heteronuclear double and triple resonance, the method of two-quanta transitions[35–37], and also replacement of the magnetic nuclei by isotopes with analysis of the signals of ^{13}C satellites, but discussion of these aspects lies outside the scope of the present Review.

III. CHEMICAL SHIFTS OF PROTONS

According to Pauling (see 2.I in Ref. 38) the electronegativity of phosphorus coincides with that of hydrogen, and the chemical shift of the methyl protons in trimethylphosphine is consistent with the correlation found between the chemical shifts of the methyl protons in a methyl derivative of an element and the electronegativity of that element[39]. However, Table 1 shows that phosphonic, thiophosphonic, and phosphonium groups have a considerable deshielding effect, due primarily to the atomic contribution of the phosphorus-containing groups to the proton chemical shifts (transmissible through chemical bonds) and governed by the electron-accepting properties of such groups in comparison with the phosphinous (P^{III}) group. On the whole, estimates of the atomic contribution[25,40] are consistent with the Hammett constants, which indicate that phosphonate groups possess weak electron-accepting properties (close to those of the carboxy-group or the bromine atom). The greater deshielding effect of thiophosphonate than of phosphonate groups, in spite of the lower electronegativity of sulphur than of oxygen, definitely indicates considerable magnetic anisotropy of the P=S group.

Although in Mavel and Martin's estimation[41] the P=O group should also possess considerable magnetic anisotropy, this has not been confirmed by later work. In particular, the almost complete coincidence of the chemical shifts of the terminal protons (*cis* and *trans* with respect to phosphorus) in the spectra of derivatives of vinylphosphonic acid (Table 2),[20,24,42] and also the small difference between the chemical shifts of *cis*- and *trans*-protons in isomeric propenylphosphonates[43] and other analogous derivatives[24,44], indicate that magnetic anisotropy plays an insignificant part in the spectra of these compounds.

The Reviewers have investigated the chemical shifts of protons H_a and the methyl protons in isomeric derivatives of 2-methylbuta-1,3-dienylphosphonic acid of types



($X = Cl$, F, OR, NR_2, C_2H_5), and established that the polar effect of the phosphonic group is decisive in these compounds, leading to formation of an intramolecular hydrogen bond between H_a and the phosphoryl oxygen in isomer (II).[45,46] Whereas the difference between the chemical shifts of the methyl protons in the two isomers lies in the range 0.15–0.22 ppm, the difference for the protons H_a is considerably larger (1–1.5 ppm), although the changes in the geometrical arrangement of H_a and CH_3 in the two isomers are approximately equivalent. The addition of trifluoroacetic acid, which ruptures intramolecular hydrogen bonds, halves the difference for H_a. On the whole it can be accepted as a general principle that protons located spatially closer to a phosphoryl or a thiophosphoryl group resonate at lower field. However, the situation is more complicated in cyclic esters of phosphoric and phosphonic acids[47–53] and in five-membered rings containing phosphorus[54–56]; in particular cyclic oxygen atoms evidently exert no less effect than does phosphoryl oxygen.

Table 1. Chemical shifts and spin–spin coupling constants J_{HP} in the p.m.r. spectra of organophosphorus compounds[17].

	Type of compound	ν, ppm	J, c/s
PH	PH_3	—	182.2
	P^+H	—	495—515
	P (O) H	—	490—710
	P (S) H	—	490—650
PCH	$P(CH_3)_3$	0.9	2.8
	$P^+(CH_3)_4$	2.5	14.4
	P (O) $(CH_3)_3$	1.9	13.4
	P (S) $(CH_3)_3$	1.8	13.0
PCCH	$P(CH_2CO_2)_3$	1.0	13.7
	$P^+(CH_2CH_2)_4$	1.3—1.6	18.0
	P (O) $(CH_2CH_2)_3$	1.1	16.3
	P (S) $(CH_2CH_2)_3$	1.8	11.3
	$R_2P[C\equiv C]_n H$ $n \neq 1,2$	2.6—3.0	0.3—1.5
	$R_2P[C\equiv C]_n CH_3$ $n = 1—3$	2.0—2.1	0.7—1.7
POCH	$P(OCH_3)_3$	3.6	10.5—11.5
	P (O) $(OCH_3)_3$	3.6	10.6—11.2
	P (S) $(OCH_3)_3$	3.7	13.0—13.4
	P (Se) $(OCH_3)_3$	3.7	14.1
PNCH	P $[N(CH_3)_2]_3$	2.5	8.5—9.2
	P (O) $[N(CH_3)_2]_3$	2.6	9.3—9.7
	P (S) $[N(CH_3)_2]_3$	2.6	10.8—11.1
PSCH	$P(SCH_3)_3$	2.3	9.8
	P (O) $(SCH_3)_3$	2.3	15.1—15.6
	P (S) $(SCH_3)_3$	2.4	17.5

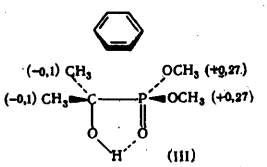
The tendency of phosphoryl compounds to form intramolecular and intermolecular hydrogen bonds is evidently the most characteristic feature distinguishing the proton resonance of these compounds. An intramolecular hydrogen bond is assumed to be the cause of the magnetic non-equivalence of the protons in compounds containing an asymmetric phosphorus atom[57,58]. The tendency of organophosphorus compounds to intermolecular hydrogen bonding has been assessed from the chemical shift of the proton in chloroform dissolved in these compounds[17]. This showed that, with compounds of the type $X_3P=O$, the tendency increases with the accumulation on the phosphorus of substituents X situated towards the end of the sequence

$$Cl < AlkS < AlkO < Alk < Alk_2N.$$

Thus the chemical shift of chloroform (7.08 and 7.28 ppm for a solution in cyclohexane and for the pure liquid)

has the values 7.53, 8.00, 8.25, 8.61, and 9.11 ppm when dissolved in $Cl_3P{=}O$, $(CH_3S)_3P{=}O$, $(CH_3O)_3P{=}O$, $CH_3PO(OC_2H_5)_2$, and $((CH_3)_2N)_3P{=}O$ respectively.

The tendency to form hydrogen bonds involving the phosphoryl group determines in some measure the effect of various solvents on the proton chemical shifts. The effect of trifluoroacetic acid on the chemical shifts of protons in derivatives of 2-methylbutadienylphosphonic acid[45] has already been noted. The intramolecular hydrogen bond in dimethyl 1-hydroxyalkylphosphonates fixes the molecules in a definite conformation. When such compounds (III) are dissolved in benzene



(III)

the solvent molecules are preferentially oriented in such a way that the magnetic anisotropy of the benzene ring produces shielding of methoxyl protons and deshielding of methyl protons[59]

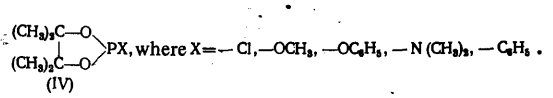
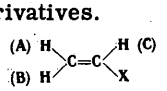

(IV)

Table 2. Parameters δ (ppm) and J(c/s) of p.m.r. spectra of vinylphosphorus derivatives.



P-containing group X	δ_A	δ_B	δ_C	J_{AB}	J_{BC}	J_{AC}	J_{AX}	J_{BX}	J_{CX}
$POCl_2$	6.41	6.51	6.60	0.3	18.2	12.3	77.6	35.0	41.6
$PO(OCH_3)_2$	6.19	6.45	6.19	2.4	18.4	12.8	49.9	24.8	21.0
$PO(OC_2H_5)_2$	6.14	6.18	6.15	2.3	18.7	12.7	50.4	25.0	21.9
$PO[N(CH_3)_2]_2$	4.90	4.93	5.19	1.2	18.2	12.3	58.0	28.6	30.9
$PO(C_6H_5)_2$	5.10	5.10	5.35	2.3	17.9	13.2	36.3	20.4	26.3
$\dot{P}(C_2H_5)_2$	—	—	—	0.05	19.0	12.8	43.8	21.7	21.2
$\dot{P}(CH_3)_2C_6H_5$	—	—	—	0.4	18.6	12.8	48.5	25.3	24.0
$P(CH{=}CH_2)_2$	5.62	5.50	6.15	2.0	18.4	11.8	30.2	13.6	11.7

In the spectra of tetramethyldioxaphospholans of type (IV) the two pairs of methyl groups are not chemically equivalent. Dissolution in benzene increases the difference between their chemical shifts, which indicates the absence of rapid invertion relative to the phosphorus[60].

Use as solvents of strong acids capable of protonating organophosphorus compounds also causes a significant change in the chemical shifts of protons in groups located close to the centre of protonation. Correlation of the change in chemical shifts with the acid function of the solvent enabled protonation constants to be determined for a series of phosphines[61], phosphonates, phosphine oxides, and andions of phosphorus acids[62-64]. In the monomethylphosphonate, which is incapable of further protonation, the proton chemical shift of the methoxyl is independent of the acidity of the solution[64].

Thus examination of proton chemical shifts of organophosphorus compounds shows that in many cases this parameter depends significantly on the state of the phosphorus atom in the molecule and on the relative positions of the proton and the phosphorus-containing group. This enables proton chemical shifts to be used to establish the structure, the geometrical configuration, and the conformational equilibria of organophosphorus compounds, as well as for physicochemical investigations. However, there are no specific differences in the chemical shifts of protons that are caused by the presence of the phosphorus-31 nucleus: the above regularities are general in character and are due to the chemical characteristics of the phosphorus-containing groups, not to the magnetic properties of the phosphorus nucleus. From this point of view the spin–spin coupling of protons and phosphorus, to be considered in the next Section, is a considerably more valuable and interesting parameter for organophosphorus compounds.

IV. SPIN–SPIN COUPLING IN ORGANOPHOSPHORUS COMPOUNDS

1. Proton–Proton Interaction Constants

Neither proton chemical shifts nor proton–proton spin–spin coupling constants are specific in character, but conform to general rules. As a consequence of the low electronegativity of phosphorus, the constants J_{HH} are of the same order of magnitude as in hydrocarbons. The geminal constant $^2J_{HH}$ between protons attached to a carbon atom bound to phosphorus is ~ 10 c/s, as also in the fragment HPH (in chloromethylphosphine $ClCH_2PH_2$ these two constants are 10.4 and 9.8 c/s, the assignment being uncertain[22]); the constant is apparently negative in both cases[65]. In vinyl derivatives of phosphorus $^2J_{HH}$ varies in the range 0.05–2.34 c/s (positive),[20,24,35,36] the lowest value corresponding to the phosphonium compound $(C_2H_5)_3P.CH:CH_2$.[36] The vicinal constant $^3J_{HH}$ between protons in an ethyl group attached to phosphorus also lies near the usual value of 7–7.5 c/s,[29,30,65] independently of the state of the phosphorus; and in ethylenic derivatives it is ~ 12.5 c/s for *cis*-protons and 18.5 to 19 c/s for *trans*-protons[20,24,35,36], an appreciable change in the values of these constants being observed only when other substituents are present at the double bond[36,43,44,66-68]. This fact has been used[69,70] for the quantitative determination of the contents of *cis*- and *trans*-enolic forms in solutions of several substituted diethyl formylmethylphosphonates of the type $R.CH(CHO).PO(OC_2H_5)_2$.

The constants $^3J_{HH}$ between *ortho*-protons in aromatic phosphine oxides also have the usual values of 8–9 c/s.[40,71,72] Values are known for the constant $^3J_{HH}$ in the H–P–P–H system which are close to the vicinal constant in a hydrocarbon fragment (10.5 and 6.8 c/s for the two vicinal constants in diphosphine $H_2P{-}PH_2$[65]). In the H–C–P–H system, however, it varies within fairly wide limits, decreasing as electron-accepting groups accumulate on the phosphorus atom[65,73]:

Compound	CH_3PH_2	$(CH_3)_3\overset{+}{P}H$	$CH_3P(O)(H)(OH)$
$^3J_{HH}$, c/s	7.98	5.48	2.0

Allenic derivatives containing phosphorus show the long-range spin–spin coupling between protons, well known with allenic systems[74], having constants $^4J_{HH}$ and

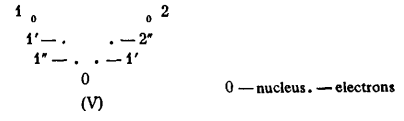
$^5J_{HH}$ of 6–7 ~ 3 c/s respectively[21,25,75–77]. Propenylphosphonic acid derivatives develop allylic spin–spin coupling between protons, with $^4J_{HH}$ being ~ 1 and ~ 1.5 c/s for *trans*- and *cis*-positions of the methyl group and the ethylenic proton[43,46,78].

The spin–spin coupling constants of protons and phosphorus are of considerably greater value for the p.m.r. investigation of organophosphorus compounds, and their intensive study during recent years has enabled the main regularities in their variation to be established. On the whole the principle rules governing magnitude and sign of the constants J_{HP} are the same as those for proton–proton spin–spin coupling, but proton–phosphorus interaction is greater in absolute magnitude and usually remains evident with a larger number of bonds separating the interacting atoms.

2. Sign of Spin–Spin Coupling Constants of Protons and Phosphorus

The relative signs of spin–spin coupling constants in molecules can be determined by analysis of complicated n.m.r. spectra, double and triple resonance, and the method of two-quanta transitions. Theoretical calculations[79] predict a positive (absolute) sign of the constant for directly bound ^{1}H and ^{13}C nuclei and for $^3J_{HH}$. During recent years new methods have been elaborated for determining the absolute signs of spin–spin coupling constants: relaxation times and saturation parameters of individual spectral lines have been shown[80] to depend on the absolute signs of the coupling constants; the dependence of the change produced by the field resulting from the action of the solvent, on the dipole moment of the test substance, has been established for the constants $^2J_{HH}$ and $^2J_{HF}$, which also enables the absolute signs of these constants to be determined[81,82]. Although the absolute signs of the constants have not been determined directly for proton–phosphorus interaction, comparison of available data on the absolute and relative signs of the constants in the spectra of various compounds enables us to elucidate for most cases the absolute signs of the spin–spin coupling constants involving ^{31}P nuclei (Table 3)[83–86].

The occurrence of particular signs of the constants (in saturated compounds) is explained theoretically[87] on the basis of Hund's multiplicity principle. In the case of two magnetic nuclei combined through two chemical bonds (V)



(V)

the Fermi contact interaction of the nuclear spins[88], which makes the chief contribution to the spin–spin coupling constant[89], can be accomplished in two ways.

(*a*) Direct overlapping of the orbitals of electrons 1′ and 2″. This leads to antiparallel pairing of the electron spins, as a result of which the nuclear spins 1 and 2, being oriented antiparallel to the electron spins, are paired together antiparallel, so that the spin–spin coupling constant between them is positive.

(*b*) Overlapping of orbitals with insertion of an intermediate atom. The spins of electrons 1′ and 1″, and independently of them the spins of electrons 2′ and 2″, are antiparallel. Since, however, 1″ and 2′ belong to the same atom, they will tend, according to Hund's rule, to be mutually parallel, the net effect of which is that electron spins 1′ and 2″, as well as nuclear spins 1 and 2, will tend to be parallel, so that the constant has a negative sign.

Table 3. Signs of spin–spin coupling constant of magnetic nuclei with phosphorus $^nJ_{PX}$.

X	n=1	n=2	n=3	n=4	X	n=1	n=2	n=3	n=4
^{1}H ^{13}C	+ +and−	+and− +and−	+ +	+and−	^{19}F ^{31}P	− −and+	+ +	+	+

Competition between the two mechanisms may lead in the case of geminal interaction to either a positive or a negative constant. Extension of this principle to other cases leads to the conclusion that, with an odd number of chemical bonds linking the interacting magnetic nuclei, the spin–spin coupling constant should assume positive values, whereas, with an even number of bonds, it may be either positive or negative. This principle is fully consistent with experimental data on the proton–phosphorus interaction constants[90], but with heavy nuclei directly attached to phosphorus negative constants are observed, for the most part contrary to predictions. The appearance of negative constants between directly bound nuclei was explained by Pople and Santry[91] by applying the molecular orbital method to spin–spin interaction. On the other hand, negative constants may also arise if not only contact interaction but also other contributions play an appreciable part in spin–spin coupling[92–94].

3. Spin–Spin Coupling of a Directly Bound Proton with Phosphorus $^1J_{HP}$

The constant $^1J_{HP}$ varies over a very wide range—from 138 c/s in the dihydrogen phosphide anion PH_2^-[95,96] to 1092 c/s in hydrogen tetrafluorophosphate HPF_4[97]—and is probably positive in all cases. The ease of identification in the spectra and the characteristic values of the constant $^1J_{HP}$, which vary fairly exactly with the valency state of phosphorus and the nature of the substituents, make this parameter extremely convenient both for establishing the structure and for assessing the electron distribution in phosphorus hydrides by means of proton magnetic resonance.

By analogy with the spin–spin coupling constant of directly bound ^{1}H and ^{13}C nuclei, the constant $^1J_{HP}$ has been generally recognised as depending on the *s*-character of the orbital in the H–P bond: $^1J_{HP} = 29.30 s_{PH}$, where s_{PH} is the *s*-character of the P–H bond in phosphine[67].

This relation explains satisfactorily the change in $^1J_{HP}$ on passing from three-coordinated compounds ($^1J_{HP} \simeq$ 200 c/s) to four-coordinated compounds (400–700 c/s), since in the former the P–H bonds are formed predominantly by p-electrons of the phosphorus with slight addition of *s*-character, whereas in four-coordinated compounds, with hybridisation of phosphorus close to sp^3,

these bonds contain 25% and more of s-character. The substantial variations in $^1J_{HP}$ within a group of compounds having the same coordination of phosphorus can be explained by the different electronegativities of the substituents: according to Bent's rule [98] the replacement of substituents on the central atom by more electronegative substituents leads to a concentration of p-character in orbitals in the direction of these electronegative substituents, with a resultant enhancement of the s-character of the coupling with hydrogen atoms. However, this approach is open to criticism.

Whereas with compounds of three-coordinated phosphorus hybridisation can vary within wide limits owing to transition of the lone pair from the s-state to sp^3-hybridisation, with phosphonium salts a significant change in hybridisation is improbable. Yet, whereas in phosphines $^1J_{HP}$ varies within comparatively narrow limits (182 to 216 c/s on passing from phosphine to diphenylphosphine [61]), phosphonium salts show a considerably larger variation (436, 506–510, and 870 c/s for $[(t\text{-}C_4H_9)_3PH]^+$, [61] $[(C_6H_5)_3PH]^+$, [61,94] and $[(C_6H_5O)_3PH]^+$ [94] respectively). The increase in $^1J_{HP}$ on passing from phosphonium salts to dialkyl hydrogen phosphites (695.5 c/s in $HO.P(CH_3O)_2$ [92,99]) and to compounds containing five-coordinated phosphorus, for which the $^1J_{HP}$ constants are especially large

R—PF_2(OR′)	RPF_2(NHR′)	ArPF_2	HPF_4
730—830 c/s[100]	850—858 c/s[101]	739—780 c/s[100–104]	900 c/s[105]	1075—1092 c/s (depending on temp.) (Ref.97)

is still less explicable from this point of view. Although increase in the s-character of the bonding orbitals occurs on passing from three-coordinated to more highly coordinated phosphorus compounds, a decrease in s-character is rather to be expected in four-coordinated compounds with electronegative substituents having a lone pair of electrons (Cl, O, N) and in compounds with five-coordinated phosphorus, owing to hybridisation involving d-orbitals [106].

An explanation of this variation in $^1J_{HP}$ was given by McFarlane and White [94], who suggested, and confirmed experimentally on protonated phosphines, that, by analogy with the behaviour of $^1J_{HC}$, [107] not only the s-character of the P–H orbital but also the charge on the phosphorus atom greatly affects the magnitude of $^1J_{HP}$. It had been shown theoretically [107,108] that the spin–spin coupling constant of directly bound nuclei depends on the cube of the charge, so that small changes in the charge may have a substantial effect on the constant. This new approach opens up wide possibilities of explaining the effects of substituents on $^1J_{HP}$ and elucidating the distribution of electron density in organophosphorus molecules. Thus the effect of solvents on $^1J_{HP}$ in dimethyl hydrogen phosphite (this parameter varies from 627.9 c/s in solution in an ammoniacal buffer (pH 11.4) to 734.3 c/s in trifluoroacetic acid [99]) can be explained by a difference in solvation of the P=O group and the accompanying change in the charge on the phosphorus. The increase in $^1J_{HP}$ in the above five-coordinated phosphorus compounds is obviously due to the accumulation of electronegative substituents, which produce an increase in the positive charge on the phosphorus.

The above regularities in the spin–spin coupling of directly bound ^1H and ^{31}P atoms can be extended in considerable measure to the longer-range interaction of these nuclei, but their relative positions in space then play a considerably greater part.

4. Spin–Spin Coupling of Proton and Phosphorus in a Geminal Position $^2J_{HP}$

Geminal proton–phosphorus spin–spin coupling constants are of considerable interest both for the identification of organophosphorus compounds and for establishing general n.m.r. rules in connection with the electron distribution in them. It is usually easy to elucidate these constants in the proton spectra, and often their signs relative to $^1J_{HP}$, $^3J_{HP}$, etc. can often be determined, which facilitates the establishment of their absolute signs. The limits of variation in $^2J_{HP}$ are fairly wide, from +59.0 c/s in *cis*-propenylphosphonic dichloride [43] to between −21 and −22 c/s in compounds of the type $R.CH_2.PO(OC_2H_5)_2$, where R is an electron-accepting group having a multiple bond (C=O, C≡N, C≡C). [109,110] It is interesting that these limits exceed only slightly the known limits of variation in geminal proton–proton constants [111], but they will undoubtedly be extended for proton–phosphorus interaction.

At least three factors—the state of hybridisation at substituents on the phosphorus atom, the substituents attached to the carbon atom, and the configuration of the molecule—govern the value of $^2J_{HP}$ in the H–C–P system. In saturated four-coordinated phosphorus compounds this parameter is usually negative, varying in the vicinity of −15 to −20 c/s, [37] but it has been found recently [29] that $^2J_{HP}$ and $^3J_{HP}$ have the same signs in ethylphosphonic dichloride and difluoride, which indicates a positive absolute sign of the geminal proton–phosphorus constant $^2J_{HP}$ (+19.6 and +14.1 c/s in $C_2H_5POF_2$ and $C_2H_5POCl_2$ respectively‡). Comparison of the relative signs of the constants in ethylenic [20,24,35,36,43] and allenic [21,76,85] organophosphorus compounds shows convincingly that the geminal H–C–P constant at an unsaturated carbon atom is always positive. On the whole substituents at a carbon atom have the same effect on $^2J_{HP}$ as on the proton–proton coupling constant $^2J_{HH}$: [111] the introduction of electronegative substituents, change in the hybridisation of carbon from sp^3 to sp^2, and also the introduction of electron-donating substituents—all produce a change in $^2J_{HP}$ towards *positive values*. Substituents on the phosphorus obviously conform on the whole to the same rule in their effect on $^2J_{HP}$: electronegative substituents, capable of moving electrons to d-orbitals of phosphorus by a conjugation mechanism, produce a change in the geminal constant towards positive values.

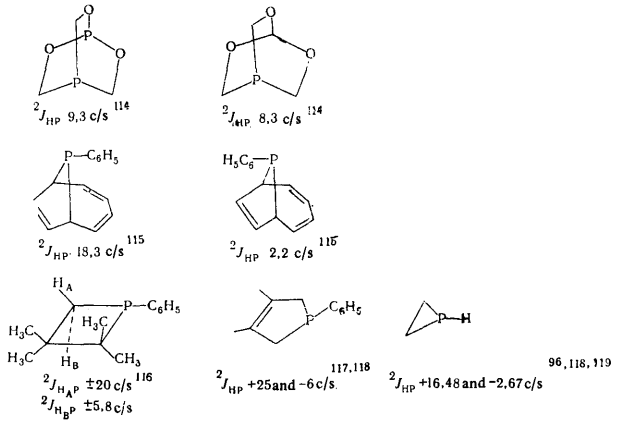
The effect of substituents on $^2J_{HP}$ is considerably smaller in three-coordinated phosphorus derivatives, although the attachment of chlorine atoms to the phosphorus or the transition from an sp^2- to an sp^3-hybridised carbon atom increases the parameter, as with the four-coordinated compounds:

Compound	$(CH_3)_3P$	$(CH_2{=}CH)_3P$	$CH_3CH_2PCl_2$
$^2J_{HP}$, c/s	+2.66[65]	+11.74[25]	+15.0§[113]

‡These results differ somewhat from the values obtained in an unpublished paper [112].

§We have adopted a positive sign for $^2J_{HP}$ in ethyldichlorophosphine on the basis that the geminal and vicinal constants in the spectrum of this compound [113] have the same sign.

In phosphines containing aliphatic and aromatic substituents $^2J_{HP}$ varies only within the narrow limits of zero to +4 c/s, but considerable departures from these limits are observed in compounds containing the phosphorus atom in a strained ring:



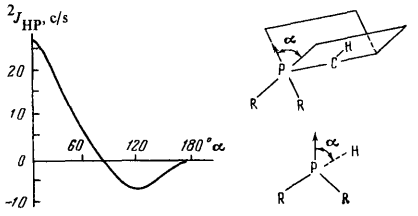
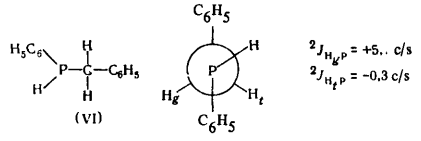


Figure 5. Angular dependence of constant $^2J_{HP}$ in phosphines.

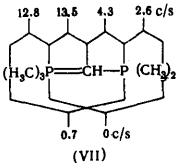
Albrand et al. [118] have analysed the above and other similar data, and have shown convincingly that the geminal constant $^2J_{HP}$ in phosphines is determined mainly by the mutual arrangement of the proton and the substituents on the phosphorus (Fig. 5). Data for compounds having a rigid configuration extend also to benzylphenylphosphine



in which the non-equivalence of the two methylene protons is due to inhibited rotation. Comparison of the proton–proton and proton–phosphorus constants enables us not only to determine the absolute signs of the latter but also to assign them to certain protons [118].

Unfortunately, so few data are available on the spin–spin coupling constants of five-coordinated phosphorus compounds that no general conclusions can be drawn.

It is interesting that the geminal constants $^2J_{HP}$ in the phosphinophosphorane



correspond exactly to the above values for three- and four-coordinated phosphorus [120].

5. Spin–Spin Coupling of Proton and Phosphorus in the Vicinal Position $^3J_{HP}$

Vicinal proton–phosphorus constants are evidently always positive, and on the whole depend on the same factors as do the geminal constants, but the mutual positioning of the interacting nuclei plays a still greater part. Analysis of vicinal constants in cyclic and unsaturated compounds [121–123], for which it is possible to estimate the dihedral angle Φ between the HC^1C^2 and C^1C^2P planes in the $H–C^1–C^2–P$ system, showed that the dependence of $^3J_{HP}$ on Φ is completely analogous to the corresponding relation for proton–proton interaction [124] (Fig. 6): (i) $^3J_{HP}$ has its maximum value at Φ = 180°; (ii) $^3J_{HP}$ has its minimum value or is zero when Φ = 90°; (iii) when Φ = 0° the constant $^3J_{HP}(0°) = (0.5–0.33)^3J_{HP}(180°)$; (iv) with other values of the angle Φ the parameter $^3J_{HP}$ assumes intermediate values.

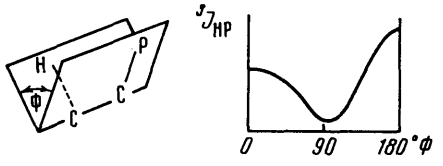
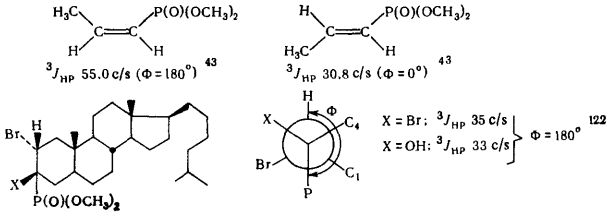
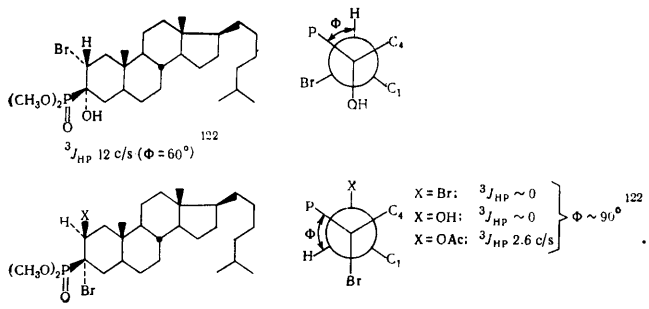


Figure 6. Angular dependence of constant $^3J_{HP}$.

The spin–spin coupling constant of the phosphorus atom in the dimethoxyphosphinyl group and a vicinal proton varies from 9 to 55 c/s with different values of Φ:





The above dependence on the dihedral angle and the considerable range of variation in $^3J_{HP}$ make elucidation of the vicinal proton–phosphorus interaction constant especially valuable in stereochemical investigations.

Substituents attached to carbon atoms have the same effect on $^3J_{HP}$ as in proton–proton interaction: electronegative substituents produce a decrease in the parameter. Thus for the bisdimethylamides of a series of vinylphosphonic acids $^3J_{HP}$ varies as follows [20,74]:

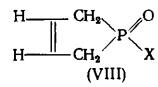
X = H	CH_3	$N(CH_3)_2$	OCH_3
$^3J_{HP}$ = 28.7	18.4	14.0	10.5 c/s

On the other hand, introduction of electronegative substituents at the phosphorus atom and the change from tervalent to four-coordinated phosphorus compounds produce increases in $^3J_{HP}$, as with geminal proton–phosphorus interaction. In a series of derivatives of vinylphosphonic acid, for example, the parameter falls in the sequence [20,21,24,35,36,43–45]

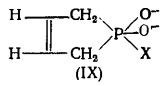
$$P(O)Cl_2 > P(O)(SC_2H_5)_2 > P(O)[N(CH_3)_2]_2 > \overset{+}{P}R_3 > P(O)R_2 > PR_3,$$

and in *cis*-prop-1-enylphosphonic dichloride the constant $^3J_{PH,trans}$ = 85.0 c/s [43] assumes the maximum value known at present for constants of this type. Electronegative substituents, capable of conjugation involving vacant *d*-orbitals of phosphorus, evidently cause rehybridisation of the orbitals and enhancement of the *s*-character in the direction of the phosphorus–carbon bond. It is possible also that the variation in the parameters is associated with a change in the charge on the phosphorus. However, variation in the substituents attached to three-coordinated phosphorus in the allenic derivatives $CH_2:C:C(CH_3).PX_2$ is accompanied by variation in $^3J_{HP}$ in the opposite sequence—8.9, 7.8, and 3.4 c/s when X represents C_6H_5, $N(CH_3)_2$, and Cl respectively [21].

Although no considerable spin–spin coupling in the =CH–C–P system has been detected in open-chain allyl compounds, the parameter $^3J_{HP}$ is quite large (36 to 40 c/s) in cyclic phospholens of the type



(VIII)



(IX)

and varies little with the coordination number of the phosphorus [124–126].

Considerable values of $^3J_{HP}$ are found also in systems containing a heteroatom, and depend more on the nature of the heteroatom than of the substituents attached to phosphorus [17,127–130]:

H–C–O–P	H–C–N–P	H–C–S–P
8–12 c/s	11–12 c/s	14–22 c/s

As with other vicinal constants this parameter, too, has been found to depend on the dihedral angle [48,58], and $^3J_{HCOP}$ is apparently also maximal with the interacting nuclei in the *trans*-position.

Thus the parameters $^3J_{HP}$, usually easily identifiable in the p.m.r. spectra of organophosphorus compounds, are extremely sensitive to their electronic structure and especially their geometrical structure, and can therefore be widely used in analysing the structure of compounds.

6. Long-range Proton–Phosphorus Spin–Spin Coupling $^nJ_{HP}$

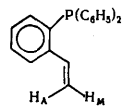
Long-range spin–spin coupling $^nJ_{HP}$ is observed in many cases through 4–8 bonds in allenic and acetylenic systems containing phosphorus atoms. A series of acetylenic phosphonates show a uniform decrease in $^nJ_{HP}$, proportional to the cube of the distance between the hydrogen and phosphorus nuclei [131], as *n* increases from 3 to 6; with *n* = 6 the constant $^6J_{HP}$ is still considerable (2.15 c/s). The long-range spin–spin coupling constant of protons and phosphorus is lower in phosphines and their oxides and sulphides than in phosphonates, but even in heptatriynyldiphenylphosphine $(C_6H_5)_2P.[C:C]_3.CH_3$ spin–spin coupling $^8J_{HP}$ = 0.7 c/s is observed [132,133]. Unfortunately, the absolute signs of the constants in such systems have not been studied in detail; double resonance has shown that the constants $^4J_{HP}$ and $^1J_{FP}$ in prop-1-ynylphosphonic acid $CH_3.C:C.POF_2$ have opposite signs [134], so that the proton–phosphorus constant is positive.

Considerable spin–spin coupling $^4J_{HP}$ and $^5J_{HP}$ is observed in allenic compounds containing a three- and four-coordinated phosphorus atom [21,25,75,77]. In compounds of the type $CH_2:C:CH.POR_2$ the constants $^4J_{HP}$ vary between –10 and –18 c/s with increase in the Taft inductive constant σ_1 of the substituents (R = Alk, Ar, NAlk$_2$, OAlk, Cl). [21] In the analogous compounds containing three-coordinated phosphorus the constant $^4J_{HP}$ is proportional to the Hammett constant σ_n, and has a negative sign in all cases except when at least one of the substituents is a dimethylamino-group; this is probably due to the ability of the lone pair of the nitrogen to conjugate with vacant 3*d*-orbitals of phosphorus [21].

The constant $^5J_{HP}$ in the allenic phosphonate $(CH_3)_2C::C:CH.POX_2$ with X = Cl is +12.1 c/s, [21,135] but in compounds with other substituents attached to phosphorus it is lower (6.1, 6.3, 7.8, 9.7, and 5.4 c/s when X = $N(CH_3)_2$, C_6H_5, [21] OC_2H_5, [136] F, [77] and C_2H_5 [75] respectively). The constant may be assumed to be positive in all compounds of this type. It is interesting that, as in other cases, the proton–proton interaction parameter in this system is considerably smaller and more constant: $^5J_{HH}$ varies in the range 3.1–3.5 c/s.

The analogy between proton–phosphorus and proton–proton long-range interaction is apparent in the considerably lower long-range coupling constants in allylic and aromatic than in acetylenic and allenic systems. In $CH_3.CH:CH.POX_2$ the constants $^4J_{HP}$ = 0–3.5 c/s (probably negative), the splitting being greater with methyl and phosphorus-containing groups in the *cis*-position than in the *trans*-isomers [43,45,66,137]. Derivatives of phosphonic acids with 1,3-diene substituents $CH_3XCH:CH.CH:CH.POY_2$ (*trans*, *trans*) exhibit splitting of the $C_{(3)}$ proton signal with the constant $^4J_{HP}$ = 1.6–1.7 c/s. [138] The constants for the methyl protons in *o*-tolylphosphorus derivatives and for the ring *meta*-protons in various phenylphosphorus compounds lie in the range 1–4.2 c/s. [40,71,72]

However, the discovery of long-range spin–spin coupling in *o*-vinylphenyldiphenylphosphine



(X)

$^5J_{H_AP}$ 1.1 c/s

$^5J_{H_MP}$ 0.1–0.05 c/s

is quite unexpected. In this case interaction is attributed to direct overlapping of the electron clouds of the proton and phosphorus through space. Such interaction is not observed in the corresponding phosphonium iodide [139].

Long-range spin–spin coupling constants in systems containing a heteroatom are extremely small [140–144]. Nevertheless, it has been possible to establish by means of double resonance that they may have different signs depending on the substituents attached to the phosphorus [140]:

Compound	$(C_2H_5O)_3P$	$(C_2H_5O)_3P{=}O$	$(C_2H_5O)_3P{=}S$
$^4J_{HCCOP}$, c/s	−0.55	+0.84	+0.73

The variation in sign may be due to the conformational constitution of the compounds, since the above constants result from the averaging of all possible conformational structures.

In the fragment P.CO.N.CH.CH the constant $^5J_{HP}$ exceeds $^4J_{HP}$, and this serves to confirm the hypothesis of two simultaneous mechanisms of spin–spin coupling, making opposite contributions to the latter constant [144].

The above relations of the proton chemical shifts and the proton–phosphorus spin–spin coupling constants with the molecular and electronic structures of organophosphorus compounds present wide possibilities for the p.m.r. investigation of these compounds. The next Section examines the most important lines of research.

V. MAIN LINES OF THE p.m.r. INVESTIGATION OF ORGANOPHOSPHORUS COMPOUNDS

The practical application of p.m.r. spectroscopy is concerned primarily with establishing the molecular and geometrical structure of organic compounds.

Proton magnetic resonance has recently been widely used to confirm the structure of five-membered phosphorus-containing heterocycles, which result from the reaction of tervalent phosphorus derivatives with conjugated systems. As already remarked, the constants $^3J_{HP}$ are quite considerable in cyclic compounds, which enables the latter to be distinguished unambiguously from open-chain compounds [124–126,145–148]. Close attention has been paid to esters of phosphonic acids with groups, potentially capable of keto–enol tautomerism [109,149,150] or containing a mobile hydrogen atom [109,151,152], which are distinguished by a considerable $^2J_{HP}$ constant (10–21 c/s). Several esters, thioesters, and amides of phosphoric, thiophosphoric, and phosphonic acids of interest as insecticides have been identified by p.m.r. for analytical purposes [127–129].

Widespread use is made of p.m.r. for the easy establishment of the geometrical structure of organophosphorus compounds, especially ethylenic derivatives. In effect only this method has provided an approach to the problem of the *cis–trans* isomerism of ethylenic phosphonates [43,66,68,121–123]; establishment of the *trans*-structure of 2-cyanovinylphosphonic esters necessitated reconsideration of the mechanism of their formation [153].

Application of this method enabled a study to be made of the aldo-*cis–trans*-enol tautomerism of substituted formylmethylphosphonates in solution [69,70].

Extremely interesting results have been obtained on the conformations of open-chain organophosphorus compounds, made possible by the phenomenon of molecular asymmetry and governed by the difference in the chemical shifts and the spin–spin coupling constants for protons in the various conformations [118,154–156]. Study of the effects of temperature and the solvent on the spectra provides additional opportunities for investigating the problem [157]. Development of research on these lines includes the question of the pseudorotation of systems that are stable at ordinary temperatures [158,159].

The appearance of the p.m.r. method gave a sharp impetus to the development of research on interactions such as hydrogen bonding and intermolecular association. The Reviewers established the presence of an intramolecular hydrogen bond in derivatives of 2-methylbutadienylphosphonic acid [45,46]; an intramolecular hydrogen bond explains the molecular association effect in the spectrum of 2,4-dichlorophenyl methyl isopropylphosphoramidate [160]; an intermolecular hydrogen bond affects the chemical shift of the proton of chloroform dissolved in organophosphorus compounds [17]. This aspect is closely connected with the problem of chemical exchange in complexes with organophosphorus ligands [161]. The investigation of complexes of organophosphorus compounds with metals is inherently a fairly complicated problem, solution of which requires the application not only of p.m.r. but also of other types of nuclear resonance spectroscopy [161–166].

We note in conclusion that the p.m.r. method has found a valuable application for studying the protonation of organophosphorus compounds by strong acids [61–64,94]. In individual cases it is possible to determine the lifetime of molecules in the protonated state [167].

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Base-catalysed Rearrangements of Epoxides

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The principal characteristics of the rearrangements of epoxides due to the elimination of α-, β-, γ-, δ-, and ϵ-protons under the influence of bases have been considered.
The bibliography includes 135 references.

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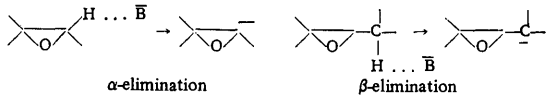
I. INTRODUCTION

Numerous monographs and reviews have been devoted to the reactions of epoxides[1-7]. Two types of reactions—addition and isomerisation—are the most characteristic of epoxides. Until recently, the study of the chemistry of epoxides was confined in most cases to reactions in which nucleophilic agents added to them and to their acid-catalysed isomerisations to carbonyl compounds. Recently new reactions of epoxides catalysed by strong bases were discovered. This review is a first attempt at a systematic account of the data which have accumulated on the isomerisation of epoxides in the presence of strong bases, i.e. processes which are not accompanied by the intermolecular addition of any external agents to the epoxides.

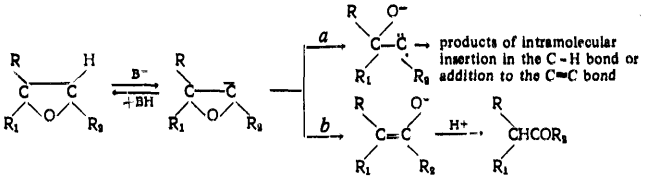
In a study of a base-catalysed isomerisation of the so called "non-functional" epoxides, i.e. epoxides without any other functional groups, Crandall showed that, depending on the reaction conditions, strong bases abstract a proton from the α- or β-position in relation to the oxygen atom of the epoxy-ring[8,9]:



When the epoxide molecule contains an electron-accepting functional group, there is a possibility of the elimination of the proton from the carbon atom adjoining this group (processes involving the elimination of a proton from a heteroatom in the functional group are not discussed in this review). In general one can consider the elimination of α-, β-, γ-, δ-, and ϵ-protons, etc. and the various reactions of epoxides due to these processes.

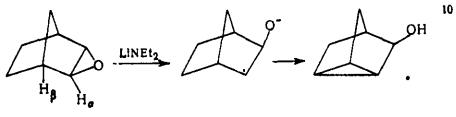
II. ELIMINATION OF AN α-PROTON

The majority of the cases of elimination of the α-proton described hitherto have been observed with non-functional epoxides or epoxides having aromatic substituents, since the introduction of any functional group into the side chain of the epoxide favours the removal of a proton from other parts of the molecule. The α-elimination results in the formation of an epoxide anion which subsequently isomerises according to a carbenoid (*a*) or an anionic (*b*) mechanism†, depending on the reaction conditions and the structure of the initial epoxide:



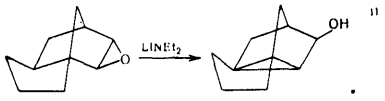
In the presence of hydrogen atoms in the α- and β-position, β-elimination takes place as a rule. Two cases constitute exceptions.

1. The approach of the base to the β-proton is greatly hindered as a result of which α-elimination takes place. For example, epoxynorbornane (I) isomerises to a nortricyclanol as a result of the intramolecular insertion of β-alkoxycarbene in the C — H bond[10], so that the approach of the base to the β-H atom is sterically hindered:



(I)

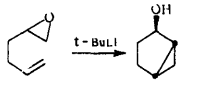
The epoxide (II) reacts similarly:



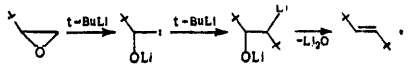
(II)

2. α-Elimination is observed with epoxycycloalkanes containing 8 — 10 carbon atoms in the ring. A characteristic property of such rings is transannular reactions owing to the closeness in space of the opposite carbon atoms[12,13]. Thus the epoxy-derivatives of *cis*- and *trans*-cyclo-octenes isomerise on treatment with $LiNEt_2$ to the corresponding bicyclo-octanols as a result of a transannular carbenoid insertion[14,15].

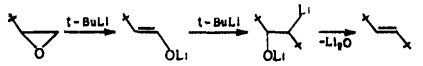
The attempt to trap the carbene in an intermolecular reaction involving addition to the C=C bond was unsuccessful, while the analogous attempt in the intramolecular reaction succeeded[16]:



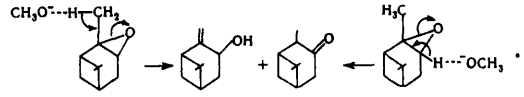
Crandall and coworkers[17] observed that, when t-butyl-epoxyethane is treated with t-butyl-lithium, *trans*-di-t-butylethylene is formed in high yield. The authors explain this finding by the formation of a carbene and its subsequent insertion in the t-butyl-lithium molecule:



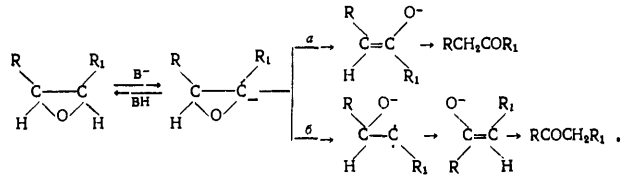
The simpler pathway for the formation of di-t-butylethylene via the intermediate formation of the product of the addition of t-butyl-lithium to the epoxide is rejected, since the product of this reaction (an alcohol) would not be dehydrated under the reaction conditions. We believe that the recently observed[18] enhanced tendency of lithium alkoxides derived from allyl alcohols to undergo addition reactions with lithium alkyls makes it unnecessary to postulate the insertion of a carbene in the t-butyl-lithium molecule, since the reaction can take place according to the mechanism



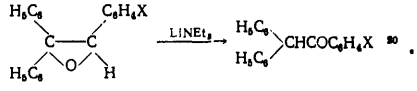
The isomerisation of alkyl-substituted epoxides in the presence of strong bases to allyl alcohols (β-elimination, see p. 405) is usually accompanied by the formation of ketones as a side reaction. For example, the isomerisation of the epoxy-derivative of α-pinene in the presence of sodium methoxide leads to pinocarveol and pinocarvone[19]:



A control experiment showed that pinocarveol isomerises only slightly to pinocarvone under the reaction conditions. Similar results were obtained also in a few other cases[8,16]. All these findings suggest that ketones are formed mainly via a pathway involving the initial elimination of the α-proton from the epoxide[8]. Further conversion of the epoxidecarbanion into the ketone can theoretically take place via two mechanisms:

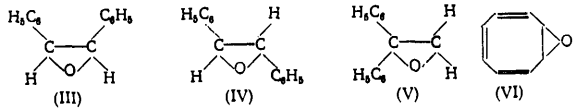


As a rule the reaction follows pathway *a*, as can be seen from the following example:



However, it is noteworthy that aryl substituents may stabilise the carbanion.

Carbonyl compounds are the main products of the base-catalysed isomerisation of the epoxides (III) — (VI)[20-22]:

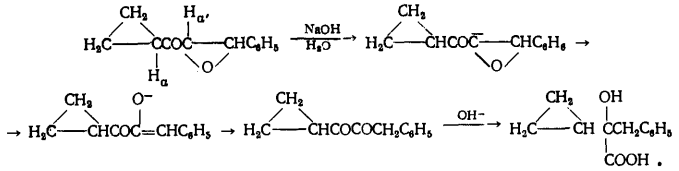


(III) (IV) (V) (VI)

The isomerisation of α-ketoepoxides in an alkaline medium does not usually stop at the stage involving the

† The mechanisms quoted do not imply that a "free" carbene or carbanion is formed during the isomerisation. The reactions are classified on the basis of the final products.

formation of a α-diketone[23-29], since the latter undergoes the benzil rearrangement under the reaction conditions[29]:

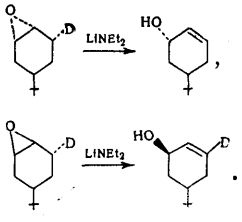


Of the two possible pathways for the conversion of the ketoepoxide—the Favorskii rearrangement (with the abstraction of a proton from the α-carbon atom as the initial stage) and the benzil rearrangement (with the abstraction of a proton from the α'-carbon atom as the initial stage)—in the above example the second actually occurs, owing to the greater mobility of the hydrogen atom in the α'-position.

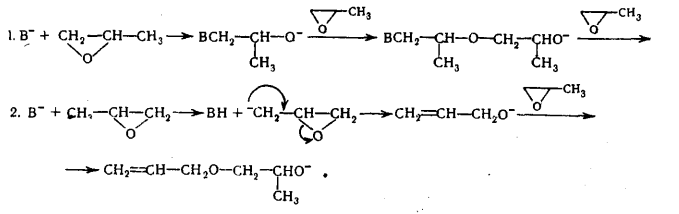
In conclusion we may note a unique case of the isomerisation of epichlorohydrin and its homologues to α-chloroketones as a result of the elimination of the α-proton under the influence of lithium orthophosphate. β-Elimination products were not detected in these reactions. According to Sheng[30], this is evidence of a considerable increase of the mobility of the proton linked to the carbon atoms in the epoxy-ring under the influence of the adjacent chloromethyl group.

III. ELIMINATION OF A β-PROTON

In a study of the mechanism of the base-catalysed isomerisation of the epoxy-derivatives of *cis*- and *trans*-oct-4-enes (labelled with deuterium in 4- and 5-positions) to allyl alcohols, Cope and Heerin demonstrated unambiguously that the first reaction stage is the abstraction of a proton from the β-position of the epoxide[31]. However, it is not clear whether the process proceeds via the intermediate formation of a carbanion or via a concerted mechanism. A further step towards the understanding of the β-elimination mechanism was taken by Thummel and Rickborn[32], who showed that the conversion of epoxides into aryl alcohols is a *cis*-elimination reaction:

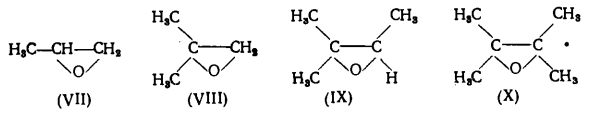


A study of epoxide polymers obtained in the presence of alkaline catalysts revealed a high content of unsaturated terminal groups[33]. It has been suggested[34] that the initiation and propagation of the polymer chain may be represented by mechanism (1), while the unsaturated terminal groups are formed as a result of the competing reaction (2):



The latter leads to a lowering of the molecular weight, since the abstraction of a proton from the β-position of the monomer by the growing polymer chain leads to chain termination[35].

In a study of the polymerisation of epoxides in dimethyl sulphoxide catalysed by potassium t-butoxide, Price and Carmelite[36] showed that the yield of the polymer and its molecular weight decrease in the series of epoxides (VII) > (VIII) > (IX) > (X). The yield of allyl alcohols increases simultaneously in the same sequence:



The ratio of the addition and β-elimination products is determined to a large degree by the basicity of the alkaline agent. As a rule, the stronger the base the lower the yield of the addition product. For example, in the presence of n-propyl-lithium or n-butyl-lithium epoxycyclohexane isomerises to cyclohex-3-enol and a small amount of 2-alkylcyclohexanol, while in the presence of allylsodium and allylmagnesium bromide, only the alkylation products were obtained[37] (see also Bedos[38,39]).

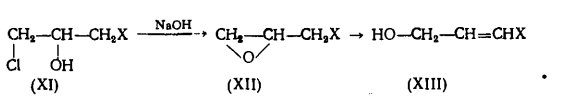
A comparative study of the effects of base strength on the relative amounts of the alkylation and β-elimination products from epichlorohydrin was made by Fabris[40].

The bulk of the base and the steric accessibility of the reaction centre have a considerable influence on the proportions of the addition of β-elimination products. It has been shown[41] that the rates of abstraction of a proton from primary, secondary, and tertiary alkyl groups decrease in the series primary $\gg$ secondary $\gg$ tertiary. The introduction of a methyl group into the epoxy-ring greatly facilitates the conversion of these epoxides into allyl alcohols. The epoxy-derivatives of 1-methylcycloalkenes[42], α-pinene[8,43-46], Δ^3-carene[44-47], β-diisobutene[8], and many others[48,49] isomerise in this way.

Methyl-substituted epoxides can isomerise to allyl alcohols under very mild conditions, for example in chromatography on alumina[50-54] and on treatment with aluminium alkoxides[55,56] and di-isobutylaluminium[57] and methoxyaluminium[58] hydrides.

The isomerisation of a series of epoxycycloalkanes to allyl alcohols as a result of the elimination of a β-proton has been described[8,43,59-64].

The elimination of a β-proton is greatly facilitated in the presence of an electron-accepting substituent in the methylene (or methylidyne) group attached to the epoxy-ring. It was noted long ago that the principal products of the dehydrohalogenation of the chlorohydrins (XI), where X = SO_2Ar,[65] CN,[66] $COOCH_3$,[67] and C≡C – R[68-72], are not the epoxides (XII) but the alcohols (XIII):

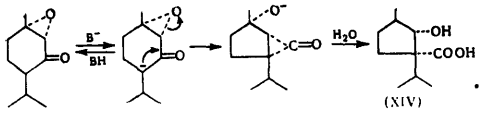


It has been shown in a number of studies that epoxides of type (XII), where X = Cl [40] (c.f. Sheng[30]), NO_2,[73] PR,[74] and CH = CHR [75] also readily isomerise to allyl alcohols.

IV. ELIMINATION OF A γ-PROTON

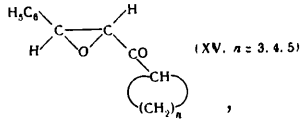
The base-catalysed abstraction of a proton from the carbon atoms in the epoxy-ring (α-elimination) is facilitated by the presence in the ring of a heteroatom and the shift of electron density towards it. Since the epoxy-ring exhibits an *I* effect[76-79], the relative ease of β-elimination is understandable. The abstraction of a proton from a carbon atom in the side chain of the epoxide is particularly easy when an adjoining electronegative group is present (C = O, CN, COOR). Rearrangements of "functional" epoxides of this kind will be considered in the present section.

The Favorskii rearrangement of α-epoxyketones is a well known example of the base-catalysed isomerisation of epoxides as a result of the elimination of a γ-proton. For example, it has been shown in a number of investigations[80-86] that, in the presence of bases (OH^-, OR^-), the epoxy-derivative of piperitone rearranges to the hydroxy-acid (XIV):



(XIV)

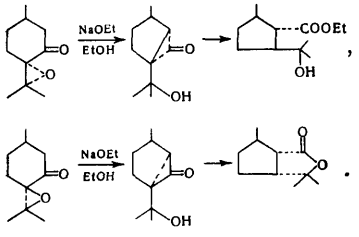
Analogous reactions of the epoxy-derivatives of isophorone and α-epoxyketones of type (XV),



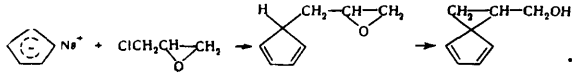
(XV, n = 3, 4, 5)

have been described[29,86].

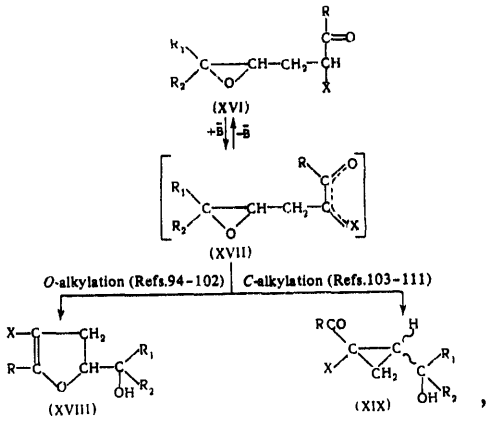
The study of the Favorskii rearrangements of the epoxy-derivatives of *cis*- and *trans*-pulegones showed that in both cases the process is stereospecific[87-90]:



Yet another example of the base-catalysed isomerisation of an epoxide as a result of the elimination of a γ-proton has been described[91]:

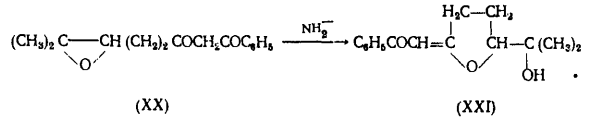


In a series of studies, Temnikova, Ershov, and coworkers investigated in detail the isomeric conversions of epoxides of type (XVI) containing in the side chain the RCO—CH—X fragment, which is capable of mesomerism. Depending on the nature of the substituents R and X, in an alkaline medium the epoxides (XVI) isomerise as a result of the intramolecular *O*-alkylation of the RCO—CH—X fragment with formation of 4,5-dihydrofurans (XVIII) or the *C*-alkylation products of the same fragment—derivatives of cyclopropane (XIX)‡:



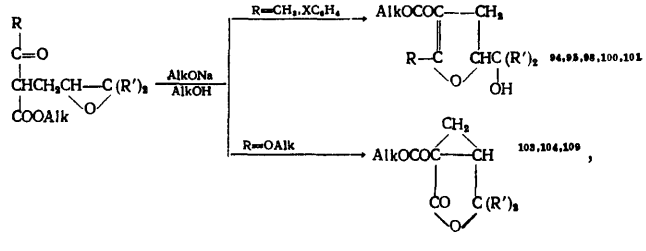
where R = CH_3, XC_6H_4, OCH_3, or OC_2H_5, X = C_6H_5, CH_3 H, OCH_3, OC_2H_5, CN, $COCH_3$, or COC_6H_5, and R_1, R_2 = H, CH_3, or XC_6H_4.

The base-catalysed isomerisation of the γε-diketo-epoxide (XX) results in the formation of exomethylene-tetrahydrofuran (XXI)[112]:



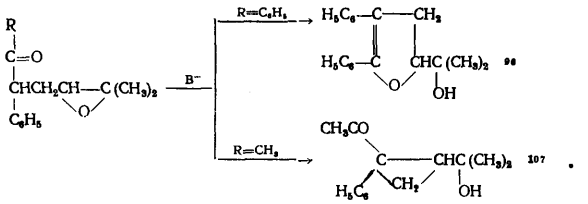
In contrast to the analogous intermolecular processes leading exclusively to *C*-alkylation products[3], intramolecular alkylation in systems of type (XVI) results as a rule in the formation of *O*-alkylation products[94-102,112,113-116]. This can be accounted for by the dominant role of steric factors in the above intramolecular reactions[118,119], since the steric requirements which must be met by the geometry of the transition state in *O*-alkylation are usually less rigorous than in *C*-alkylation; moreover, *O*-alkylation leads to less strained systems than does *C*-alkylation.

Another important factor determining the mode of intramolecular alkylation in systems (XVI) with a similar structure is the degree of delocalisation of the charge in the intermediate carbanion (XVII). A high degree of delocalisation of the charge in the anion leads to the formation of *O*-alkylation products, i.e. in this case alkylation takes place at the most electronegative reaction centre[117]:



‡ The possibility of the base-catalysed isomerisation of cyclopropyl ketones to 4,5-dihydrofurans has been discussed[92,93].

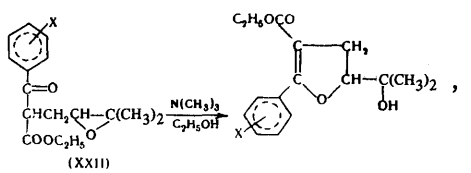
where R' = CH_3 or XC_6H_4 and Alk = CH_3 or C_2H_5.



Experimental data agree qualitatively with the calculations by the LCAO-MO method[120].

The mode of base-catalysed isomerisations of epoxides (XVI) is determined mainly by internal (structural) factors. A change in external conditions (the solvent, the basic catalyst, and temperature) does not as a rule affect the site of intramolecular alkylation.

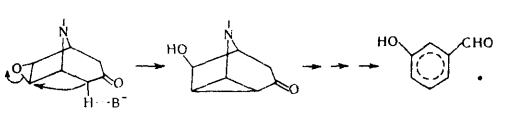
Kinetic studies on the mechanism of the isomerisation reaction[121]



(XXII)

where X = H, *p*-CH_3, CH_3O, Br, or *m*-Cl, show that the reactions of epoxides (XXII) having electron-donating substituents (particularly with X = *p*-CH_3O) involve predominantly a relatively non-polar transition state and a synchronous mechanism including the abstraction of a proton from the carbon atom of the keto-form (XXII) with the subsequent intramolecular *O*-alkylation accompanied by a transfer of the reaction centre. In the case of epoxides (XXII) with electron-accepting substituents, a proton is abstracted in the first stage from the oxygen atom of the enolic form of the β-ketoester (XXII); subsequently the oxygen atom of the enolate anion formed attacks the carbon atom of the epoxy-ring. A characteristic feature of the last transition state is the *cis*-orientation of the negatively charged oxygen atom and the residue containing the epoxy-rings§.

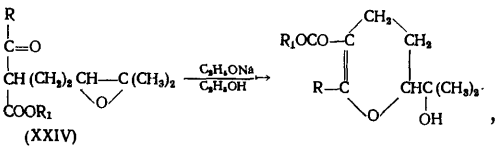
The above reactions include certain rearrangements in the benzonorbornene series and certain alkaloids[123-125]. For example the alkaloid skopinone (XXIII) is converted into *m*-hydroxybenzaldehyde in the presence of bases. It is suggested that the initial stage in this rearrangement is the elimination of a γ-proton with subsequent intramolecular *C*-alkylation[124,125]:



(XXIII)

V. ELIMINATION OF δ- AND ε-PROTONS

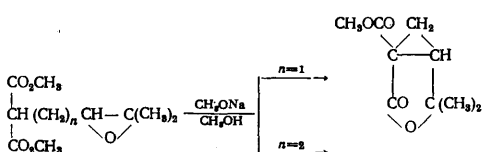
Temnikova, Ershov, and coworkers showed that epoxides of type (XXIV) isomerise in an alkaline medium as a result of intramolecular *O*-alkylation with formation of 5,6-dihydro-1,4-pyrans[113-116,126]:



(XXIV)

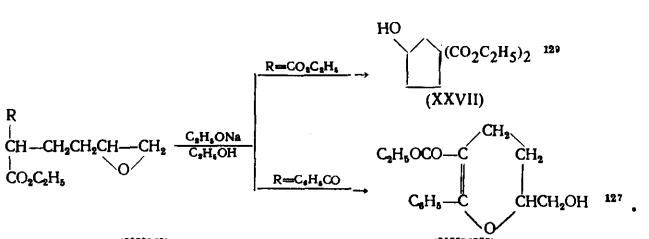
where R = CH_3 or XC_6H_4 and R_1 = CH_3 or C_2H_5.

According to a kinetic study, the first stage of the process is the elimination of a δ-proton under the influence of the base. This results in the formation of a mesomeric carbanion, which isomerises to the corresponding dihydropyran[127]. Derivatives of cyclobutane or cyclopentane, i.e. *C*-alkylation products, were not detected in the reactions investigated[113-119]. Nor are they formed on treating with bases under severe conditions the epoxide (XXV, *n* = 2), the homologues of which, for example (XXV, *n* = 1), isomerise under analogous conditions to cyclopropane derivatives[103,104,109]:



(XXV)

Another homologue of the epoxide (XXV, *n* = 2), namely (XXVI, R = $COOC_2H_5$), readily rearranges to a substituted cyclopentane (XXVII), while the epoxide (XXVI, R = C_6H_5CO) isomerises under analogous conditions as a result of intramolecular *O*-alkylation with formation of the dihydropyran (XXVIII):



(XXVI) (XXVIII)

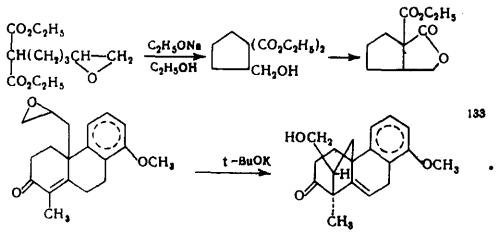
This difference in the mode of isomerisation emphasises yet again the relation between the degree of delocalisation of the charge in the intermediate mesomeric anion and the mode of isomerisation of epoxides with mobile hydrogen atoms in the carbon side chain[118] (cf. p. 406).

The difference between the reactivities of the epoxides (XXV, *n* = 2) and (XXVI, R = $COOC_2H_5$) may be accounted for by steric hindrance to cyclisation. It is noteworthy that derivatives of cyclobutane are not formed in either case owing to the comparative difficulty of the formation of a four-membered ring[130].

Several examples of the isomerisation of epoxides to allyl alcohols as a result of the elimination of a δ-proton have been described[131,132].

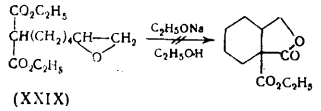
§ ^1H NMR spectroscopic data indicate rotation about the C=C bond in the enolate anions of carbonyl compounds even at comparatively low temperatures[122].

The elimination of a ϵ-proton with subsequent intramolecular *C*-alkylation leads as a rule to the formation of cyclopentanes[129,133-135]:



In the examples quoted intramolecular attack is directed to the sterically more hindered secondary carbon atom of the epoxy-ring. These results agree with kinetic studies[130], according to which the rate of formation of a five-membered ring in the intramolecular *C*-alkylation reaction is approximately 1000 times faster than the rate of formation of a six-membered ring.

The difficulty of the formation of a six-membered ring is demonstrated by the unsuccessful attempts at the isomerisation of the epoxide (XXIX):



(XXIX)

In conclusion we may note that the study of the base-catalysed rearrangements of epoxides is not only of purely chemical interest, since epoxides are biogenetic precursors of many natural products[131-135]. The isomeric transformations discussed above can probably serve as models of certain natural processes.

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Reactions of Derivatives of Phosphorus(III) Acids with Carbonyl Compounds

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The review describes the reactions of fully esterified phosphorous acids, phosphoramidites, and the mixed anhydrides of dialkylphosphorous and carboxylic acids with carbonyl compounds not containing halogens: unsaturated and saturated aldehydes and ketones, α-diketones, and carbonyl compounds activated by ethoxycarbonyl, phosphoryl, nitrile, or any other electronegative group. The modes and mechanisms of these extremely varied and interesting reactions, which are important for progress in the chemistry of organophosphorus compounds and theoretical organic chemistry, have been examined.
The bibliography includes 188 references.

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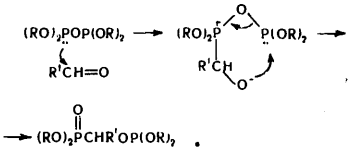
I. INTRODUCTION

One of the most important and interesting reactions in the chemistry of organophosphorus compounds is the Arbuzov reaction (A.E. Arbuzov) in which fully esterified phosphorus(III) acids react with alkyl halides and other halogen-containing organic compounds. However, in recent years there has arisen another extremely interesting and promising trend in the research on the chemistry of organophosphorus compounds involving reactions of fully esterified phosphorous acids, phosphoramidites, and mixed anhydrides with various organic compounds not containing halogen atoms. These reactions lead to the formation of compounds with a tetra- or penta-coordinate phosphorus atom. Reactions of this type proved to be extremely varied owing to the fact that the phosphorus atom exhibits biphilic properties under these conditions, which allows both electrophilic and nucleophilic interactions. Vigorous study of these reactions greatly extended synthetic possibilities in organic chemistry, led to the discovery of a number of extremely interesting types of reactions of organophosphorus compounds, and resulted in the introduction of many new features in the investigation of their mechanisms. A particularly large number of studies have been made on the reactions of derivatives of phosphorus(III) acids with various carbonyl compounds, which are the most important and interesting reactions of this type. Despite their specificity, in many cases they may be regarded as varieties of the Arbuzov reaction, proceeding via a general two-stage mechanism in which the first or both phases of the Arbuzov reaction take place. It is noteworthy that individual reactions of carbonyl compounds, mainly with phosphites, have been described in monographs dealing with particular aspects of the chemistry of organophosphorus compounds published abroad in previous years[1,2] and also in reviews and research reports in which the results of the investigators' own work are discussed[3-8]. In the present review, the authors' aim was to examine fully and systematically the reactions of derivatives of phosphorus(III) acids with carbonyl compounds without halogen atoms which have been described in the literature. Reactions of this type with phosphorus(III) acid chlorides were discussed in the review of Pudovik and Khairullin[9].

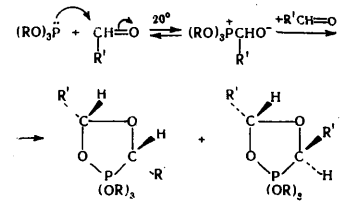
II. REACTIONS OF DERIVATIVES OF PHOSPHORUS(III) ACIDS WITH ALDEHYDES AND KETONES

1. Reactions with Saturated Aldehydes and Ketones

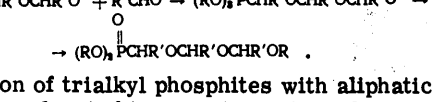
The reactions of phosphorus(III) acid esters with aldehydes were investigated for the first time by Arbuzov and Alimov, who established that pyrophosphites react with aldehydes to form products containing tri- and tetracoordinate phosphorus atoms[10]:



At room temperature aliphatic aldehydes react extremely slowly with trialkyl phosphites[11]. As a result of attack by the phosphorus atom on the carbon atom of the carbonyl group, an unstable 1:1 adduct is formed, further reaction of which with a second aldehyde molecule leads to diastereoisomeric 1,2,4-dioxaphospholans[11]:



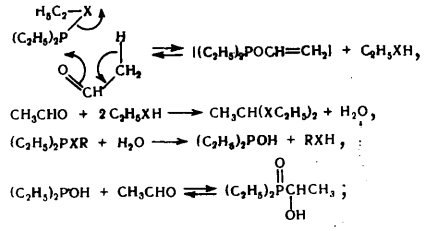
In the presence of an excess of the aldehyde, a 3:1 adduct is formed, which is stabilised by conversion via intramolecular dealkylation into the corresponding phosphonate[4]:



The reaction of trialkyl phosphites with aliphatic aldehydes at an elevated temperature also takes place with formation of products resulting from the addition of two

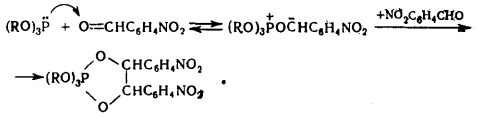
and three aldehyde molecules and having a linear structure[12].

The esters of diethylphosphinous and diethylphosphinothious acids react differently with acetaldehyde: the products are α-hydroxyethyldiethylphosphine, and diethylphosphine oxides and the diethylmercaptal or diethylacetal of acetaldehyde[13]. According to the authors, these reactions involve nucleophilic substitution with formation of a cyclic transition complex:

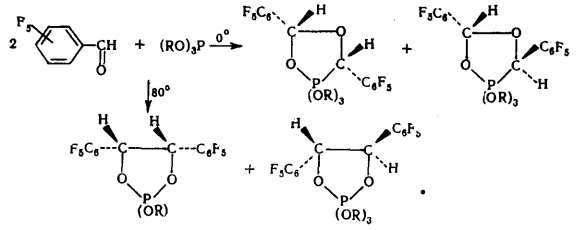


where X = O or S and R = C_2H_5 or CH = CH_2.

In contrast to data published previously[14], Ramirez showed that *o*- and *p*-nitrobenzaldehydes condense under mild conditions with trialkyl phosphites to form 1,3,2-dioxophospholans[15]. He postulates that the presence of electronegative substituents in the aldehyde molecule may be responsible for the direct attack of the phosphorus atom on the oxygen atom of the carbonyl group, which leads to the formation of an intermediate adduct with a P — O — C linkage:

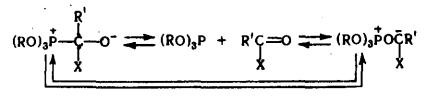


However, the possibility of the attack by the phosphorus atom also on the carbon atom of the carbonyl group, by analogy with unsubstituted aldehydes, resulting in the formation of an intermediate adduct having a P — C bond, which subsequently rearranges further to an adduct with a P — O — C linkage, is not ruled out in these reactions. This hypothesis is confirmed by the reaction of pentafluorobenzaldehyde with trialkyl phosphites which takes place with formation of 1,4,2-dioxophospholans at a low temperature and 1,3,2-dioxaphospholans at an elevated temperature[16,17]:

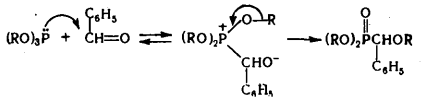


On dissolution, 1,4,2-dioxophospholan may be converted into 1,3,2-dioxaphospholan. It is suggested that this process involves the dissociation of the P — O and C — O bonds in 1,4,2-dioxaphospholan with regeneration of the aldehyde molecule and the formation of a 1 : 1 adduct with a P — C — O linkage, which rearranges into a 1 : 1 adduct with a P — O — C linkage; this adduct subsequently reacts with an aldehyde molecule to form 1,3,2-dioxaphospholan.

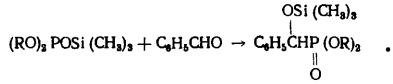
Thus it proved possible to demonstrate for pentafluorobenzaldehyde the initial formation of an adduct with a P — C — O linkage and its transformation into one with a P — O — C linkage. The mechanism proposed is probably general for reactions of tervalent phosphorus with activated carbonyl compounds. Possibly in these reactions there is equilibrium between the initial reactants and the adducts with P — C — O and P — O — C linkages[18]:



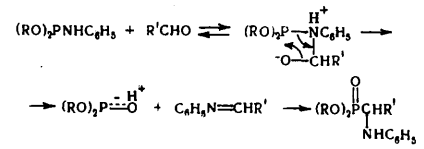
m-Nitrobenzaldehyde and aromatic aldehydes with electropositive substituents are inert with respect to trialkyl phosphites below 100°C.[18] At elevated temperatures aromatic aldehydes react with trialkyl phosphites via a mechanism involving the Arbuzov rearrangement with formation of alkoxyalkylphosphonic acid esters[19]:



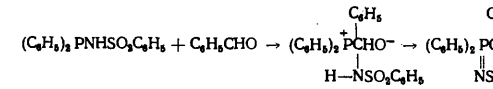
These reactions are accompanied by the oxidation of phosphites to phosphates[20]. Reactions of aromatic aldehydes with alkyl trialkylsilyl phosphites take place similarly[21]:



The reactions of aldehydes with phosphoramidites are extremely interesting and varied. Dialkyl *NN*-dialkylphosphoramidites and phenylphosphonamidous acids[24] react with aldehydes to form esters of α-aminoalkylphosphonic acids[25]. Evdakov postulated that in these reactions the phosphorus atom attacks the carbon atom of the carbonyl group, but subsequently Hudson and other investigators showed that in most cases these reactions involve the initial attack by the nucleophilic nitrogen atom on the carbon atom of the carbonyl group. Dialkyl *N*-phenylphosphoramidites react with aldehydes similarly. The intermediates formed are dialkyl phosphites and Schiff bases, the interaction of which leads to the final reaction product[26-28]:

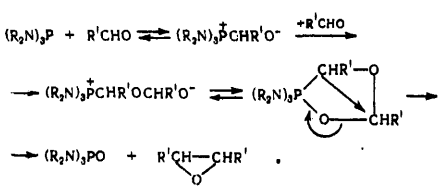


Earlier another reaction mechanism was suggested for dialkyl *N*-phenylphosphoramidites[29,30]. Pudovik and Batyeva showed that the reaction of *N*-diphenylphosphinobenzenesulphonamide and benzaldehyde takes place differently. In the benzenesulphonamide the nucleophilic activity of the nitrogen atom is reduced owing to the electron-accepting group linked to it, as a result of which the reaction takes place via the phosphorus atom[31]:



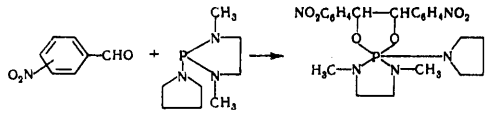
Phosphorous tris(dialkylamides) react with aliphatic, aromatic, and heterocyclic aldehydes with formation of various products. When there are electropositive substituents in the aldehyde, a 1 : 1 adduct having a dipolar structure and a P — C bond is formed. The presence of electronegative substituents promotes the interaction of the 1 : 1 adduct with a second aldehyde molecule to form *NNN*-tris(dialkyl)phosphoramides and epoxy-compounds.

It is suggested that the epoxy-compounds are formed via an intermediate 1,4,2-dioxaphospholan[32]:

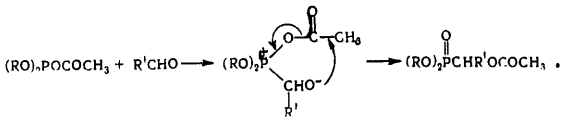


According to Ramirez[18], the formation of an epoxide in the reaction of phosphorous tris(dimethylamide) with nitrobenzaldehyde takes place via intermediate 2:1 adducts which have the structure of dipolar ions with a P—O—C linkage.

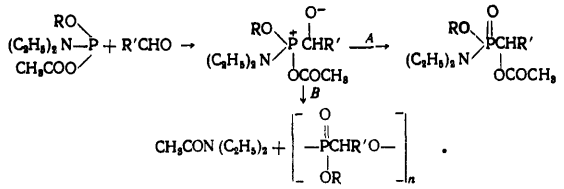
When nitrobenzaldehyde reacts with cyclic phosphorous triamides, stable spiro-1,3,2-dioxaphospholans are formed[18]:



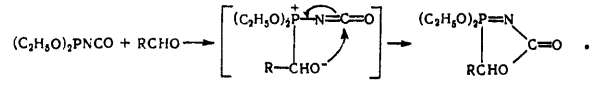
Mixed anhydrides of phosphorous and carboxylic acids readily react with aldehydes via a mechanism involving the Arbuzov rearrangement with formation of acyl derivatives of α-hydroxyalkylphosphonic acid esters[33-36]. In this case the attack by the negatively charged oxygen atom in the intermediate dipolar ion is directed to the electrophilic and sterically accessible carbon atom of the acetyl group:



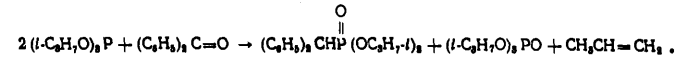
When phosphoramidoacetatidites react with aliphatic aldehydes, the reaction takes place predominantly according to mechanism *A*, while with benzaldehyde mechanism *B* obtains[36]:



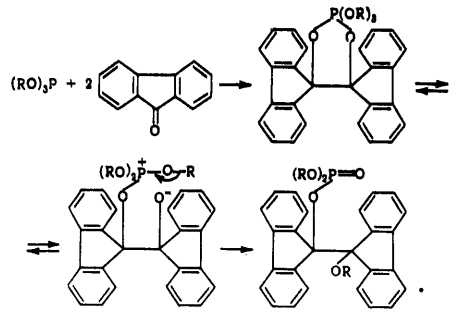
Diethyl phosphoroisocyanatidite reacts with benzaldehyde, *p*-chloro-, *p*-bromo-, and *p*-methoxy-benzaldehydes, and butyraldehyde to form cyclic esters of alkyldiethoxyphosphazocarbonic acid and polymeric 1:1 adducts; the cyclic bromobenzyldiethoxyphosphazocarbonic acid ester is converted on heating into a polymeric adduct[37]:



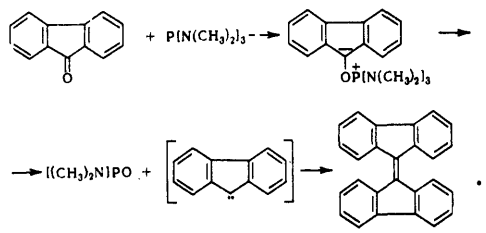
In many cases ketones react with trialkyl phosphites somewhat differently than aldehydes. Thus the reactions of tri-isopropyl phosphite with benzophenone and 4,4′-dichlorobenzophenone take place slowly on prolonged heating with formation of tri-isopropyl phosphate, di-isopropyl diphenylmethylphosphonate, and propene[38]:



Fluorenone reacts with trialkyl phosphites at room temperature to form 1,3,2-dioxaphospholans. In a polar solvent the phospholan may exist partly in an open-chain dipolar form and may be converted into phosphate as a result of dealkylation[39]:

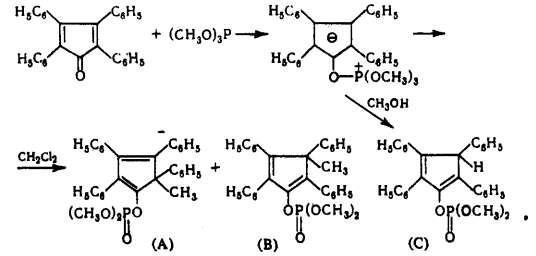


In the reaction with tri-isopropyl phosphite, tri-isopropyl phosphate and phenanthrone were isolated[38], while in the presence of an excess of phosphite the reaction proceeds via a mechanism analogous to that described above for benzophenone[38]. The reaction of fluorenone with phosphorous tris(dialkylamide) results in the formation of *NNN*-tris(dialkyl)phosphoramide and dibiphenyleneethylene, the latter probably resulting from the dimerisation of a carbene[40]:



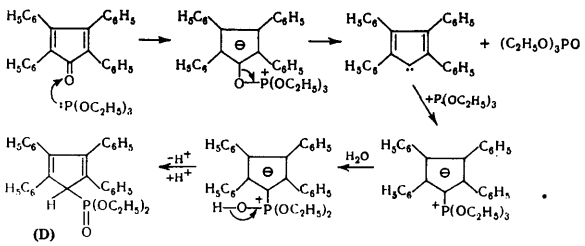
Cyclic phosphorous triamides form with fluorenone spiro-1,3,2-dioxaphospholans[40].

The mode of reaction of trialkyl phosphites with tetraphenylcyclopentadienone depends on the conditions[41,42]: a mixture of isomeric enol phosphates (A) and (B) is formed in dichloromethane and in methanol the product is compounds (C)[41]:

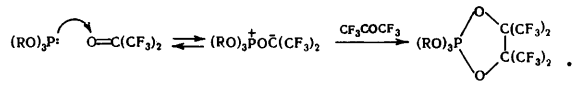


When tetracyclone reacts with trialkyl phosphites in aqueous ethanol, a more complex mixture of products is

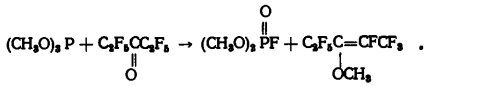
formed, the main component of which is the phosphonate (D). The proposed reaction mechanism includes the formation of a carbene and an ylide as intermediates[42]:



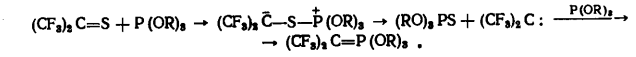
The reaction of derivatives of phosphorus(III) acids with perfluoroketones takes place very readily. Hexafluoroacetone reacts with trialkyl phosphites, phosphonites, phosphinites[43-46], *NN*-dialkylphosphoramidites[47], phosphorous tris(dialkylamides)[40,46], and cyclic phosphorous triamides[40] at low temperatures with formation of 1,3,2-dioxaphospholans:



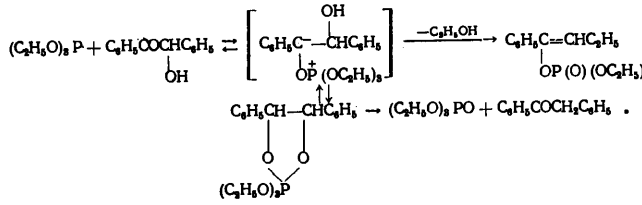
At an elevated temperature perfluoroketones form with trialkyl phosphites dialkyl phosphorofluoridites and enolic ethers derived from ketones[48]:



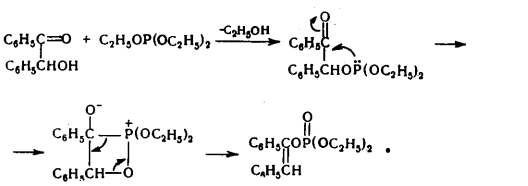
A more complex mixture is formed at an elevated temperature with phosphorous tris(dialkylamides)[46,49]: the main product is bis(dialkylamino)difluorophosphorane[46]. Trialkyl phosphites were found to react differently with hexafluorothioacetone[50]:



Reactions of trialkyl phosphites with α-hydroxyketones and their derivatives have been described. Benzoin reacts with triethyl phosphite at 180°C: the formation of an intermediate dipolar ion, which is stabilised by conversion into an enol phosphate with elimination of an alcohol or is converted into 1,3,2-dioxaphospholan, has been suggested. 1,3,2-Dioxaphospholan decomposes under the reaction conditions into triethyl phosphate and deoxybenzoin[51]:

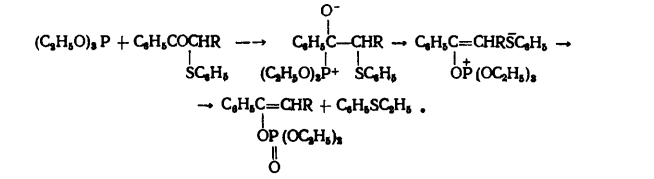


An enol phosphate is formed in the reaction of benzoin with triethyl phosphite in the presence of sodium[52]. In this case a somewhat different mechanism has been proposed:

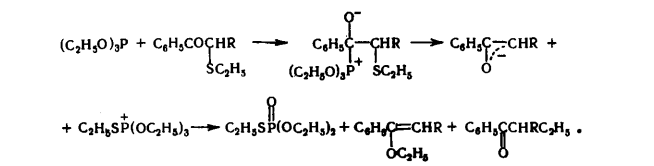


Benzoin acetate also reacts with the phosphite to form an enol phosphate[51].

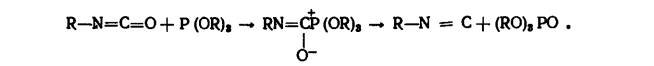
Depending on their structure, α-ketosulphides react with triethyl phosphite in two ways[53]. If the alkyl(aryl)-thio-group can be split off as an anion, the corresponding enol phosphate and ethyl phenyl sulphide are formed:



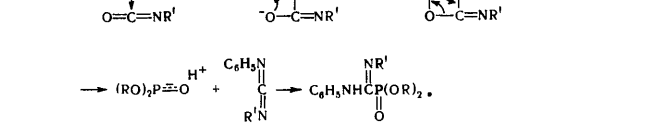
In the case of benzyl ethyl sulphide, the ethylthio-group is split off as an anion with greater difficulty and the reaction proceeds preferentially with formation of a vinyl ether or ketone derivatives[53]:



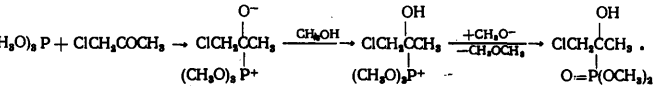
The reactions of isocyanates with trialkyl phosphites result in the formation of trialkyl phosphates and isonitriles[54]:



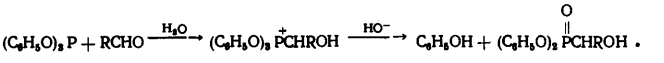
Dialkyl *N*-phenylphosphoramidites react with aromatic isocyanates to form dialkyl *NN'*-diphenylamidinophosphonates[55]. The reaction proceeds according to a mechanism involving the initial attack by the nitrogen atom on the carbon atom of the carbonyl group:



When the reactions of aldehydes and ketones with trialkyl phosphites are carried out in the presence of proton-donating agents, the intermediate dipolar ions are stabilised by the addition of a proton; the subsequent intramolecular dealkylation leads to the formation of α-hydroxyalkylphosphonates[56]:



Similar reactions probably occur also between triphenyl phosphite and aldehydes and ketones in an aqueous medium[2,57]:



When carbonyl compounds react with trialkyl phosphites in the presence of phosphorus trichloride or other acid chlorides, the intermediate addition product reacts with them to form tris-(α-dialkoxyphosphonoalkyl) phosphites[58]:

Ivanov showed recently that trialkyl phosphites are capable of condensing with formaldehyde and compounds containing a mobile hydrogen atom in the methylene group, forming the corresponding phosphonomethyl derivatives[59-61]:

$$(RO)_3P + CH_2O + HCHXY \rightarrow (RO)_2\overset{O}{\overset{\|}{P}}CH_2CHXY + ROH .$$

Aliphatic and aromatic aldehydes and furfural undergo this reaction. It is suggested that it proceeds according to the following mechanism[60]:

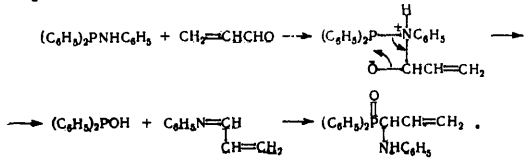
$$(RO)_3P + R'CHO \rightleftarrows (RO)_3\overset{+}{P}CHR'O^- \rightarrow [(RO)_3\overset{+}{P}CHR'OH] \rightarrow$$

$$\rightarrow [(RO)_3\overset{+}{P}CHR'CHXY]OH^- \rightarrow (RO)_2\overset{O}{\overset{\|}{P}}CHR'CHXY + ROH .$$

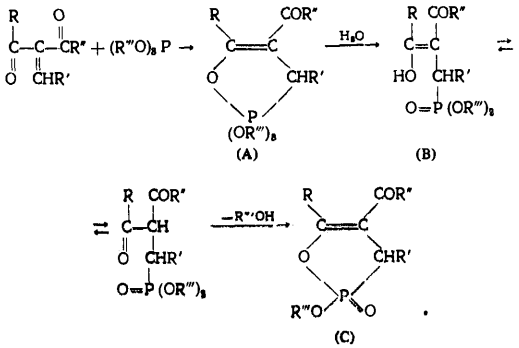
2. Reaction with $\alpha\beta$-Unsaturated Aldehydes and Ketones

The reactions of phosphites and phosphoramidites with $\alpha\beta$-unsaturated aldehydes and ketones proved to be extremely interesting; in many cases it was possible to follow clearly the formation of intermediate dipolar ions and to elucidate the effect of structural factors on their stability. Extensive studies in this field have been carried out by B. A. Arbuzov and coworkers. In a study of the reaction of triethyl phosphite with the simplest unsaturated aldehyde—acrolein—they showed that under mild conditions the reaction leads to the formation of 2,2,2-trialkoxy-Δ^4-oxaphospholen[62-64]. The earlier hypothesis of the isomerisation of Δ^4-phospholens to esters of γ-alkoxyalkenylphosphinic acids was not confirmed[65-67].

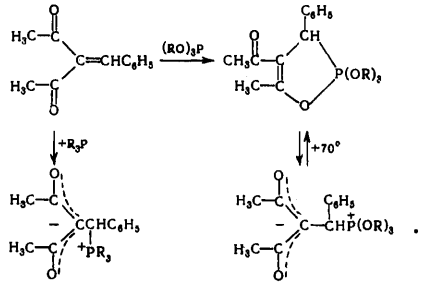
Pudovik and Batyeva showed that in reactions of $\alpha\beta$-unsaturated aldehydes with diphenylphosphinous anilide, products with the phospholan structure are not formed. The reactions probably take place with initial attack by the nitrogen atom on the carbonyl carbon atom and leads to the formation of α-arylamino-γ-aryl(alkyl)allyl(diphenyl)phosphine oxides[28]:



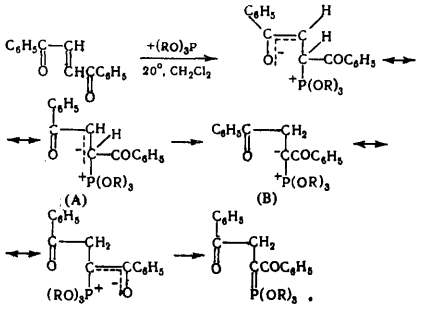
The reaction of trialkyl phosphites with ethylideneacetylacetone and with ethylidene- and benzylidene-acetoacetic esters leads to very stable 1,2-oxaphospholens[68,69]. On hydrolysis, the phospholen rings (A) are opened and the enols (B) are formed; on vacuum distillation, these split off an alcohol molecule and are converted into cyclic phosphonates (C)[70]:



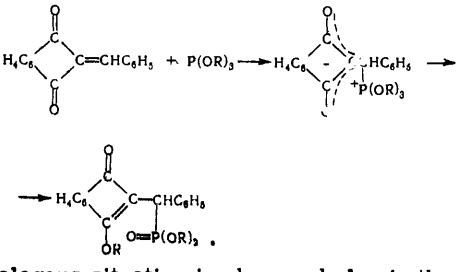
Stable phospholens with a P—C bond in the ring were also obtained by Ramirez in the reaction of 3-benzylidenepentane-2,4-dione with triethyl phosphite[71], phenylphosphonite, and diphenylphosphinite[72]. The study of the NMR spectra of solutions of the phospholens showed that at 70°C they are in equilibrium with dipolar ions, while at 125°C they have been fully converted into the dipolar form. Stable dipolar ions are formed by the reaction of 3-benzylidenepentane-2,4-dione with tertiary phosphines[73]:



The products of the reaction of trialkyl phosphites, phosphonites, and phosphinites with dibenzoylethylene have the structure of alkylidenephosphoranes[74-77] and not Δ^4-oxaphospholens as suggested earlier[78,79]. The reaction proceeds via the dipolar ion (A) which isomerises as a result of proton migration to the more stable dipolar ion (B):

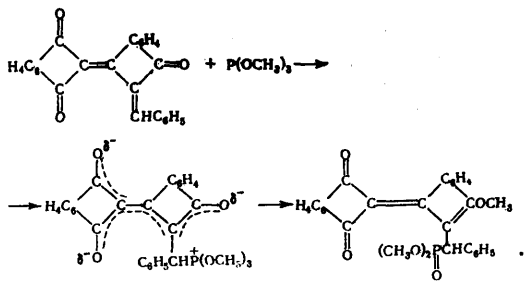


The reaction of dibenzoylethylene with a trialkyl phosphite in alcoholic solution and at an elevated temperature yields a complex mixture of products containing a trialkyl phosphate, 2,5-diphenylfuran, 1,2,3,4-tetrabenzoylbutane, and 1,2-dibenzoylethane[78,79]. The products of the addition of trialkyl phosphites to 2-benzylideneindan-1,3-dione at a low temperature exist in the form of dipolar ions, isomerising readily to esters of the enolic form of 1,3-dioxoindan-2-ylbenzylphosphonic acid[80]. At room temperatures the esters are formed immediately[81,82]:



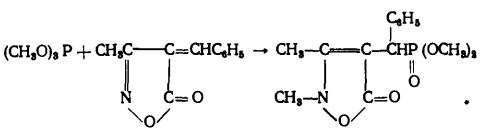
An analogous situation is observed also in the reaction of trimethyl phosphite with 2-benzylidene-3(2*H*)-thianaphthenone-1,1-dioxide[83,83]. As a result of the increase in the length of the conjugated chain and the equalisation

of electron density, even more stable dipolar ions are formed in the reactions of trialkyl phosphites with benzylidenebindone[82], 5-benzylidenebarbituric acid, and 5-benzylidene-1,3-diphenylbarbituric acid[84]

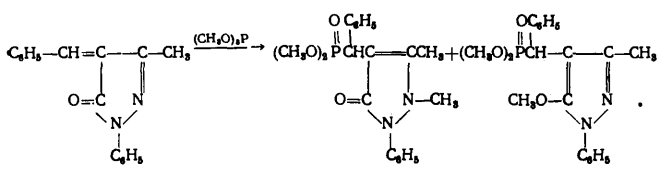


The reactions of phosphorous tris(dimethylamide) with 2-benzylideneindandione, 1,3,2-benzylidene-3(2*H*)-thianaphthenone-1,1-dioxide, benzylidenebindone, 5-benzylidenebarbituric acid, and 5-benzylidene-1,3-diphenylbarbituric acid also yielded stable crystalline dipolar ions with a P — C bond, the structure of which has been demonstrated by infrared, ultraviolet, and NMR spectroscopy and by dipole moment measurements[82,84,85].

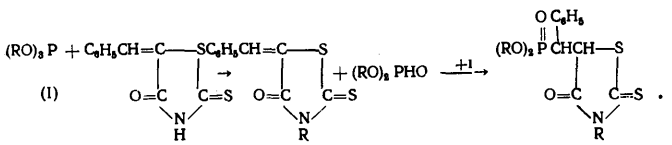
Heterocyclic carbonyl compounds containing a semicyclic double bond in the α-position relative to the carbonyl group do not form dipolar ions or phospholens on reaction with trialkyl phosphites. The reaction with 4-benzylidine-3-methyl-5-isoxazolone involves the $-N=C-C=C-$ system of conjugated bonds and leads to phosphonates[86]:



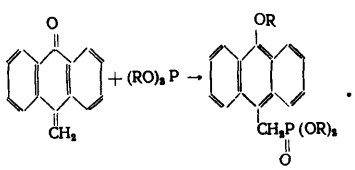
In the reaction with 4-benzylidene-3-methyl-1-phenyl-5-pyrazolone, trimethyl phosphite adds simultaneously to the $C=C-C=N-$ and $C=C-C=O$ bonds[87]:



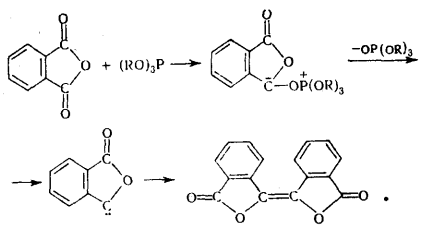
In the reaction with benzylidenerhodanine, the latter was found to be *N*-alkylated, the dialkyl phosphite formed in this process adding to the benzylidene double bond[88]:



Trialkyl phosphites react with methyleneanthrone via the conjugated system incorporating the methylene group[89]:

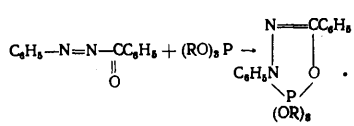


Phthalic anhydride does not react with trialkyl phosphites at room temperature; after prolonged heating, biphthalyl is formed[90]. The intermediate formation of a carbene which subsequently isomerises to biphthalyl is postulated. An alternative mechanism involves the formation of an epoxide, which is reduced by phosphite to an olefin[91]:

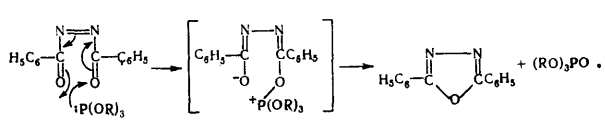


Similarly, thiophthalic anhydride undergoes reductive dimerisation by triethyl phosphite with formation of *trans*-bithiophthalide[91]. The reaction of thiophthalic anhydride with phosphorous tris(diethylamide) takes place via a different mechanism and leads to a mixture of lactones and thiolactones[91]. Dimethyl- and diphenylmaleic anhydrides react with triethyl phosphite to form the corresponding bifurandiones[92].

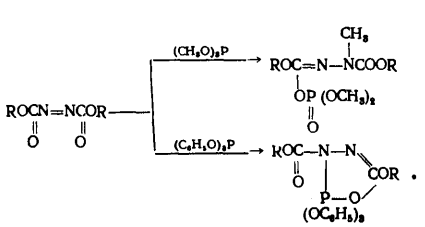
B. A. Arbuzov and coworkers showed that the conjugated system $-N=N-\underset{|}{C}=O$ may be also involved in the formation of cyclic phosphoranes[93,94]:



In the reaction of azodibenzoyl with trialkyl phosphites, the intermediate dipolar ions decompose into a trialkyl phosphate and diphenylfurodiazole owing to the difficulty of the closure of a seven-membered phosphorane ring[94,95]:

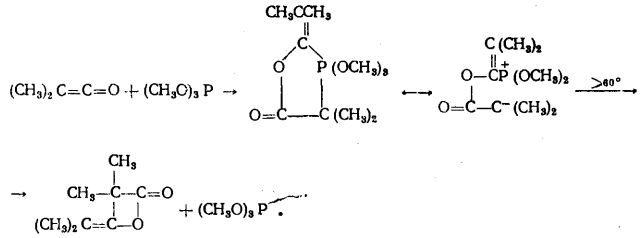


According to the data of Ginsburg and Yakubovich[95], the reaction of diethyl azodicarbonate with trimethyl and triphenyl phosphites yields linear phosphates and cyclic phosphoranes: their structure was recently confirmed by infrared and NMR spectroscopy[94]:

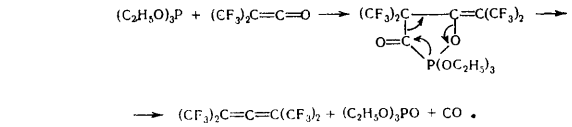


Ketens readily enter into reactions with phosphites, but the addition products are frequently unstable and undergo further reactions. Dimethylketen forms with

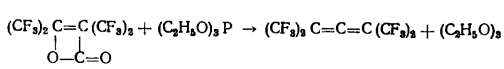
trimethyl phosphite a 2 : 1 adduct with a cyclic phosphorane structure, which is converted at 60°C into a dimer of dimethylketen and trimethyl phosphite[97,96]:



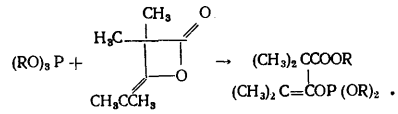
The product of the reaction of trimethyl phosphite with diphenylketen probably also has a phosphorane structure[96-98]. Bis(trifluoromethyl)keten reacts with triethyl phosphite to form tetrakis(trifluoromethyl)allene, triethyl phosphate, and carbon monoxide[99]:



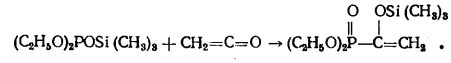
Possibly the first stage in this reaction is the formation of a β-lactone dimer, since this dimer yields the same products on reaction with triethyl phosphite[99]:



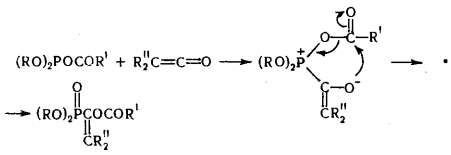
Dimethylketen dimers form with trialkyl phosphites 1 : 1 adducts containing a tervalent phosphorus atom. The reactions involve ring opening and migration of the alkoxy-group[100]:



Trialkylsilyl dialkyl phosphites react with ketens very readily[21]:



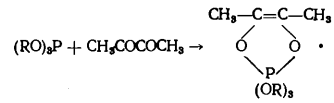
The reactions of mixed anhydrides of dialkylphosphorous and carboxylic acid anhydrides with keten and diphenylketen result in the formation of α-acyloxyvinylphosphonic acid esters[101,102]:



III. REACTIONS OF DERIVATIVES OF PHOSPHORUS(III) ACIDS WITH ALDEHYDES AND KETONES ACTIVATED BY ELECTRONEGATIVE GROUPS

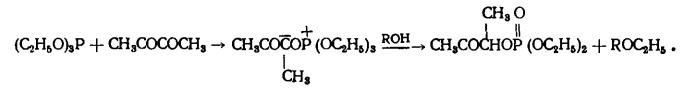
1. Reactions with α-Diketones

The reactions of trialkyl phosphites with α-dicarbonyl compounds have been investigated by a number of workers using diacetyl, the simplest α-diketone, as an example[103-107]. They take place very vigorously and result in the formation of 1 : 1-adducts for, which Ramirez et al.[107] and Kukhtin et al.[108] suggested and later proved the structure of 1,3,2-dioxaphospholens:

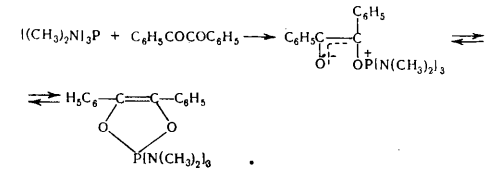


1,3,2-Dioxaphospholens are formed when trialkyl phosphites react with benzil, phenanthrenequinone[109,110], pentane-2,3-dione[106,107,111], dibenzoyl ketone[112], phenylglyoxal[112], 1,2-naphthoquinone[109,113], cyclohexane-1,2-dione[114], methylphenylglyoxal[115], and *o*-chloranil[109], and also when *NN*-dialkylphosphoramidites and phenyl- and methyl-phosphinous amides react with diacetyl[24,116], benzil[46,117], and cyclohexane-1,2-dione[118]. Cyclic phosphites and phosphoramidites form with α-diketones stable spirodioxaphospholens[5,119-121].

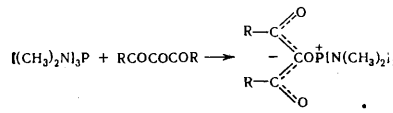
The reactions of trialkyl phosphites with α-diketones in proton-donating solvents lead to the corresponding phosphates, which confirms the intermediate formation of dipolar ions[122]:



In many cases it proved possible to demonstrate that 1,3,2-dioxaphospholens are in equilibrium with the dipolar ions. Thus phosphorous tris(dialkylamides) form with benzil a 1 : 1 adduct having the dioxaphospholen structure, which in solution is in equilibrium with the open-chain dipolar form. These data were obtained from a study of ^{31}P NMR spectra[120,121,123].

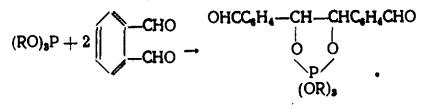


In benzene the main product is 1,3,2-dioxaphospholen but in methylene chloride the equilibrium is displaced towards the open-chain dipolar form[5,121]. The products of the reaction of phosphorous tris(dialkylamide) with dibenzoyl ketone[124] and 9,10-phenanthrenequinone[124] are generated only in the dipolar form[124]:

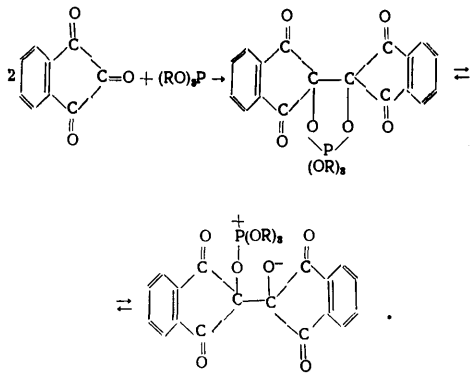


In reactions of phosphorous tris(dialkylamides) with polycarbonyl compounds, the cyclic phosphorane structure predominates over the dipolar structure on passing from α-diketones to *o*-quinones and triketones. An increase of the degree of delocalisation of the negative charge at the carbon atom promotes the formation of the open-chain dipolar form[121]. The stability of the dioxaphospholen structure increases on passing from acyclic phosphoramidites to five-membered cyclic phosphoramidites[125]. In the reaction of trialkyl phosphites with acenaphthenequinone[126], isatin[127], and phthalalhyde[128], 1 : 1 adducts were not isolated, since at the dipolar ion stage

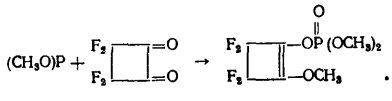
they react rapidly with a second molecule of the carbonyl compound and form 1,3,2-dioxaphospholans:



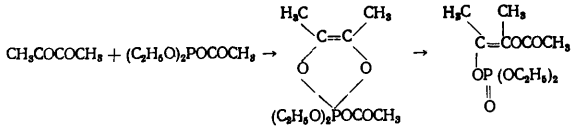
In the reaction with indantrione, 1,3,2-dioxaphospholans are in equilibrium with dipolar ions[129]:



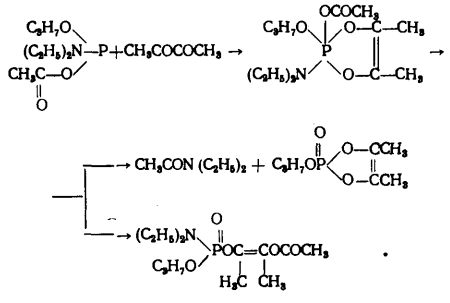
In the reactions of trialkyl phosphites with alloxan[130] and tetrafluorocyclobutane-1,2-dione[48], the intermediate dipolar ions are stabilised as a result of dealkylation to enol phosphates:



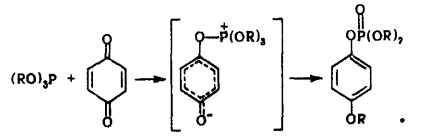
Dialkyl phosphoracetatidites react with α-diketones like trialkyl phosphites and phosphoramidites. The intermediate products of the addition of diethyl phosphoracetatidite to diacetyl—1,3,2-dioxaphospholen with a pentaco-ordinate phosphorus atom—was detected by ^{31}P NMR.[131] However, the presence of the anionoid acetyl group makes dioxaphospholens unstable and they react further via the mechanism of the second stage of the Arbuzov rearrangement with ring opening and the formation of an $\alpha\alpha$-endiol phosphate[36,131]:



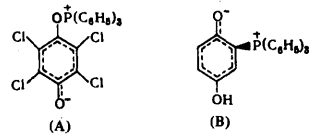
When phosphoramidoacetatidites react with α-diketones, two competing processes occur; the process leading to the retention of the dioxaphospholen ring predominates[36]:



The reactions of trialkyl phosphites with *p*-quinones are of considerable interest. *p*-Benzoquinone, 2,5-dimethylbenzoquinone, duroquinone, 1,4-naphthoquinone, anthraquinone, and 1,8-dichloroanthraquinone react with trialkyl phosphites via the 1,6-conjugated system with formation of *p*-alkoxyphenyl dialkyl phosphates[24,27,89,109,132-139] and not via a 1,4-addition mechanism as suggested previously[140,141]:



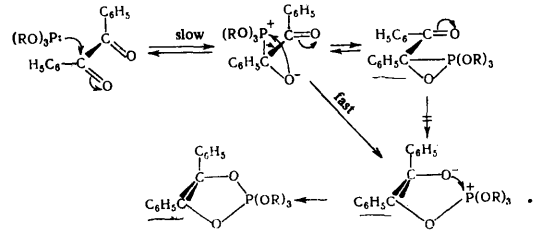
The intermediate dipolar ions were not isolated owing to their rapid conversion into phosphate esters. A stable dipolar ion (A) with a P—O—C linkage is formed when triphenylphosphine reacts with chloroanil and in the reaction of triphenylphosphine with *p*-benzoquinone the product is a dipolar ion (B) with a P—C bond[142,143]:



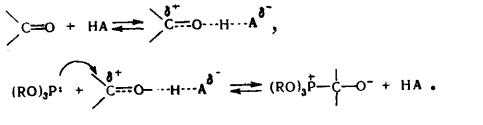
In the reaction of chloroanil with tri-isoalkyl phosphites, the substitution of all the chlorine atoms by di-isoalkoxyphosphono-groups was observed[144].

A spectrophotometric kinetic study of the reactions of trialkyl phosphites with benzil in anhydrous dioxan and benzene showed that the reaction is of second order with an activation energy of 8.41 kcal mole^{-1} and an activation entropy of −47.5 e.u.[145]. The rate of reaction increases in the following series of trialkyl phosphites: $(CH_3O)_3P < (s\text{-}C_4H_9O)_3P < (C_2H_5O)_3P < (iso\text{-}C_3H_7O)_3P$, which agrees with the increasing nucleophilicity of the phosphorus atom in these compounds.

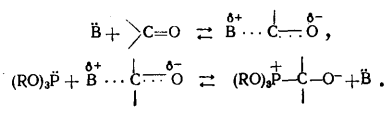
In the reaction involving tri-s-butyl phosphites, the steric effect has a significant influence. The following reaction mechanism was proposed on the basis of the results:



The nucleophilic attack by the phosphorus atom on the carbonyl carbon atom determines the rate of reaction. When an acid is added, the carbonyl group is activated by the formation of a hydrogen bond and the rate increases:



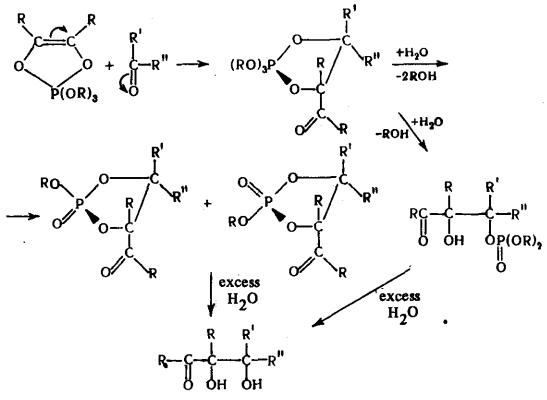
When a base adds to the carbonyl carbon atom it reduces its electrophilicity, which results in a lowering of the rate of reaction:



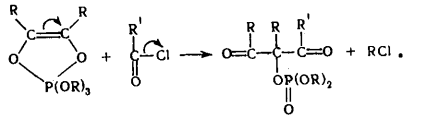
The low activation energy shows that the rate-determining stage does not require much energy and probably does not involve the dissociation of the P — C bond. The high negative activation entropy indicates a high degree of orientation of the transition state. The relatively slight dependence of the rate of reaction on solvent polarity can be accounted for by the fact that the transition state resembles an ion pair with a minimal charge separation owing to $2s - 3p$ bonding between the oxygen and phosphorus atoms. The conversion of the ion with a P — C bond into one with a P — O — C linkage takes place as a three-centre rearrangement with nucleophilic attack by the negatively charged oxygen on the phosphorus atom. The rearrangement of the ion with intermediate formation of a three-membered ring is less likely since the energy barrier preventing the complete dissociation of the P — C bond is higher.

However, there is as yet no unanimity concerning the mechanism of the reactions of phosphites, phosphoramidites and mixed anhydrides with dicarbonyl compounds. Together with the hypothesis of the initial attack by the phosphorus atom on the carbonyl carbon atom with subsequent isomerisation of the dipolar ion with a P — C bond, developed in the work of Ogata and Yamashita[145] discussed above and in the present authors' earlier investigations[146,147], it has been suggested in the literature, mainly in the publications of Ramirez, that there is a possibility of an initial attack by the phosphorus atom on the oxygen atom with direct formation of a P — O — C linkage. Such attack is most likely in the reactions of phosphites with quinones and also in the reactions of phosphorous tris(dialkylamides) with α-dicarbonyl compounds[38]. The possibility of synchronous or almost synchronous transfer of the lone electron pair of the phosphorus atom to the conjugated system of the α-diketone with subsequent incorporation of π electrons in the phosphorus d orbitals has also been suggested. Depending on the groups surrounding the phosphorus atom, the latter can exhibit in the initial reaction step both nucleophilic and electrophilic properties[131]. It is extremely probable that, depending on the nature of the reactants and the conditions, these reactions can involve different mechanisms.

1,3,2-Dioxaphospholens formed from α-diketones and phosphites are extremely reactive. They enter into condensation reactions involving the carbonyl groups of symmetrical[148-150] and asymmetric α-diketones[151], monoaldehydes[151-153], phthalaldehyde and terephthalaldehyde[154], monoketones[155], $\alpha\beta$-unsaturated aldehydes[156,157], phenyl isocyanate[158], p-quinones[159], and keten[160] with formation of 1,3,2-dioxaphospholans. Cyclic and linear phosphoric acid esters and also polyoxycarbonyl compounds were obtained from the latter by hydrolysis and alcoholysis[152,161-163]. The nucleophilic addition of 1,3,2-dioxaphospholens to the carbonyl group of mono- and polycarbonyl compounds constitutes a new stereoselective method of formation of a carbon — carbon bond; it has been called the oxyphosphorane condensation[156,157]:



The 1,3,2-dioxaphospholen ring opens on interaction with carboxylic acid chlorides, phosgene[161], bromine[164], oxygen[107], and ozone[165,166]:

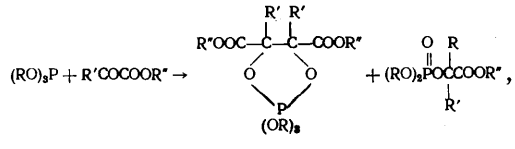


On irradiation with light, 1,3,2-dioxaphospholens decompose into a trialkyl phosphite, an α-diketone, and a trialkyl phosphate[167]. When acted upon by an excess of a trialkyl phosphite at 215°C, they give rise to a trialkyl phosphate and diaryl- or alkylaryl-acetylenes[98]. In the reactions with alcohols, there is partial exchange of substituents in the alkoxy-groups[168].

Ramirez has made interesting studies on the structure and stereochemistry of dioxaphospholens[4,5,8].

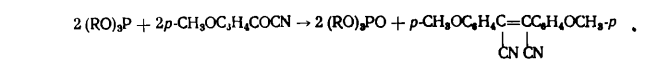
2. Reactions with Aldehydes and Ketones Activated by Alkoxycarbonyl, Phosphoryl, and Nitrile Groups

Reactions of derivatives of phosphorus(III) acids with carbonyl compounds in which the carbonyl group is activated by electron-accepting substituents are of considerable interest. The present authors' studies showed that the reactions of trialkyl phosphites with pyruvate, glyoxylate, and mesoxalate esters take place in two ways. At a low temperature trialkyl phosphites react preferentially with two molecules of the carbonyl compound forming 1,3,2-dioxaphospholans; at an elevated temperature, the corresponding α-substituted dialkyl alkyl phosphates are formed together with the dioxaphospholans[146,147,169-171]:

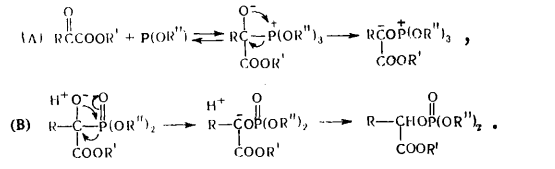


where R′ = H, CH_3, or COOAlk, and R, R″ = alkyl.

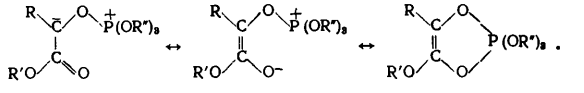
In reactions of trialkyl phosphites with pyruvate[172] and mesoxalate esters[5], Ramirez observed the formation of dioxaphospholans alone. Knunyants and coworkers demonstrated the formation of 1,3,2-dioxaphospholans in reactions of phosphites with trifluoropyruvate esters[173]. The reactions of trialkyl phosphites with the nitriles of benzoylformic and *p*-nitro-, *p*-chloro-, and *p*-methylbenzoylformic acids[174] also give rise to 2:1 adducts with the dioxaphospholan structure. The nitrile of *p*-anisoylformic acid gives an unstable addition product, as a result of which a trialkyl phosphate and $\alpha\alpha$-dicyano-*pp'*-dimethoxystilbene were isolated from the reaction mixture[174]:



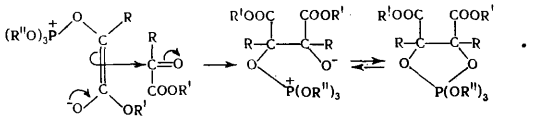
We suggested[146,147] that in reactions of trialkyl phosphites with α-ketoesters the rate-limiting process is nucleophilic attack by the lone electron pair of the phosphorus on the carbon atom of the carbonyl group as the most electrophilic centre in the molecule, which results in the formation of a dipolar ion [reaction (A)] with a P—C bond. Next there is a rapid intramolecular rearrangement of the type of nucleophilic substitution at the phosphonium centre with formation of a dipolar ion having a P—O—C linkage. This reaction resembles the phosphonate—phosphate rearrangement (B) of α-hydroxyalkylphosphonate esters, which was investigated in detail by the present authors for carbonyl compounds of the same type; the decisive role of electron-accepting substituents in this rearrangement has been demonstrated[175,176]:



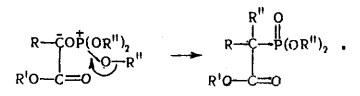
This mechanism has found definite confirmation in the work of Ogata and Yamashita[145], mentioned above, who investigated the kinetics of the reactions of trialkyl phosphites with benzil. However, there is as yet no direct proof for this mechanism, which does not allow a complete elimination of the possibility that these reactions take place also via the oxygen atom of the carbonyl group. The resulting dipolar ion with a P—O—C linkage can be stabilised further in two ways: (a) there is a possibility of the conversion of this ion into the more stable enolate—phosphonium system with a definite contribution by a pentacovalent structure[2]:



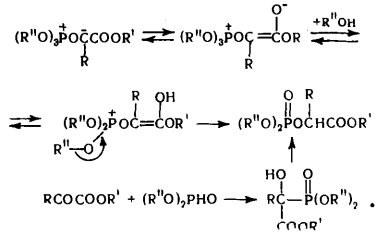
As a result of the attack by the carbon atom of the enolate group on the carbonyl group of a second α-ketoester molecule, a new dipolar ion is formed and stabilised by conversion into 1,3,2-dioxaphospholan:



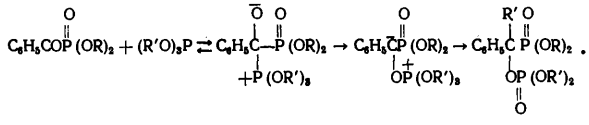
(b) The dipolar ion can also be stabilised in a different way—as a result of dealkylation in accordance with the second stage of the Arbuzov rearrangement:



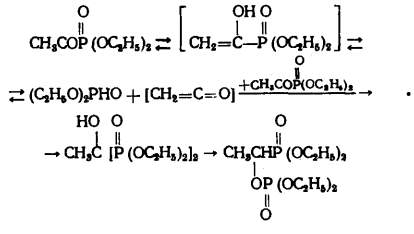
When reactions of trialkyl phosphites with pyruvate esters are carried out in proton-donating solvents (acetic acid, methanol), the dipolar ions are stabilised as a result of protonation with subsequent dealkylation to the corresponding phosphates; the formation of dioxaphospholans is not observed[177]:



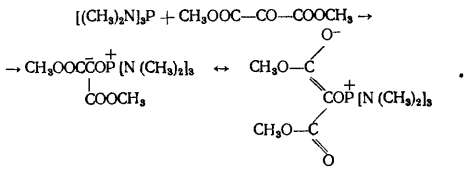
The phosphates formed proved to be identical with those obtained in the isomerisation of dialkyl α-alkoxycarbonyl-α-hydroxyalkylphosphonates[178]. The tendency towards the formation of phospholans in the reactions of phosphites with carbonyl compounds depends on the structure of the carbonyl compounds and diminishes in the series $RCOCOOR' > HCOCOOR' > R'OOC-CO-COOR' \gg RCOP(OR')_2$. The esters of α-ketophosphonic acids are relatively unreactive in reactions with trialkyl phosphites—they do not form products of the phospholan type. The esters of benzoylphosphonic acids react with trialkyl phosphites after prolonged heating of the reaction mixture. In contrast to earlier data[179], the present authors showed that the intermediate dipolar ions are stabilised as a result of their intramolecular dealkylation and conversion into dialkyl α-phenyl-α-dialkoxyphosphonoalkyl phosphates[180]:



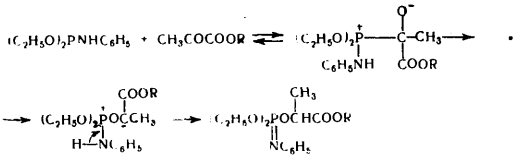
The reactions of phosphites with acetylphosphonic ester takes place similarly[181]. At a high temperature, thermal cleavage of the acetylphosphonic ester and the formation of diethyl α-(diethoxyphosphono)ethyl phosphate predominate[181]:



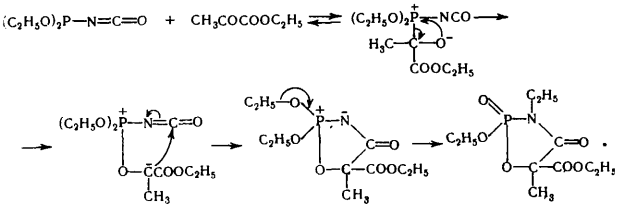
The mode of reaction depends also on the structure of the phosphorus(III) derivative. Thus, on passing from trialkyl phosphites to phosphoramidites and aminophosphines, the tendency towards the formation of dioxaphospholans is reduced[169,182]. One of the causes responsible for this decrease may be steric hindrance arising in the trigonal-bipyramidal configuration and increasing when the alkoxy-substituents at the phosphorus atom are replaced by dialkylamino-substituents. This lowers the stability of the phospholan structure relative to the open-chain dipolar form. Accordingly, the product of the addition of phosphorous tris(dialkylamide) to mesoxalate ester exists in the form of a dipolar ion[124] and not in the form of phospholen as suggested previously[183]:



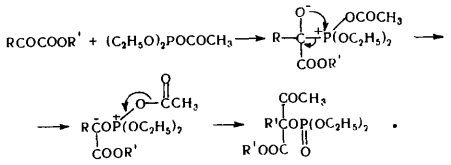
In the reaction of phosphorous tris(dialkylamides) with pyruvate and glyoxylate esters, only oxidation products were isolated[184]. The formation of 1,3,2-dioxaphospholans was not observed also in the reactions of pyruvate esters with dialkyl *N*-phenylphosphoramidites. In this case the dipolar ions are stabilised as a result of the migration of the anilino-proton to the carbanion with formation of dialkyl α-alkoxycarbonylalkyl *N*-phenylphosphorimidites[185]:



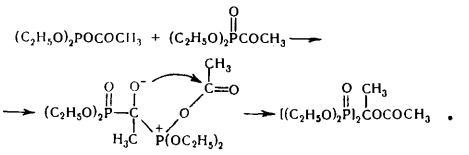
The present authors showed that pyruvate esters react vigorously with diethyl phosphoroisocyanatidite. In this case the dipolar ion is stabilised as a result of the attack by the carbanion on the electrophilic carbon atom of the isocyanate group and leads to the closure of a five-membered ring. Subsequent dealkylation yields an addition product—2-ethoxy-5-ethoxycarbonyl-3-ethyl-5-methyl-2-oxa-2-phosphaoxazolidin-4-one[186]:



Mixed anhydrides of phosphorous and carboxylic acids react with α-ketoesters in only one way with formation of substituted dialkyl α-acetylalkyl phosphates. In this case the dipolar ion is stabilised as a result of the migration of the acetyl group to the carbanion[187]:



The reactions of mixed anhydrides of diethylphosphorous and carboxylic acids with α-ketophosphonates yielded alkylbis(diethoxyphosphono)methyl acetates[101,188]:



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Effect of d_π–p_π Interaction in Organic Compounds of Group IVB Elements

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The behaviour of organic derivatives of Group IVB elements is markedly influenced by d_π–p_π interaction in the ground and excited states. Chemical and physical techniques are nowadays widely used to investigate d_π–p_π interaction. This review deals with the results of certain spectroscopic (NMR and infrared) studies on this effect. The experimental data obtained by NMR and infrared spectroscopy have been compared in a number of cases with the results obtained by other research techniques. The bibliography includes 222 references.

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I. INTRODUCTION

Silicon, germanium, tin, and lead atoms have vacant d orbitals in contrast to carbon. The orbitals have energies close to those of the s and p orbitals in the outer electronic shell. As a result, organic derivatives of these elements have some chemical and physical properties which are not typical of the carbon analogues with the same structures and are due to the presence of d orbitals in the central atom[1]. Of these properties, the present review deals only with the phenomenon of d_π–p_π bonding. The formation of a bond of this type is possible only if the substituent X in the M–X (M = Si, Ge, Sn, or Pb) group is an atom with lone electron pairs (F, Cl, O, N, etc.) or a group with multiple bonds (CH=CH$_2$, C≡C–H, etc.). The atom M in the M–X group may be regarded as an acceptor of the p electrons of the atom X, the electron transfer process resulting in the formation of a dative d_π–p_π bond. The idea of partial double bonding involving silicon using d levels was put forward by Brockway and Wall[2]. The concept of d_π–p_π conjugation was introduced by Pauling[3], who suggested this phenomenon in order to account for the shortening of the Si–Hal and Si–O bonds. d_π–p_π interaction was considered theoretically by Craig[4–7] Jaffé[8], Moffitt[9], and Cruickshank[10,11]. Calculation of the overlap integrals shows[4,5,8,9] that the outer d orbitals can form a strong directed π bond. The degree of double bonding can then be considerable only in the presence of a partial positive charge at the silicon atom. Moreover, the degree of d_π–p_π interaction depends markedly on the steric disposition of the d orbitals relative to the σ bonds. Fairly effective overlap can be achieved only when the σ bond coincides with the plane of the maximum density of the d orbital. This is indicated by the significant dependence of the d_π–p_π overlap integrals on molecular geometry[8]. We may also note quantum-chemical data[12–14] indicating the occurrence of d_π–p_π interaction in Si–aryl and Si–vinyl bonds.

The reviews by Stone and Seyferth[15], Bürger[16], Ebsworth[1], and Attridge[17] deal with the problems of the experimental study of d_π–p_π interaction involving elements of the silicon subgroup. In these reviews the problem of d_π–p_π interaction has been considered as a whole, but, because of the large amount of new spectroscopic data on this problem, these reviews have become to a large extent obsolete. We decided to examine the results obtained by NMR and infrared spectroscopic methods, since we believe that these procedures are the most fruitful in spectroscopic studies on d_π–p_π interaction. We confined ourselves to the consideration of studies which appear to be the most significant. At the same time we may note that a fairly large number of publications have appeared in which the effect of d_π–p_π interaction is either ignored or is taken into account incorrectly. The reasons for the incorrect or invalid conclusions concerning d_π–p_π interaction are failure to take into account all the factors influencing the chemical shift in ^{1}H NMR spectra[18,19], the complex mode of the C=C stretching vibration in the infrared spectra of the vinyl derivatives of Group IVB elements[20–22], incomplete allowance for the factors influencing the frequencies of the C=O stretching vibrations and =CH$_2$ deformation vibrations in the vibrational spectra of organic derivatives of the elements[23–28], failure to take into account other conjugation effects[29,30], and low sensitivity of spectroscopic parameters to the effect of substituents[31,32]. Thus the necessary conditions for a correct interpretation of d_π–p_π interaction include the following: (1) allowance for the polarity of the chemical bond influenced by the inductive effect of substituents and conjugation effects other than d_π–p_π interaction; (2) the availability of fairly large series of compounds in which the spectroscopic parameters of the molecular fragments (a) depend only on the electronic effect of the substituents and (b) are fairly sensitive to these effects.

So far there have been no Russian reviews of spectroscopic studies on d_π–p_π interaction.

II. NMR STUDY OF d_π–p_π INTERACTION

There have been three main trends in studies of the effect of d_π–p_π interaction in organic derivatives of Group IVB elements by NMR: (1) analysis of the spin–spin coupling constants; (2) analysis of the chemical shifts in the proton magnetic resonance (^{1}H NMR) spectra; (3) the study of the basic and acidic properties of organic derivatives of Group IVB elements. We shall examine the results of studies of each type.

1. Analysis of the Spin–spin Coupling Constants

The extensive data accumulated on the spin–spin coupling constants (SSCC) between the nuclei of the ^{13}C and ^{1}H isotopes in compounds of the type $CH_{4-n}X_n$ show that the constants $J(^{13}C-^1H)$ are proportional to the amount of s

character of the carbon orbital in the direction of the C–H bond. However, the relation between $J(^{13}C-^{1}H)$ and the parameters of the polarisation of the C–H bond under the influence of substituents X (for example, the electronegativity of X) does not hold for all substituents without exception [33]. Moreover, it has been shown that, for strongly electronegative substituents (X, Y, and Z) in the molecules CHXYZ, the experimental values of the SSCC differ from the constants calculated assuming additivity on the basis of the SSCC for compounds of the type CH_3X, CH_3Y, and CH_3Z. The above remarks should be borne in mind in the interpretation of the ^1H NMR data for organic derivatives of Group IVB elements within the framework of $d_\pi-p_\pi$ interaction. We shall now consider certain SSCC data in the Table.

Spin–spin coupling constants.

Compound	$J(^{13}C-^{1}H)$, Hz	Compound	$J(^{13}C-^{1}H)$, Hz
$(CH_3)_4Si$	118.0	$(CH_3)_3SiOPb(CH_3)_3$	115.0
$(CH_3)_3SiOLi$	116.0	$(CH_3)_3SiSSi(CH_3)_3$	119.5
$(CH_3)_3SiONa$	115.0	$(CH_3)_3SiSeSi(CH_3)_3$	120.5
$(CH_3)_3SiOSi(CH_3)_3$	118.0	$[(CH_3)_3Si]_3N$	118.0
$(CH_3)_3SiOGe(CH_3)_3$	117.8	$[(CH_3)_3Si]_2NGe(CH_3)_3$	118.0
$(CH_3)_3SiOSn(CH_3)_3$	116.8	$[(CH_3)_3Si]_2NSn(CH_3)_3$	118.0

The constancy of the SSCC on passing from tetramethylsilane to hexamethyldisiloxane, despite the replacement of the methyl groups by the electronegative oxygen atom, is striking. These data are usually regarded as evidence of a strong effect of $d_\pi-p_\pi$ interaction in the Si–O bond [34]. In compounds with Si–O–M groups, the variation of M in the series Ge–Sn–Pb results in a lowering of the amount of s character of the C–H bond in the $(CH_3)_3Si$ fragment and the contribution of $d_\pi-p_\pi$ interaction to the Si–O bond increases. The degree of double bonding in the Si–O fragment increases also on passing from hexamethyldisiloxane to alkali metal trimethylsilanoxides [35].

The characteristics of the $d_\pi-p_\pi$ interaction in the Si–O bonds of heterosiloxanes have been investigated by NMR and infrared spectroscopic methods also in other studies [36–41].

In the compounds $(CH_3)SiXSi(CH_3)_3$, the SSCC increase in the series O < S < Se (in opposition to the variation of the electronegativities of the X), which indicates a decrease of $d_\pi-p_\pi$ interaction on passing from oxygen to selenium derivatives [34]. Comparison of the SSCC for methoxysilanes and their carbon analogues also confirms the occurrence of $d_\pi-p_\pi$ interaction in the Si–O bond [42]. The low values of the SSCC for compounds with Si–N bonds, despite the considerable electronegativity of the nitrogen atom have been interpreted on the basis of the $d_\pi-p_\pi$ interaction in the Si–N bond [34,43]. Analysis of the $^{13}C-1H$ SSCC for the $N-CH_3$ fragment in the compounds $(CH_3)_3MN(CH_3)_2$ and $M[N(CH_3)_2]_4$ showed [43] that the inductive effect of the $(CH_3)_3M$ group diminishes when M varies in the series Si > C ≥ Ge > Sn. Comparison of the effective electronegativities, which vary in the same sequence, with Batsanov's electronegativities [44] which do not take into account the effect of π bonding (C > Ge ≃ Sn > Si) shows that the capacity of Group IVB elements for $d_\pi-p_\pi$ interaction diminishes in the series Si > Ge > Sn. In the monohalogeno-derivatives $(CH_3)_3SiX$ with X varying in the series F–Cl–Br–I, the SSCC increase correspondingly (118.8, 120.5, 121.0, and 121.5) in a sequence opposite to that in the variation of the I effect of the halogen atom. According to Schmidbaur [34], this indicates a decrease of the capacity of the halogens for $d_\pi-p_\pi$ interaction in the series F > Cl > Br > I. However, this conclusion is not entirely correct, since in methyl halides the SSCC also increase from the fluoride to the iodide derivative [45].

The effect of the $d_\pi-p_\pi$ interaction in the Si–N bond was investigated by Zuckerman and coworkers [46–48], who showed that the $J(^{15}N-^{1}H)$ SSCC for the compounds $(CH_3)_3M^{15}NHC_6H_5$, where M = Si, Ge, or Sn, and for aniline are similar but differ from the SSCC for the pyridinium ion, the orbitals of the nitrogen atom of which are sp^2 hybridised. On this basis, it was concluded that there is no stereochemical evidence for $d_\pi-p_\pi$ interaction in M–N bonds. However, according to other data [13,49], sp^3 hybridisation of the orbitals of the nitrogen atom by no means rules out its $d_\pi-p_\pi$ interaction with the silicon atom.

2. Analysis of Chemical Shifts in ^1H NMR Spectra

^1H NMR is mainly employed to investigate organic derivatives of Group IVB elements (however, ^{19}F NMR also yields information about the $d_\pi-p_\pi$ interaction [50]). The attempts to isolate the contributions to chemical shifts associated with the $d_\pi-p_\pi$ interaction encountered considerable difficulties. This is because the chemical shift is a function of a large number of intramolecular factors [51] the most important of which are the inductive effects of the substituents and the effects of the anisotropy of the magnetic susceptibility and of the intramolecular electric field [52]. Therefore experimental chemical shifts must be treated with much caution in attempts to obtain information about $d_\pi-p_\pi$ interaction. We shall consider certain data obtained after approximate allowance for the above factors.

The idea of the first series of studies [53–55] consisted in a comparison of the relations in the ^1H NMR spectra of organic derivatives of silicon, germanium, and tin with the similar relations for carbon compounds. It was shown that in the series $(CH_3)_4-nMR_n$, where M = Si, Ge, or Sn and R = Cl, Br, I, OAlk, C_6H_5, or $CH=CH_2$, there is a linear correlation between the chemical shifts and the inductive constants σ^* of the substituents R for each R and M. Similar relations hold also for carbon compounds. Therefore the points corresponding to different R for carbon compounds on the plot of τCH_3 against $\Sigma\sigma_R^*$ were transferred onto the chloride straight line in the direction parallel to the $\Sigma\sigma^*$ axis. The values of σ_{eff}^* were then obtained for each R. When the σ_{eff}^* were used for correlation with the τCH_3 for silicon, germanium, and tin derivatives, the points corresponding to certain compounds deviated from the correlation owing to $d_\pi-p_\pi$ interaction. Analysis of the deviations indicates a considerable contribution of $d_\pi-p_\pi$ interaction to the τCH_3 for R = OCH_3, OC_2H_5, and $CH=CH_2$. Bromine and iodine apparently enter into $d_\pi-p_\pi$ interaction less than does chlorine. Together with their advantages, these studies suffer from the evident disadvantages due to the assumption that the intramolecular factors influencing the chemical shifts in organic derivatives of Group IVB elements do not differ from those in carbon compounds.

Therefore in a second series of studies [56–58] an attempt was made to take into account these factors for methyl and ethyl derivatives of silicon and germanium more rigorously. The chemical shifts τ for the CH_3 and CH_2 groups in

compounds with substituents incapable of d_π–p_π interaction, in which there is almost no contribution to τ due to the anisotropy of the magnetic susceptibility and of the electric field, were considered initially. A linear correlation between the τ and the inductive constants σ^* of the substituents was found for these compounds. This made it possible to take into account accurately the changes in bond polarities in compounds with any substituents and hence to calculate the values of τ due solely to the I effect. Subsequently corrections were applied to these chemical shifts, taking into account approximately, on the basis of the appropriate formulae, the magnetic anisotropy and the electric field of the substituents, and the τ_{calc} were obtained. The discrepancies between the τ_{calc} and τ_{exp} were attributed to the effect of d_π–p_π interaction, decreasing in the series F > OCH_3 > Cl > C_6H_5 > Br and Si > Ge.

Because data concerning the involvement of the vinyl group in π bonding with elements of the silicon subgroup were contradictory [28], a series of studies were undertaken to investigate this problem by ^{1}H NMR. [59-61] Analysis of the chemical shifts in the ^{1}H NMR spectra of the compounds $(CH_3)_3MCH{=}CH_2$, $(C_2H_5)_2M(CH{=}CH_2)_2$ (M = C, Si, Ge, or Sn), and $Cl_3MCH{=}CH_2$ (M = Si or Ge) taking into account the effects of the magnetic anisotropy and the electric field showed that the capacity of Group IVB elements for d_π–p_π interaction with the vinyl group diminishes in the sequence Si > Ge > Sn. This conclusion was confirmed by infrared spectroscopy [62].

In some studies conclusions concerning the d_π–p_π interaction were reached on the basis of a simple analysis of the experimental chemical shifts. Although, owing to the complex nature of the chemical shift, the results of these investigations cannot pretend to a high objectivity, we shall examine some of the most important of them. Despite the failure to take into account intramolecular factors influencing the proton chemical shifts, the data for d_π–p_π interaction obtained in these studies agree qualitatively with the results of the investigation of this effect by other physical and chemical methods. The reason for this is probably as follows. It has been shown [58] for the compounds R_nMX_{4-n} (where R = CH_3 or C_2H_5, M = Si or Ge, and X = F, Cl, Br, OCH_3, or C_6H_5) that the principal factors affecting the proton chemical shift in the Group R are the inductive I effect of X and the intramolecular electric field of X (except for the case where X = C_6H_5, the effect of the anisotropy of the magnetic susceptibility of the M–X bond is extremely small). Both factors lead to a decrease of proton screening in the groups R. d_π–p_π interaction between M and X is opposed to the I effect and increases the screening of the protons in R. Therefore the conclusions concerning d_π–p_π interaction based on the anomalously high chemical shifts in certain methyl and ethyl derivatives of Group IVB elements can agree qualitatively with the results of more exact investigations. In studies of this type, a decrease of the capacity of Group VI elements for d_π–p_π interaction with Group IVB elements in the series O > S > Se > Te was established [34, 63, 64]; the occurrence of d_π–p_π interaction in bonds formed by silicon with oxygen, nitrogen, fluorine, and chlorine was discovered [65-73]; it has been shown that the amount of π character of the Sn–Cl bond is less than that of the Si–Cl bond [74] and a decrease of d_π–p_π interaction in Si–O bonds with increasing number of such bonds in the molecule was established [75, 76].

We shall now consider the results of studies in which the specific features of molecular structure make it possible to arrive at conclusions about d_π–p_π interaction without introducing corrections into the experimental chemical shifts for magnetic anisotropy and the electric field. In a study of the chemical shifts in the compounds $(CH_3)_nCl_{3-n}SiOR$, where n = 0–3 and R = alkyl group, Brune [77] demonstrated the occurrence of d_π–p_π interactions in the Si–O bond [77]. In the compounds $R'Cl_nSi(OR)_{3-n}$, d_π–p_π interaction in the Si–O fragment diminishes as chlorine atoms or alkoxy-groups accumulate; the chlorine atom is more actively involved in d_π–p_π interaction than oxygen [78-80]. Analysis of the effective electronegativities of the oxygen atoms in alkoxydisilanes showed that the delocalisation of the lone electron pairs of oxygen in the Si–Si–O fragment is accompanied by a strong d_π–d_π–p_π interaction [81]. Subsequently the characteristics of d_π–p_π interaction in organic derivatives of ethoxysilanes and also in aminoalkoxysilanes were studied by Voronkov and Pestunovich [82-85], who showed, in particular, that the conclusions [77] concerning the greater capacity of chlorine compared with oxygen for d_π–p_π interaction is erroneous. The distribution of electron density in aminoalkoxysilane molecules depends both on d_π–p_π interaction and on the effect of p, σ conjugation.

The aromatic systems of benzene, furan, and thiophen containing organometallic substituents have also been studied by ^{1}H NMR. It has been established both experimentally [86] and theoretically [87] that in compounds of this type the chemical shifts of certain ring protons are almost independent of the magnetic anisotropy and the electric field of the substituents. Therefore in many cases it is possible to relate these chemical shifts to the electronic effects of the substituents and to obtain information about the d_π–p_π interaction in the bond between the Group IVB element and the ring. Analysis of the ^{1}H NMR and ^{19}F NMR spectra of the compounds $XC_6H_4M(CH_3)_3$ (where M = Si, Ge, or Sn [88]) and $(FC_6H_4)_nSn_{4-n}$ (where R = CH_3, C_2H_5, [89] or C_6H_5 [90]) established that d_π–p_π interaction occurs in the M–ring bond, the interaction being a minimum for M = Sn and almost absent in lead derivatives [90].

As in other investigations [91-95], Angelelli et al. [96] concluded on the basis of the dipole moments of aryl derivatives of elements of the silicon subgroup that π bonding increases with increasing electron-donating properties of the *para*-substituent X, completely ignoring the contributions of the effects due to direct polar conjugation. The linear relation between the chemical shifts of the *para*-protons and Hammett's σ_n constants [97] showed that the d_π–p_π interaction between the phenyl ring and the atom M in the $M(C_2H_5)_3$ group diminishes in the sequence Si > Ge ≃ ≃ Sn > Pb as M is varied [98]. However, for compounds with the substituents MCl_3 the degree of d_π–p_π interaction in the M–Ph bond varies in a different sequence: Sn > > Ge > Si, which the authors explain [98] by a decrease of the capacity of silicon and germanium atoms for d_π–p_π interaction with the ring owing to their involvement in the energetically more favourable interaction with chlorine atoms. Reikhsfel'd and coworkers [99-105] showed that the d_π–p_π interaction in Si–Ph bonds competes with the intermolecular interaction involving the d orbitals of the silicon atom.

That the bonds between silicon subgroup elements and the phenyl ring are of the π type is also indicated by the ^{19}F NMR data for substituted fluorobenzenes [106] and the ^{14}N data for *p*-trimethylsilylnitrobenzene [107]. The problems of d_π–p_π interaction were examined in greater detail for organosilicon derivatives of furan and thiophen [108-110]. The trialkylsilyl group linked to the furan [108] or thiophen [108] ring behaves as a typical electron acceptor. At the same time the $(CH_2)_nSiAlk_3$ fragment is an electron donor. This demonstrates the occurrence of d_π–p_π inter-

action in furyl- and thienyl-silanes in which the silyl group is linked directly to the ring. It has been shown that the silicon atom in the $SiCl_3$ and $Si(OHAlk)_3$ groups is less strongly conjugated to the ring than the silicon atom in the $SiAlk_3$ group [110] owing to the competing $d\pi-p\pi$ interaction in the Si–Cl and Si–O bonds.

According to infrared spectroscopy [111] and electron diffraction [112] data, the lone electron pairs of the oxygen atom in compounds of the type $C_6H_5OSiH_3$ are involved in two conjugation processes—with the ring π electrons and the silicon 3*d* orbitals. This conclusion has also been confirmed by ^1H NMR. [113]

It has been shown by ^1H NMR that the $d\pi-p\pi$ character of the Si–N bond reduces the barrier to conformational transitions via an intermediate sp^2 state in *N*-trimethylsilyl derivatives of aziridine [114] and piperidine [115] compared with their carbon analogues. The $d\pi-p\pi$ interaction of silicon and germanium atoms with the nitrogen atoms of the pyrazole rings has also been established by ^1H NMR. [116]

3. The Basic and Acidic Properties of Organic Derivatives of Group IVB Elements

As already mentioned above, the chemical shift in the NMR spectra is a complex function of a large number of intramolecular and intermolecular factors. Therefore, in correlating the acid–basic properties of organic derivatives of the elements with molecular structure, correct experiments are necessary. In studies on basicity, the formation of hydrogen bonds between molecules having bonds of the type M–X (where M = Si, Ge, or Sn and X = O or N) and proton donors was investigated. Chloroform was mainly employed as the proton donor. The chemical shift of the proton in chloroform at infinite dilution or the $^{13}C-^1H$ spin–spin coupling constant of chloroform served as a measure of the strength of the hydrogen bond (and hence of the basicity of X).

It was found that the basicity of siloxanes and alkoxysilanes is much lower than that of their carbon analogues [117], which indicates, in agreement with infrared spectroscopic data [118], a strong $d\pi-p\pi$ interaction in the Si–O bond. The basicity of various compounds with M–N bonds has been investigated [43,119] and a decrease of $d\pi-p\pi$ interaction on passing from M = Si to M = Sn has been established, which in broad outline is also consistent with the results of earlier infrared spectroscopic studies [120].

The study of the acidic properties of alcohol derivatives of the elements is based on the finding [121] that alcohols form very stable [H-bonded (Ed. of Translation)] complexes with dimethyl sulphoxide. Other possible types of association are then suppressed and therefore the chemical shift of the OH proton is a measure of the acidity of the alcohol (we may note that this method has been recently criticised [122]). Organosilyl alcohols containing the $\rangle SiOH$ fragment are more acidic than their carbon and germanium analogues [123]. Comparison of the chemical shifts of the OH protons in silyl-substituted benzoic acids and phenols with their carbon analogues indicates $d\pi-p\pi$ interaction between the aromatic ring and the silicon atom, which is more pronounced in phenols [124]. The $(CH_3)_3SiSi(CH_3)_2$ group is a more powerful acceptor of π electrons from the aromatic ring than the trimethylsilyl group [125]. An appreciable $d\pi-p\pi$ interaction in the Si–O bond is also indicated by the greater strength of the hydrogen bonds in $(CH_3)_3SiOH$ than in $(CH_3)_3COH$; [122,126] for the Si–Cl bond, this follows from a comparison of the proton-donating properties of chloroform [127].

The greater capacity of silicon for $d\pi-p\pi$ intera tion compared with germanium follows from data obtained in a ^1H NMR study of the hydrogen bond in compounds of the type $(CH_3)_3M-C\equiv CH$. [128] For M = Si, the hydrogen of the $\equiv CH$ group is more mobile than for M = Ge owing to the reduced electron density in the multiple bond as a result of the interaction of the π electrons of this bond with the *d* orbitals of the silicon atom. The acidic properties of certain other acetylene derivatives of Group IVB elements have been studied by Petrov et al. [129]

The ^1H NMR study of the hydrogen bond between compounds of the type $(C_2H_5)_3MXH$ (where M = Si or Ge and X = S or Se) and proton-accepting solvents showed that silicon forms stronger $d\pi-p\pi$ bonds than germanium. The effect of the $d\pi-p\pi$ interaction in M–S bonds is more appreciable than in M–Se bonds [130].

III. STUDY OF $d\pi-p\pi$ INTERACTION BY VIBRATIONAL SPECTROSCOPIC METHODS

The effect of $d\pi-p\pi$ interaction in organic derivatives of Group IVB elements has been studied in three different ways by vibrational spectroscopic methods (infrared and Raman spectroscopy): (1) the study of the basic and acidic properties of the compounds; (2) the study of the vibration frequencies and intensities for certain bonds in organic derivatives of the elements, (3) analysis of the stretching vibration frequencies of the Si–H bond in substituted silanes.

1. The Basic and Acidic Properties of Organic Derivatives of Group IVB Elements

On formation of the hydrogen bond, organic derivatives of the elements can behave both as acids and bases. When compounds with a bond between a Group IVB element and a Group VI element form a hydrogen bond with proton donors (alcohols, pyrrole, chloroform), the compound behaves in the hydrogen bond as a base. On formation of a hydrogen bond between compounds with fragments of the type O–H, S–H, and N–H linked to a Group IVB element and hydrogen bond acceptors (dioxan, tetrahydrofuran, ethyl ether), the compound behaves as an acid. In studies of this kind it is assumed that the shift of the X–H frequency of the proton donor in the hydrogen bond on passing from the non-associated to the associated state is proportional to the hydrogen bond energy [131,132]. (In a more rigorous treatment, a linear relation was demonstrated between the νO-H frequency shift and the square of the hydrogen bond energy in phenol–base systems [133]. This is probably true also of other proton donors [133].) On the other hand, it is clear that the hydrogen bond energy is closely related to the electron density at the Group VI atom of the base or at the X atom of the X—H group of the proton donor in the hydrogen bond. The electron density at these atoms in turn depends directly on the contribution of the $d\pi-p\pi$ interaction in the M–X bond, where M is an element of the silicon subgroup. The stronger is the $d\pi-p\pi$ interaction, the lower the electron density at the atom X. Study of hydrogen bonding showed [131] that the silanols $(C_6H_5)_2SiH(OH)$ and R_3SiOH (where R = CH_3, C_2H_5, or C_6H_5) are much more acidic but only slightly less basic than the corresponding carbinols. This is evidence of $d\pi-p\pi$ interaction in silanols involving only one of the two lone electron pairs of oxygen. In the compounds $(C_6H_5)_3MOH$ (where M = C, Si, Ge, Sn, or Pb), the silanol is much more acidic

than the other hydroxy-derivatives[134,135]. In the absence of d_π–p_π interaction the acidity of the hydroxides should be determined by the electronegativity of the element M. This fact and also data for the basicity of the hydroxides leads to the following sequence in terms of capacity for d_π–p_π interaction: Si > Ge > Sn ≃ Pb. On passing to the alcohols $(C_6H_5)_3MCH_2OH$ (where M = C, Si, or Ge), one would expect that the carbinol would be the most acidic, since carbon is the most electronegative of the three elements M. However, the following acidity series was obtained experimentally: $(C_6H_5)_3GeCH_2OH > (C_6H_5)_3SiCH_2OH > > (C_6H_5)_3CCH_2OH$,[122] which according to the authors is evidence of intramolecular coordination between the oxygen and germanium atoms due to the *d* orbitals of the latter. In the silyl analogue this effect is less pronounced and in the carbinol it is absent altogether. It probably occurs in 2-substituted cyclohexanones and cyclohexanols[136] and also in the compound $H_3GeCH_2OCH_3$.[137] In the alcohols $(C_6H_5)_3MCH_2CH_2OH$ the effect is probably absent. The acidity of such alcohols is almost independent of the nature of the element M,[122] since the *I* effect of the $(C_6H_5)_3MCH_2CH_2$ group changes little as M is varied. In a study of intramolecular hydrogen bonding in the hydroperoxides $(C_6H_5)_3MOOH$ (where M = C, Si, Ge, or Sn) and their hydrogen bonding with tetrahydrofuran, it was established that the acidity of the hydroperoxides diminishes in the following sequence as M varies: Si > Ge > C > Sn.[138] This is evidence of a decrease of d_π–p_π interaction in the M–O bond in the series Si > Ge > Sn and it is consistent with the results obtained for the hydroxides $(C_6H_5)_3MOH$.[135] The effect of d_π–p_π interaction in the M–C_6H_5 bond is much less than in the M–O bond. Therefore the main factor determining the energy of the intramolecular (as well as intermolecular) hydrogen bond is the acidity of the hydroperoxides.

Studies of a series of ethers, siloxanes[118,139], alkoxysilanes, and alkoxygermanes[140-142] led to the discovery that the basicity of the oxygen atom diminishes in the series C–O–C > C–O–Si > Si–O–Si. The decrease of basicity was interpreted as a result of a shift of the oxygen *p* electron to the silicon *d* orbital. The difference between the basicities of monoethoxygermane and monoethoxysilane corresponds to a greater d_π–p_π interaction in the Si–O bond than in the Ge–O bond. On the other hand, tetraethoxygermane is only slightly more basic than tetraethoxysilane. This is because in tetraethoxysilane π-bonding with each of the oxygen atoms is weaker compared with the d_π–p_π interaction in monoethoxysilane[142]. Evidence for stronger π-bonding of oxygen to silicon than to germanium or tin was also obtained in other studies[143,144]. Thus the following series of decreasing basicity of organic derivatives of the elements with an M–O bond have been established:: SiOC > $Si(OC)_2$ > $Si(OC)_3$ > SiOSi, GeOGe > > GeOC > $Ge(OC)_2$ > $Ge(OC)_3$, and SnOSn > SnOC > > $Sn(OC)_2$.[145] It has also been shown[146] that the low basicities of compounds with the $(CH_3)_3SiO$ and $(CH_3)_3CO$ fragments is due not only to d_π–p_π interaction in the Si–O bond but also to steric hindrance to the formation of a hydrogen bond generated by the $(CH_3)_3C$ and $(CH_3)_3Si$ groups.

The force constants of the Group IVB element–Group VI element bonds have been analysed[147-149] on the basis of the vibrational spectra of compounds containing such bonds. Thus an enhanced multiplicity of the Si–O and probably Sn–S bonds has been established[147,148] but data supporting the π character of Si–S, Ge–S, Pb–S, and Sn–O bonds were not obtained[147-149]. In view of the large number of factors influencing the force constants (this is discussed in greater detail in the next section of the review), the reliability of these data[147-149] for d_π–p_π interaction is low. Studies on the basicity of organic derivatives of the elements with a Group IVB element–Group IV element bond are therefore of considerable interest. The problem of d_π–p_π interaction between elements M of the silicon subgroup and oxygen and sulphur (as well as nitrogen) atoms has been discussed[150] in a study of the basicity of compounds containing bonds involving these elements. The study showed that the capacity of M for d_π–p_π interaction with nitrogen or oxygen atoms decreases in the sequence Si > Ge > Sn. An appreciably weaker d_π–p_π interaction was observed in the Si–S bond. The authors' view that the d_π–p_π interaction of germanium with sulphur is more pronounced than with oxygen appears to be supported by insufficient evidence.

The order of the acidities of silanethiols and mercaptans, $(C_6H_5)_3SiSH \gg C_6H_5SH > (CH_3)_3SiSH > (C_6H_5)_3CSH > > (CH_3)_3CSH$,[151] proved to be similar to that obtained previously for the acidities of oxygen-containing compounds: $(C_6H_5)_3SiOH \gg C_6H_5OH > (CH_3)_3SiOH > (C_6H_5)_3COH > > (CH_3)_3COH$.[131] In the two pairs of compounds with the same structures $(C_6H_5)_3SiSH$–$(C_6H_5)_3CSH$ and $(CH_3)_3SiSH$–$(CH_3)_3CSH$ the silicon compounds are more acid. This is consistent with dative Si–S π bonding in silanethiols, which makes them stronger acids than mercaptans.

Whereas only one lone electron pair of the oxygen atom is involved in the d_π–p_π bonding in the Si–O–C group and to such pairs in the Si–O–Si group[118], the sulphur atom is probably capable of giving up only one electron pair in all cases[150].

These studies were developed further in an investigation[152] of the basicity of compounds of the type $(C_2H_5)_3MXM'(C_2H_5)_3$ (where M and M' = Si, Ge, or Sn; X = O, S, Se, or Te) and also the compounds $(C_2H_5)_3MXH$ (where M = Si or Ge; X = S or Se). The shift of the stretching vibration frequency of the C–D bond in non-associated deuterochloroform on formation of a hydrogen bond with the above compounds was studied. The shift $\Delta\nu$ was treated as a measure of the basicity of organic derivatives of the elements. Bearing in mind that (1) the basicity of organic derivatives of Group VI elements decreases in the sequence O > S > Se > Te[132] (the capacity of these elements for d_π–p_π interaction with Group IVB elements decreases in the same sequence), (2) the capacity of the elements for d_π–p_π interaction diminishes in the sequence Si > Ge > Sn,[63,111,130] and (3) the d_π–p_π interaction in the Si–Te bond (and even more so in the Ge–Te and Sn–Te bonds) is extremely weak[111,153], the authors[152] interpreted the results as follows. For all the tellurides $[(C_2H_5)_3M]_2Te$, the values of $\Delta\nu$ are similar. This shows that the steric hindrance and the d_π–p_π interaction have only a slight effect on the basicity. Nevertheless $\Delta\nu$ is a minimum for $[(C_2H_5)_3Si]_2Te$. The contribution of d_π–p_π interaction to the Si–Te bond is small, but it can be detected in the measurement of the basicity, since the latter is directly related to the electron density at the tellurium atom.

For organic derivatives of the elements with the general formula $[(C_2H_5)_3M]_2X$, the following sequences of decreasing basicity were obtained: O > Te > Se > S for M = Sn, O > Te > Se > S for M = Ge, and Te > Se > S > O for M = Si. None of them is identical with the O > S > Se > Te sequence quoted above for the series of carbon compounds. The reason for this is that the relatively small effect of d_π–p_π interaction, which, however, increases systematically in the sequence Te < Se < S, influences the basicity of the Group VI elements even in the series of organotin compounds. For the series $[(C_2H_5)_3Ge]_2X$, the

d_π–p_π interaction in the Ge–X bonds plays a more significant role. The basicity $[(C_2H_5)_3Ge]_2S$ and $[(C_2H_5)_3Ge]_2Se$ is lower than that of the corresponding tin derivatives. This is evidence of d_π–p_π interaction in the Ge–Se bond, which becomes even more pronounced in the Ge–S bond. In the series of compounds $[(C_2H_5)_3Si]_2X$, the values of $\Delta\nu$ are much lower than in the organogermanium and organotin series. This shows that the d_π–p_π interaction with silicon is stronger than with germanium or tin. From this point of view, examination of the series of compounds $[(C_2H_5)_3M]_2O$, $[(C_2H_5)_3M]_2S$, and $[(C_2H_5)_3M]_2Se$ yields striking results. In each of these series the basicity falls on passing from M = Sn to M = Ge and Si, which is also evidence of a decrease of the capacity of Group IVB elements for d_π–p_π interaction in the sequence Si > Ge > Sn. The degree of d_π–p_π interaction in the Si–O, Si–S, and Si–Se fragments varies approximately in the proportions 4 : 2 : 1, as shown by the analysis of the infrared spectra of substituted silanes containing these fragments[111]. Therefore the extremely low basicity of hexaethyldisiloxane is a result of a more pronounced effect of d_π–p_π interaction in silicon derivatives in general and in the Si–O bonds in particular. Moreover, as already mentioned[146], $\Delta\nu$ for $[(C_2H_5)_3Si]_2O$ is low also because of steric hindrance to the formation of a hydrogen bond due to triethylsilyl groups.

A strong d_π–p_π interaction in the Si–N groups was established in a study of the basicity of a series of organosilicon amines[120]. It was shown that the shift $\Delta\nu_{C-D}$ of the stretching vibration frequency of the C–D bond in mixtures of Cl_3CD with silylamines, characterising the basicity of the nitrogen atom, is in the range 50–80 cm^{-1} for compounds of the type $(CH_3)_3SiNR_2$, 30–35 cm^{-1} for the cyclic compounds $[(CH_3)_2SiNR]_3$, and 15 cm^{-1} for $(CH_3)_3SiNHPh$, $(CH_3)_3SiNPh_2$, and $[(CH_3)_3Si]_2NPh$. If one assumes that with decrease of basicity the effect of d_π–p_π interaction increases, then in the last of compounds the effect is a maximum. In trisilylamines the $\Delta\nu_{C-D}$ effect was not observed, which is evidence of an extremely low basicity of the nitrogen atom. However, the basicity data conflict with the conclusion of Randall and Zuckerman[46] that there is no stereochemical evidence for d_π–p_π conjugation in the Si–N bond, which was based on a study of the infrared and NMR spectra of *N*-trimethylsilyl-, *N*-trimethylgermyl, and *N*-trimethylstannyl-derivatives of aniline. This apparent contradiction can be resolved if one remembers that the lone electron pair of the nitrogen atom can interact both with *nd* orbitals and with the phenyl ring. While the data of Abel et al.[120] indicate conjugation of the lone pair of the nitrogen atom and those of Randall and Zuckerman[46] demonstrate the absence of d_π–p_π interaction, a common conclusion of both investigations is that the interaction of the lone electron pair of the nitrogen with the phenyl ring is much stronger than with *nd* orbitals.

The results obtained in the determination of the basicities of two series of compounds, $(CH_3)_3MN(CH_3)_2$ and $M[N(CH_3)_2]_4$ (where M = C, Si, Ge, or Sn), show that the silicon derivatives form weak hydrogen bonds: this is due to the delocalisation of the *p* electrons in the Si–N bond. According to Mack and Yoder[43], d_π–p_π interaction is more pronounced in silicon derivatives, is much weaker in germanium derivatives, and is probably absent in tin derivatives. The study of the basicity of ethyl(dimethylamino)germanes also indicates a smaller contribution of d_π–p_π interaction to the Ge–N bond compared with Si–N.[154]

Infrared spectroscopic data for silylamines[155] and trimethylsilyldiazomethane[156] as well as the results obtained in a study of the relative basicities of disilazanes[157] have been interpreted on the basis of the d_π–p_π interaction in the Si–N bond.

It was established by infrared spectroscopy[158,159] that the basicities of arylsilanes and organosilicon derivatives of thiophen are much lower than those of their carbon analogues. This is a consequence of d_π–p_π interaction, as a result of which the SiR_3 (R = alkyl or H) substituents in the benzene or thiophen rings become less effective electron donors than the corresponding substituent CR_3. The basicity of the vinyl derivatives of Group IVB elements is much lower than that of the corresponding carbon analogues; with increase of the atomic number of the Group IVB element, the basicity increases[160]. This is caused by the effect of d_π–p_π interaction, which decreases in the sequence Si > Ge > Sn.

The infrared spectra of compounds of the type $(CH_3)_3M$–C≡CH, where M = C, Si, Ge, Sn, or Pb, have been studied in various electron-donating solvents. It has been noted[161–162] that all the compounds except carbon derivatives form hydrogen bonds with the solvent, which is evidence of a considerable acidity of the hydrogen atom in the –C≡CH fragment. The acidity of organic derivatives of the elements increases as a result of intramolecular interaction of the π electrons of the triple bond with the *nd* orbitals of the Group IVB element. Thus the presence of d_π–p_π interaction in ethynyl derivatives of the elements has been convincingly confirmed by NMR[128,129] and infrared spectroscopic[161,162] methods.

2. Vibration Frequencies and Absorption Band Intensities of Certain Bonds in Organic Derivatives of Group IV Elements

Since the contribution of the effect of d_π–p_π conjugation in the M–X fragment to the total MX bond energy is comparatively small, considerable caution must be exercised in drawing conclusions concerning d_π–p_π interaction on the basis of an analysis of the force constants. For such conclusions to be valid, it is necessary to have rigorous proof that the changes in force constants (including the changes under the influence of the d_π–p_π conjugation) are caused by electronic effects. As a rule it is necessary to carry out a theoretical analysis of the vibrations of the molecules investigated and to obtain proof that the vibration, on the basis of the changes in frequency of which conclusions concerning intramolecular effects of the type of d_π–p_π interaction are arrived at, is characteristic. Unfortunately the latter requirement has not been fulfilled in all the studies dealing with this problem.

It has been established that the bonds formed by silicon with elements such as N, O, F, and Cl have relatively high force constants[147,163]. On this basis, Kriegsman[147,164] concluded that d_π–p_π interaction must play an important role in compounds containing such bonds. According to Kriegsmann[165], the order of the Si–N bond in hexamethyldisilazane is 0.18. The Ge–N and Sn–N bonds also have partial double bond character, which is indicated by the M–N force constants in the compounds $M[N(CH_3)_2]_4$.[166]

Subsequently the vibrational spectra of compounds of the type $(H_3Si)_nX$ and $[(CH_3)_3Si]_nX$, where X is an element in Groups IV–VI and *n* is the valence, were studied systematically by Bürger (see Bürger's review[167] and the paper summarising his results[168]). In the analysis of the force constants of the Si–X bonds of these compounds, account was taken of the contribution of the d_π–p_π interaction in the bonds between silicon and elements in Groups V–VII. The effect of d_π–p_π interaction was studied on the basis of the

vibration spectra of the compounds SiX_4 and Si_2X_6,[169] where X = Cl, Br, or I. Detailed studies of the d_π–p_π interaction in compounds with Si–O–Si and Si–O bonds and related germanium derivatives were made by Lazarev and coworkers[170-174].

Investigation of the stretching frequencies of the C=O bond in the compounds $R_3MOC(O)R'$ (R and R' = CH_3, C_2H_5, or C_6H_5; M = silicon subgroup elements) showed[175] that in the compounds with M = Si or Ge there is competition between πp conjugation ($R_3M-\ddot{O}-\underset{\|}{C}-R'$) and d_π–p_π interaction. As a result, the d_π–p_π conjugation in the Ge–O bonds of these compounds proved to be comparatively weak; the Si–O bond has a much greater amount of π character. In tin and lead derivatives, the amount of ionic character of the M–O bond is very high, owing to the transition of the M element to the sp^3d or sp^3d^2 valence states and the formation of M...O coordinate bonds.

The Si_3N skeleton of trisilylamines is planar, which is believed to be a result of the delocalisation of the lone electron pair of nitrogen to the silicon *d* orbitals, i.e. d_π–p_π interaction in the Si–N bond[176-178]. In contrast to trisilylamines, the heavy atoms in trigermylamines are not coplanar[179], since the d_π–p_π interaction in the Ge–N bonds is weaker than in Si–N bonds. Analysis of infrared spectroscopic and electron diffraction data for silicon and germanium compounds led to the conclusion that germanium has a smaller capacity for d_π–p_π interaction[179].

Contradictory data concerning the possibility of d_π–p_π interaction between the silicon atom and the carbonyl group were obtained in a study of silyl ketones[23-27,180]. Thus, according to Brook and coworkers[23-27], the stretching frequencies of the C=O bond indicate the presence of intramolecular coordination in α- and γ-silyl ketones. In β-silyl ketones, such interaction is prevented by steric hindrance. However, physicochemical studies on 1-trimethylsilylpropan-2-one[180] indicate the occurrence in this compound of coordination between the carbonyl oxygen and the silicon atom even in the gaseous state. The above investigations[23-27,180] are closely related to later studies[122,136,137] indicating the possibility of intramolecular coordination between the germanium (and also probably silicon) atoms and oxygen in organic derivatives of the elements with alcoholic groups of the type R_3MCH_2OH, where M = Ge or Si. However, it is noteworthy that this type of expansion of the valence shell of the silicon subgroup element as a result of the involvement of their *d* orbitals in the formation of additional bonds may differ significantly from the d_π–p_π interaction between atoms which are linked directly by a chemical bond. This is indicated also by experiment. Indeed, it has now been finally established that in the M–X fragment (where M is an element of the silicon subgroup and X an element of Groups V–VII or an α-unsaturated hydrocarbon substituent) the capacity of the atoms M for d_π–p_π interaction with X increases in the sequence Sn < Ge < Si, i.e. has a maximum for silicon. The *d* orbitals of the atoms M of the type d_ϵ (d_{xy}, d_{xz} d_{yz}) are used for π bonding[8]. The element M can also be involved in the formation of additional σ bonds on passing to the quinquevalent and hexavalent state (sp^3d and sp^3d^2). Bonds of this kind are achieved with the aid of *d* orbitals of the type d_γ (d_{z^2}, $d_{x^2-y^2}$). The capacity of the element M for σ bonding increases in the sequence Si < Ge < Sn.[1] Data on the acidic properties of the alcohols $(C_6H_5)_3MCH_2OH$ show[122] that intramolecular coordination is most characteristic of germanium (the tin derivative was not studied) and is least pronounced for the silyl analogue. These results suggest that intramolecular coordination is achieved with participation of d_γ orbitals. We may also note that, since silicon exhibits a comparatively weak capacity for coordination of the above type, the data for silyl ketones[23-27] must be interpreted with much caution. Thus, in order to isolate the contribution associated with intramolecular coordination to the stretching vibration frequency of the C=O bond in the β-silyl ketones $R_3SiCH_2\overset{O}{\overset{\|}{C}}-R'$, one must take into account rigorously not only the inductive effect of the substituent R_3SiCH_2 but also the effect of σ, π conjugation.

Infrared and NMR spectroscopic data for dialkoxydialkylstannanes were accounted for on the basis of the hypothesis of d_π–p_π interaction between the tin and oxygen atoms[181]. However, in a study of the vibrational spectra of compounds of the type $R_3Sn-O-SnR_3$, where R = alkyl or C_6H_5, the double bond character of the Sn–O fragment was not demonstrated[148]. The contradictory nature of the results of these investigations arises because the d_π–p_π bonds in tin compounds are energetically fairly weak. Therefore experimental accuracy for these compounds constitutes a particularly urgent task. Even for silicon compounds, where d_π–p_π bonds play a much more important role, allowance for all the factors influencing the force constant, necessary for the estimation of the contribution of d_π–p_π interaction, has not yet been finally achieved[167,168]. However, the literature shows that the search for a solution of this problem is being continued. A study[182] where it was established that in the absence of d_π–p_π interaction in M–X bonds the ν_{M-C} frequencies for the compounds $[(C_2H_5)_3M]_nX$ (M = Si or Ge; X = element in Groups I–VII; *n* = valence of X) are linearly related to the electronegativities of the substituents X is particularly instructive in this respect. An increase in the electronegativity of X increases the amount of *p* character of the M–X bond and the amount of *s* character of the M–C bond[183]. The ν_{M-C} frequencies in the compounds where the M–X bonds have π character are reduced compared with the values expected on the basis of the above linear relations. Analysis of the deviations leads to the following sequence in terms of the capacities of the substituents X for d_π–p_π interaction with the silicon or germanium atom: $F \geq O > Cl > Br > I \simeq S > Se > Te > Sb > Bi$. The deviations for silicon derivatives are greater than for germanium derivatives, which indicates a greater capacity of silicon for d_π–p_π interaction compared with germanium. Thus the fact that in different Groups of the Periodic System the capacity of the elements for d_π–p_π interaction decreases with increasing atomic number of the element was confirmed yet again in this investigation. This applies both to elements which behave as lone electron pair donors (elements in Groups V–VII) and to Group IVB elements with vacant *d* orbitals.

Numerous studies have been made on the effect of d_π–p_π interaction in compounds with an α-unsaturated hydrocarbon substituent linked to a Group IVB element[184-193]. It has been shown that in compounds of the type $(CH_3)_3M-C\equiv CH$ (where M = C, Si, Ge, Sn, or Pb) d_π–p_π interaction decreases on passing from silicon to lead derivatives. In compounds with several ethynyl groups, $(CH_3)_4$-nSi(C≡CH)n, one may expect that the vibrations of the individual ethynyl groups will be independent and therefore the intensities of the absorption bands of the ≡C–H and –C≡C– bonds will increase additively with increasing number of such bonds. The experimental deviations from these expectations

were accounted for by two types of intramolecular interactions—the inductive effect and the effect of the d_π–p_π interaction[185]. The conclusion that the π electrons of the acetylenic bonds interact with the 5*d* orbitals of the tin atom was based on a study of the vibrational spectra and the measurement of the integral intensities of certain absorption bands of the ethynyl compounds $(C_2H_5)_3SnC{\equiv}CX$, where X = H, CH_3, $CH{=}CH_2$, C_6H_5, or $Si(CH_3)_3$.[186] The results of these studies agree with the data obtained in the study of the acidic properties of the hydrogen atom in the ethynyl group by NMR[128,129] and infrared spectroscopy[161,162].

The conclusion that there is d_π–p_π interaction between the silicon atom and the π electrons of the triple bond was arrived at in a series of studies of Zeil and coworkers[187–190] of the vibrational and microwave spectra as well as NQR spectra of the compounds $(CH_3)_3MC{\equiv}CX$ and $(CH_3)_3MC{\equiv}CM(CH_3)_3$, where M = Group IVB element and X = H or Cl. The electron-accepting properties of the silicon atom linked directly to the triple bond are also indicated by NMR[191] and infrared spectroscopic[192] data and studies on the vertical ionisation potentials[192] of compounds of the type $R_3MC{\equiv}CH$ and $R_3M(C{\equiv}C)_nMR_3$, where M = C or Si, R = H, CH_3, or C_6H_5, and n = 1–3.

Thus in the M–C≡C system (where M = Si, Ge, or Sn) there is d_π–p_π interaction between the *d* orbitals of M and the π electrons of the triple bond, although in lead derivatives such interaction was not detected by infrared spectroscopy[193].

Many studies have been made on the d_π–p_π interaction between the *d* orbitals of Group IVB elements M and the π electrons of the ethylenic bond in compounds containing the M–C=C grouping. It has been shown that the vibration attributed to the presence of the C=C bond in the molecules has a wave-number of about 1650 cm^{-1} in alkenes, while in the corresponding vinylsilanes it is reduced by about 50 cm^{-1}. According to the authors of these investigations[20–22], this indicates the existence of a structure of the type $\bar{Si}$–$\overset{\frown}{C}$=$\overset{+}{C}$ in which the electron density in the double bond is reduced owing to d_π–p_π interaction. Subsequently Bock and Seidl[194,195] carried out a series of studies on silyl-substituted ethylenes and butadienes by physical methods among which they examined in detail the $\nu_{C=C}$ frequencies in these compounds. Comparison of these results with the vibrational spectra of alkylbutadienes enabled them[194,195] to conclude that trimethylsilyl substituents exhibit electron-accepting properties in consequence of the d_π–p_π interaction in the Si–C=C fragments. Therefore the force constants and the ν_{C-C} frequencies in silyl derivatives are reduced. Despite the agreement between the data for π bonding and the results obtained by other methods, Egorov and coworkers[28] showed that the complex mode of vibration with a wave-number of about 1600 cm^{-1} does not permit correct conclusions concerning d_π–p_π interaction on the basis of changes in the frequency of this vibration. It was noted that the intensity of the absorption bands corresponding to this vibration in the compounds $(CH_3)_3MCH{=}CH_2$ decreases in the following sequence as M is varied: Si > Ge > Sn. On the other hand, in allyl derivatives the intensity of this vibration actually increases in the same sequence. This type of variation of the intensity was tentatively interpreted[21,22,196] within the framework of the d_π–p_π interaction between the vinyl group and the Group IVB elements. However, according to Leites et al.[28] the intensity data can also be accounted for by the involvement in the above vibrations of all the coordinates of the $\diagdown C{=}C \diagup_{M}$ fragment.

Analysis of the absorption bands due to the fanwise vibrations of the $=CH_2$ group in substituted vinylsilanes led Eisch and Trainor[197] to the conclusion that there is d_π–p_π interaction in these compounds. Other workers[20–22,194,195,198] support this view. The spectra of vinyl derivatives were interpreted from a different standpoint by Leites et al.[28] The frequency shift of the $=CH_2$ fanwise vibrations of the vinyl group when the central carbon atom is replaced in succession by silicon, tin, and germanium was explained primarily by the inductive effect of the atom M. Leites et al.[28] believe that, even if a d_π–p_π interaction effect exists, it is so weak that it does not influence the parameters of the vibrational spectra. Egorov[30,199] examined the optical properties of methyl and vinyl derivatives of Group IVB elements on the hypothesis that such elements have a duel function—both electron-donating and electron-accepting ("C-effect"). Since the "C-effect" and d_π–p_π interaction act in the same direction, it is believed[200] that it is difficult to obtain information about the d_π–p_π interaction in vinyl and phenyl derivatives in Group IVB elements. The problems of the d_π–p_π interaction in vinyl derivatives of Group IVB elements were examined in greater detail by Egorochkin and coworkers[62,201]. The frequencies ωCH_2 of the out-of-plane deformation vibrations of the CH_2 group in the compounds $CH_2{=}CHX$ are known to be highly characteristic[28] and sensitive to the electronic effects of the substituents X.[202] Therefore if X is not conjugated with the vinyl group, the ωCH_2 are linearly related to the inductive constants of X.[62] The points corresponding to compounds with substituents capable of conjugation with the vinyl group deviate from this linear relation. Analysis of the deviations established[62,201] (1) an analogy between the effects of conjugation with the vinyl group and the phenyl ring, (2) a decrease of d_π–p_π interaction in the M–vinyl bonds in the sequence Si > Ge > Sn, (3) a competition between the d_π–p_π interaction in the M–vinyl and M–halogen bonds in the compounds $Hal_3MCH{=}CH_2$,[203] and (4) a decrease of the effect of σ,π conjugation in the allyl derivatives $R_3MCH_2CH{=}CH_2$ in the sequence Sn > Ge > Si and the dependence of this effect on the nature of the substituent R. These data are consistent with the results obtained by the ^1H NMR method[59–61].

Petrov and coworkers[204,205] showed that the vibrational spectra and dipole moments of silyl-substituted 1,3-dienes indicate a shift of the electron clouds of the substituent towards the silicon atom. The d_π–p_π interaction has a significant influence also on the reactivities of compounds of this class.

A number of studies[88–97,206,207] indicate the occurrence of d_π–p_π interactions between the Group IVB element and the aromatic ring. The majority of data suggest that this effect diminishes in the sequence Si > Ge > Sn. The changes in the positions and intensities of certain characteristic vibrations of the phenyl group in the phenylsilane derivatives C_6H_5SiXYZ indicate the occurrence of d_π–p_π interaction between the *d* orbitals of the silicon atom and the π electrons of the phenyl ring[31]. However, a similar study of phenylgermanes did not yield a direct answer to the question of the possibility of π bonding in the Ge–C_6H_5 fragment[32]. The reason for the contradictory nature of the results[31,32] is low sensitivity of the spectroscopic parameters of the phenyl group to the electronic effects of the substituents. The study of Egorochkin et al.[208], where conclusions concerning the electronic effects of the aryl substituents C_6H_4X were based on an analysis of the stretching vibration frequencies of the Si–H bond (these investigations are considered in greater detail below) in

compounds with the H–Si–C_6H_4X fragments, was free from this defect. The degree of $d\pi$–$p\pi$ interaction in the Si–aryl bond varies over a wide range and increases approximately linearly with increasing inductive effect of the aryl substituent at the silicon atom, i.e. with increase of the positive charge of the central element.

The linear correlation between the stretching frequency of the C=O bond in substituted acetophenones and the Brown–Okamoto σ^+ constants of the substituents[209] was used in an investigation of the electronic properties of the substituents X in the compound $CH_3CO-C_6H_4-X$, where X = $(CH_3)_3Si$, $(CH_3)_3SiSi(CH_3)_2$, $(CH_3)_3SiO$, or $(CH_3)_3SiSi(CH_3)_2O$.[125] It was established that the group $(CH_3)_3SiSi(CH_3)_2$ has a more pronounced $+I$ effect than the trimethylsilyl group but at the same time the pentamethyldisilyl group forms more stable $d\pi$–$p\pi$ bonds than does the trimethylsilyl group with both the aromatic ring and the oxygen atom. This investigation[125] was not the only one in which the enhanced electron-accepting capacity of the pentamethyldisilyl group in relation to the trimethylsilyl group was demonstrated. A similar phenomenon was observed, for example, also by Brune[81] in a study of the NMR spectra of alkoxydisilanes. Probably, in compounds with Si–Si–O or Si–Si–C_6H_5 fragments, the lone electron pairs or π electrons are probably not delocalised solely over the d orbitals of the nearest silicon atom. Both silicon atoms are involved in this process with formation of a single d_π–d_π–p_π interaction system.

3. Analysis of the Stretching Vibration Frequencies of the Si–H Bonds in Substituted Silanes

As already mentioned frequently in this review, in a spectroscopic study of the effect of $d\pi$–$p\pi$ interaction it is particularly important to select a series of compounds such that their molecular fragments are sensitive to the electronic effects of substituents; on the other hand, it is desirable that the spectroscopic parameters should depend only on electronic effects. The vibrational spectra of substituted silanes are particularly interesting from this point of view. The vibration of the Si–H bond involves almost exclusively changes in the Si–H coordinate. The mass of the substituents R in the silanes R_3SiH does not affect the Si–H stretching vibration frequency (ν_{Si-H}) and there is no mechanical interaction between the Si–H bond and the vibrations of organic substituents[210]. Thus the vibration of the Si–H bond is highly characteristic. Moreover examination of the literature data for the vibrational spectra of substituted silanes[211–214] reveals a significant dependence of ν_{Si-H} on the nature of the substituent. On the basis of the foregoing, substituents influence ν_{Si-H} only via their electronic effects. All these factors make silanes with organic substituents ideal objects for the investigation of the effect of substituents (in particular the effect of $d\pi$–$p\pi$ interaction) on the stretching frequency of Si–H bonds. However, for a long time little attention was paid to this problem in the literature.

In the first studies dealing with the effect of substituents on the ν_{Si-H} frequency in vibrational spectra, the frequency change was attributed exclusively to the inductive effect of substituents[211–214]. Thus Thompson[212] obtained the equation $\nu_{Si-H} = 17.5\,\Sigma\sigma^* + 2106$ relating the ν_{Si-H} frequency to the sum of Taft's inductive constants σ^* for the three substituents in the silanes R_3SiH. The substituents R were both alkyl groups and groups potentially capable of $d\pi$–$p\pi$ interaction with the silicon atom (for example, halogens and the phenyl group). The accumulated experimental data on the vibrational spectra of silanes revealed that inductive hypotheses alone are clearly insufficient to describe the variation of the ν_{Si-H} frequency as the substituents are varied. It was shown that the analysis of the ν_{Si-H} frequency in the silanes $R_{3-n}X_nSiH$, where X is a substituent capable of $d\pi$–$p\pi$ interaction with the silicon atom, yields information about the double-bond character of the Si–X fragment. It was established in this way that the amount of double-bond character in the linkage between the vinyl or phenyl groups and the silicon atom is considerable even in the presence of three such groups in the molecule. Another situation is observed in alkoxysilanes. The ν_{Si-H} frequency in monoalkoxysilanes differs little from the frequency in trialkylsilanes owing to the considerable contribution of $d\pi$–$p\pi$ interaction between the oxygen and silicon atoms. In di- and tri-alkoxysilanes the ν_{Si-H} frequency is higher mainly because of the inductive effect of the alkoxy-groups. The contribution of each alkoxy-group to the $d\pi$–$p\pi$ interaction with the silicon atom becomes less than in monoalkoxysilanes[198]. Attridge[215] observed that, for each series of silanes $R_{3-n}X_nSiH$ [R = alkyl; X = $N(CH_3)_2$, C_6H_5Cl, or OCH_3], the plot of $\Sigma\sigma^*$ against ν_{Si-H} is linear.

The presence of several straight line correlations was explained by the transfer of electron density from X to the silicon d orbitals. The anomalously high ν_{Si-H} frequencies in alkoxychlorosilanes, which could not be accounted for on the basis of earlier correlations[211–213], were interpreted as due to a decrease of $d\pi$–$p\pi$ electron donation caused by the competition between substituents for the silicon d orbitals. However, the series of substituents in terms of their capacities for $d\pi$–$p\pi$ interaction proposed by Attridge does not agree satisfactorily with the current hypotheses in this field.

These studies were developed further[58,111,208,216–222]. It was shown[216,217] that, for trisubstituted silanes R_3SiH with substituents R incapable of $d\pi$–$p\pi$ interaction with the silicon atoms and exerting only an inductive effect on the ν_{Si-H} frequency, we have $\nu_{Si-H} = 23.1\,\Sigma\sigma^* + 2112$. This equation relates the ν_{Si-H} frequency to the sum of Taft's inductive constants $\Sigma\sigma^*$ for three substituents. It was used to calculate the frequencies ν_{calc} in the silanes $R_{3-n}X_nSiH$ with substituents X capable of $d\pi$–$p\pi$ interaction with the silicon atom. It was found that the ν_{calc} are higher than the experimental frequencies ν_{exp}. Under the influence of the effect of $d\pi$–$p\pi$ interaction operating in a direction opposed to that of the I effect of X (this can be conventionally treated as a decrease of the inductive effect of X), the force constant and the stretching vibration frequencies of the Si–H bond decrease. The differences $\Delta\nu = \nu_{calc} - \nu_{exp}$ are a result of the $d\pi$–$p\pi$ interaction in the Si–X bonds. The values of $\Delta\nu$ in several series of compounds have been analysed: R_2XSiH, RX_2SiH, and X_3SiH, where X = F, Cl, Br, I, OAlk, SAlk, SeAlk, $NAlk_2$, PH_2, $CH{=}CH_2$, $C{\equiv}CH$, C_6H_5, C_4H_3O, C_4H_3S, OC_6H_5, SC_6H_5, $OCOCH_3$, $C{\equiv}N$, $NH(C_6H_5)$, NCS, and N_3. Next it was established[218] that the following equations are valid for di- and mono-substituted silanes R_2SiH_2 and $RSiH_3$ with substituents R incapable of $d\pi$–$p\pi$ interaction: $\nu_{Si-H} = 23.1\,\Sigma\sigma^* + 2121$ and $\nu_{Si-H} = 23.1\,\Sigma\sigma^* + 2132$, relating the ν_{Si-H} frequency to the sum of the inductive constants σ^* for the three substituents. The ν_{exp} frequencies in the silanes $RXSiH_2$, X_2SiH_2, and $XSiH_3$ with substituents X capable of $d\pi$–$p\pi$ interaction with the silicon atom differ from the ν_{calc} calculated from these equations. The differences $\Delta\nu = \nu_{calc} - \nu_{exp}$ for di- and mono-substituted

silanes agree with the corresponding $\Delta\nu$ obtained from the spectra of trisubstituted silanes[216,217]. Analysis of the values of $\Delta\nu$ in halogenosilanes[219], in compounds with silicon–Group VI element bonds[111], and silanes with Si–N and Si–P bonds[220] showed that the capacity for $d\pi$–$p\pi$ interaction with the silicon atom decreases within the Groups of the Periodic System from above downwards. It was established[203] that in silanes having only one substituent entering into the $d\pi$–$p\pi$ conjugation with the silicon atom, the values of $\Delta\nu$ are related to the constants $\sigma_n - \sigma'$, characterising the conjugation of these substituents with the phenyl ring, by the linear equation $\Delta\nu = -65.6(\sigma_n - \sigma') + 3$. These data and also the results of Egorochkin et al.[62] are evidence of a considerable analogy between the effects of conjugation with the silicon atom, the phenyl ring, and the vinyl group. In compounds of the type C_6H_5–X–SiH_3, where X = O, S, or NH, there is competition between two conjugation effects: p,π and $d\pi$–$p\pi$.[111,220] Since the dominant effect is that of p,π conjugation, the values of $\Delta\nu$ for these compounds are appreciably lower than the $\Delta\nu$ in silanes of the type Alk–X–SiH_3, where X = O, S, or NH.

It was also shown that the points corresponding to the compounds Alk_2NSiH_3 deviate markedly from the linear equation $\Delta\nu = -65.6(\sigma_n - \sigma') + 3$ towards lower values of $\Delta\nu$.[220] This is caused by the effect of p,σ conjugation in $Alk_2\overset{\curvearrowright}{N}-Si\begin{smallmatrix}H\\H\end{smallmatrix}$, which leads to a decrease of $\Delta\nu$. The effect of p,σ conjugation in this compound is associated with the unique properties of the Alk_2N group: a low-I effect and a high capacity for conjugation. The effect of p,σ conjugation is observed also in the compounds $(Alk_2N)_2ClSiH$ and $(Alk_2N)Cl_2SiH$, as shown by the deviation of the experimental $\Delta\nu$ from the values calculated assuming an additive contribution of the dialkylamino-groups and chlorine atoms to $\Delta\nu$.[220] A similar phenomenon has been observed also in chloromethoxysilanes[217]. Likewise it was established that the degree of $d\pi$–$p\pi$ interaction in the Si–N bond increases with the increasing $-I$ effect of the substituent having a nitrogen atom in the α-position relative to the silicon atom[220]. In agreement with theoretical postulates[4–8], this is caused by the increase of the capacity of the silicon atom for $d\pi$–$p\pi$ interaction when its positive charge increases. The latter relation can be clearly seen also in the study of the $d\pi$–$p\pi$ interaction in silanes having several substituents capable of such interaction[221]. A positive charge may be induced on the silicon atom by electronegative substituents. It would appear that the introduction of a second substituent X should stabilise the $d\pi$–$p\pi$ linkage between the silicon atom and the first substituent X. However, by virtue of its $-I$ effect, the second substituent X decreases the σ electron density at the silicon atom, but, being involved simultaneously in the $d\pi$–$p\pi$ conjugation, it increases the π electron density at the central atom. Thus, depending on the relative contributions of the electron-donating and electron-accepting properties of the substituents, their effect on the $d\pi$–$p\pi$ conjugation in the silane molecule can be extremely varied. This problem was investigated by Egorochkin and Vyazankin[221]. The values of $\Delta\nu$ in two series of compounds were determined: $(C_2H_5)_2XSiH$ and $(C_2H_5)X_2SiH$, where X = C_6H_5, CH_2=CH, Br, Cl, F, CH_3S, or CH_3O. The compounds $(C_2H_5)X_2SiH$ may be regarded as products of the substitution of the ethyl group in $(C_2H_5)_2XSiH$ by X. The effective charge of the silicon atom in $(C_2H_5)_2XSiH$ depends both on the $-I$ effect of X and on the electronic effect of the $d\pi$–$p\pi$ conjugation in the Si–X bond, which is opposed to it. The strength of the second $d\pi$–$p\pi$ linkage between Si and X and hence the overall effect of the $d\pi$–$p\pi$ interaction in molecules of the type $(C_2H_5)X_2SiH$ are determined by the magnitude and sign of this effective charge. These studies explain the experimental finding that the series of relative capacities for $d\pi$–$p\pi$ interaction in the silanes R_2XSiH (AlkO > F > $CH_3S \simeq$ Cl > Br > CH_2=CH > C_6H_5), RX_2SiH (Br > Cl > F > CH_3S > C_6H_5 > CH_2=CH > AlkO), and X_3SiH (Br > Cl > CH_3S > C_6H_5 > CH_2=CH > F > AlkO) are not the same. The extent of $d\pi$–$p\pi$ interaction in the molecule depends on the inductive and mesomeric effects of the substituents which alter the charge of the silicon atom. Therefore in silanes with several substituents the extent of the electron-donating properties of each substituent is determined significantly by the number and nature of its partners in $d\pi$–$p\pi$ interaction.

The equation $\nu_{Si-H} = 23.1\,\Sigma\sigma^* + 2112$, relating the ν_{Si-H} frequency to the sum of Taft's inductive constants σ^* of substituents incapable of $d\pi$–$p\pi$ conjugation was used to determine the values of σ^* for the groups C_2H_5Te (+0.4),[153] $(CH_3)_3Si$ (−0.9), $(C_2H_5)_3Si$ (−1.1), and $(C_2H_5)_3Ge$ (−0.8).[222] The higher electronegativity of germanium compared with silicon in the absence of the effects of $d\pi$–$p\pi$ conjugation involving these elements was thereby confirmed.

By taking into account rigorously the inductive effects of the substituents on the infrared spectra of substituted silanes and on the ^1H NMR spectra of alkylsilanes and alkylgermanes, it was possible to establish the effect of σ,σ conjugation in methyl derivatives of silicon and germanium[58].

The data described show that considerable advances have been achieved in the study of the effect of $d\pi$–$p\pi$ interaction in organic derivatives of Group IVB elements. Summarising the principal results of studies in this field, the following conclusions may be formulated. In compounds containing one M–X bond (M = Si, Ge, or Sn; X = element or Groups V–VII) or a group M–X–M (X = O, S, or Se), the capacity for $d\pi$–$p\pi$ interaction between the atoms M and X in a given Group of the Periodic System decreases with the atomic numbers of the elements M and X. The decrease of the capacities for $d\pi$–$p\pi$ interaction between the atoms M and X in the given Group on passing from a substituent X in the Second Period to one in the Third Period is greater the lower the number of the group to which X belongs. The mechanism of the $d\pi$–$p\pi$ interaction between the atoms Si and X is formally similar to the effects of the conjugation of the substituent X with an aromatic ring or the vinyl group. In compounds containing one Si–H bond, the relative capacity for the formation of $d\pi$–$p\pi$ linkages with the silicon atom is correlated with their Hammet resonance constants. In silane derivatives containing two or three similar substituents X capable of $d\pi$–$p\pi$ interaction, the extent of the latter is determined by the effective charge of the silicon atom, which depends on the inductive and mesomeric effects of X.

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Reactivity of Organic Compounds in an Excited Electronic State

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The review deals with the reactivities of complex organic compounds in an excited state; the characteristics of the electronic structure of the molecules, which play a fundamental rule in photochemical reactions, are discussed.
The bibliography includes 79 references.

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I. INTRODUCTION

On absorption of a light quantum, the molecule passes to an excited singlet state (a direct transition to a triplet level is usually forbidden). The energy of this state is determined both by the magnitude of the absorbed quantum and by the position of the energy levels in the molecule. In the condensed phase, a series of relaxation processes takes place very rapidly (over a period $\leq 10^{-12}$–10^{-13} s). Among these, the most important is spontaneous transition from the highest to the lowest excited levels and the establishment of the equilibrium configuration of the nuclei for the given state (the excess vibrational energy is then transmitted to the medium).

At the lowest excited level, the molecule can persist for a longer period (10^{-9}–10^{-7} s at the singlet level and 10^{-6}–10^{-1} s at the triplet level). The transition to the ground state now involves both the possibility of non-radiative deactivation of the molecule and the emission of excess energy as luminescence.

Photochemical reactions can in general occur at any instant after the absorption of light by the molecule and therefore can compete with both rapid and slow deactivation processes.

As an example, we shall consider the homolytic photochemical decomposition of a molecule. On absorption of light, the molecule can easily pass to an antibonding excited level and its dissociation takes place over a period of about 10^{-12}–10^{-13} s. If there is sufficient time for the molecule to pass to a lower level, which may prove stable, its decomposition can be caused either by the fact that its vibrational energy exceeds the dissociation energy of any one bond or by pre-dissociation. Dissociation processes are also possible during the return to the ground level. In the latter case the molecule in the ground state has a much higher vibrational energy than the thermal energy of the molecules in the surrounding medium. For such a "hot" molecule to undergo a chemical transformation, the process must be very rapid, since the excess vibrational energy is dissipated over a period of about 10^{-12} s.

Naturally this approximate scheme does not exhaust all possible situations, since triplets states, $n\pi^*$ states, and charge-transfer states may play a major role in the chemical reactions of the excited molecule. Moreover, different levels can exert a mutual influence on one another, becoming mixed, which also precludes a rigorous classification.

Fortunately, in many photochemical reactions (this applies also to the majority of the reactions considered in the review) the molecules involved in them pass to the lowest excited levels which have minima on their potential surfaces, greatly facilitating the consideration of the process mechanism. We can assume that, owing to their fairly long lifetime, such excited molecules are in a thermal quasiequilibrium with the surrounding medium and the mode and rates of their reactions are determined by the energy barrier on the reaction pathway. This approach is potentially similar to that employed in the discussion of reactivities of molecules in the ground state. Therefore, in order to estimate the reactivities of excited molecules, one should consider the same parameters—the rate constant and the activation energy—as for dark processes. However, in photochemical reactions this is not a simple task, since usually it is possible to measure only the quantum yields of the processes. For a unimolecular reaction, the quantum yield $\varphi = k\tau$ and for a bimolecular process $\varphi = k\tau c$, where k is the reaction rate constant, τ the lifetime of the excited molecules of the absorbing species, and c the concentration of the second component. However, τ can be by no means always determined.

The second factor which hinders the study of the reactivities of various excited molecules is the absence of activation energy in many photochemical reactions. In particular, this casts doubt on the possibility of employing the transition state theory for the interpretation of the results, since the fundamental postulate of the theory concerning the equilibrium between the activated complex and the initial molecules breaks down. It may be that the excited molecule in such reactions should be regarded as the species which has already risen above the reaction "hump". Then the rate of the process will be determined solely by the probability factors which enter into the pre-exponential factor.

It must be emphasised that the reactivity of an excited molecule is not caused solely by the fact that it has greater energy available than the surrounding molecules. The electronic structure of the excited molecule differs from its structure in the ground state. Therefore the equilibrium positions of the nuclei must be different. We are dealing essentially with a new molecule having new properties. In other words, the excited molecule can react in a completely different manner than the molecule in the ground state.

In the present review an attempt has been made to describe the current approaches to the study of the reactivity of excited organic molecules. For this purpose, we have chosen classes of photochemical reactions which

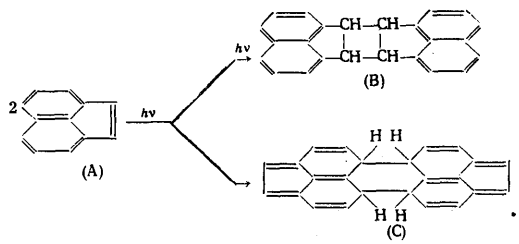
have been most thoroughly investigated in this respect. There are good reviews of many of these reactions and some are described in monographs [1-10]. Nevertheless it is desirable to consider these data in one review from a single standpoint.

II. PHOTOCHEMICAL FORMATION AND OPENING OF RINGS

1. Elementary Treatment

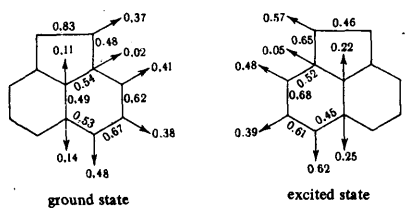
When an attempt is made to explain why the action of light on a molecule causes preferential dissociation or formation of a particular bond, the first idea that comes to mind is to examine how the reactivity indices change when the molecule passes to an excited state. The success of this simple approach may be illustrated using as an example the photocyclisation reactions of certain aromatic hydrocarbons.

This was first done by Crawford and Coulson [11] in a study of the photodimerisation of acenaphthylene [12], which might proceed in two different ways:



(I)

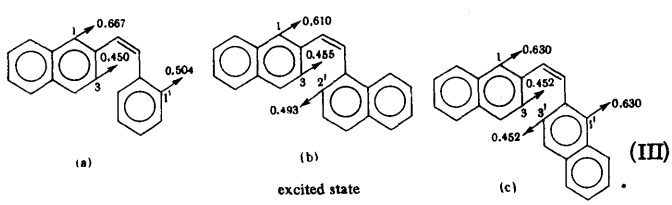
In fact the photochemical reaction leads to the formation of compound (B) only. In order to account for this finding, Crawford and Coulson compared the free valence indices and the bond orders of the molecule (A) in the ground and first excited states calculated by the simple Hückel molecular orbital method:



(II)

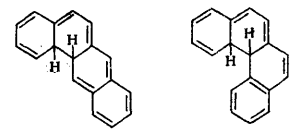
Scheme (II) shows that, on excitation of the molecule (A), the greatest decrease of bond order and increase of the free valence index of the atoms occurs in the ethylenic bond. This in fact leads to preferential dimerisation at this bond. The absence of the dimer of type (C) can probably be accounted for by the fact that this involves the formation of the energetically less favourable quinonoid structure, although the free valence indices in the para-α-positions of the naphthalene ring of substance (A) increase appreciably in the excited state.

The photocyclisation reactions of a number of naphthyl-substituted ethylenes have been interpreted similarly [13]:



(III)

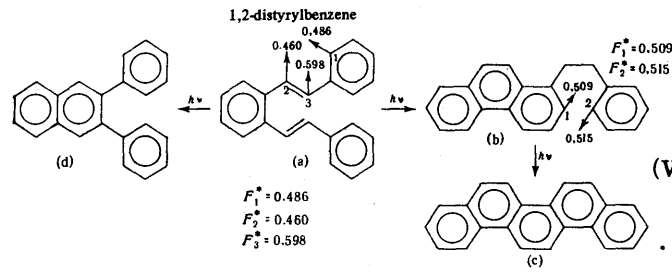
The cyclisation reaction can take place at both the α- and β-positions of the naphthalene ring. For example, with compound (a) one must consider the possibility of forming the following two isomers:



(IV)

The free valence indices for the excited molecules shown in scheme (III) suggest that the cyclisation should involve the formation of a 1,1'-bond (the sum of the F_1^* and F_8^* indices is a maximum). Indeed, experiment showed that cyclisation takes place only at the α-positions, although this mode of reaction is sterically more hindered.

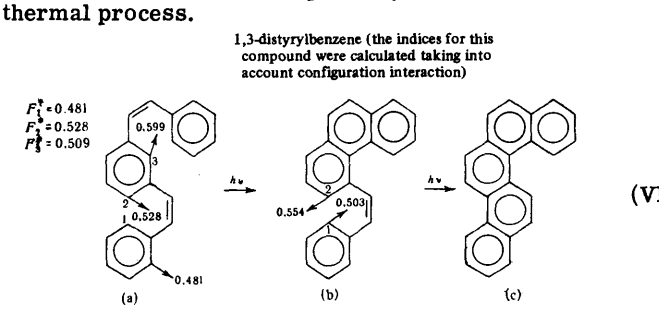
The photocyclisation reactions of distyrylbenzenes (V)-(VII) have been interpreted similarly [14]:



(V)

As in the preceding case, the cyclisation of distyrylbenzene should involve ring closure at the sites of the maximum values of $F_8^* + F_r^*$. For 1,3- and 1,4-distyrylbenzenes or their cyclisation products, this rule indeed holds. However, the reaction of 1,2-distyrylbenzene follows the (a) → (b) → (c) pathway instead of (a) → (d), probably owing to the steric hindrance in the formation of (d).

The ambiguity of the treatment of alternant hydrocarbons based on a comparison of the reactivity indices in the excited state arises because the positions in the molecule which are the most reactive in the excited state (for example have the highest free valence) are also the most reactive in the ground state. Therefore, in the absence of additional data, it is difficult to rule out the possibility that the reaction involves vibrationally excited molecules in the ground electronic level, which are formed when the electronic excitation energy is degraded. The reaction of such "hot" molecules is probably similar to the thermal process.



(VI)

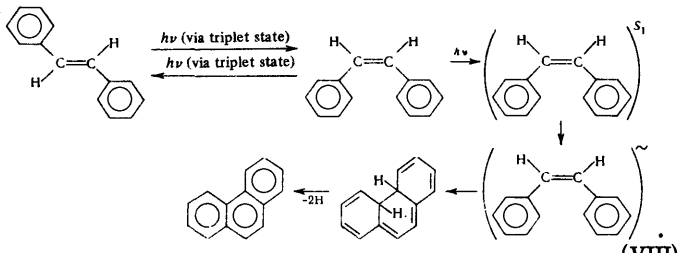
(VII)

According to Gusten and Klasing[15], the cyclisation of stilbene to 4a,4b-dihydrophenanthrene takes place in the same way (in the presence of oxidants, oxygen, air, iodine, etc., the reaction proceeds as far as the formation of phenanthrene). In a study of the photochemical cyclisation of various *m*- and *p*-substituted stilbenes, Gusten and Klasing found that for *m*-substituted stilbenes there is a satisfactory linear correlation between the sum of electron densities in the ground state at the *o*-carbon atoms involved in the new bond and the quantum yield of the reaction. For the excited electronic state of *m*-substituted stilbenes and also for the ground and excited states of *p*-substituted stilbenes, there is no correlation whatever between the electron densities and the quantum yield of the cyclisation reaction. Gusten and Klasing[15] explain this finding by postulating that the cyclisation takes place in a vibrational excited state of the molecule for stilbene and its derivatives. The absence of an effect by *p*-substituents on the rate of reaction was explained by the fact that these substituents are in the *m*-position relative to the reacting carbon atoms and therefore have little influence on the electron densities at these atoms.

On the other hand, *p*-substituents cause a significant shift of the absorption band maximum of stilbene towards longer wavelengths. There is a linear relation between the frequency of the absorption maximum and the quantum yield of the cyclisation reactions of the *p*-substituted derivatives. The authors believe that the higher the energy of the excited electronic level from which the molecule passes to the ground level, the greater its store of vibrational energy and the faster its cyclisation reaction.

A number of facts[16] indicate that the photochemical cyclisation of stilbene involves a stage in which *cis*-stilbene molecules in a singlet excited electronic state are formed. For example, on excitation to the triplet level via a triplet–triplet energy transfer, cyclisation does not occur[17,18]. Possibly the vibrational energy of the "hot" molecule formed on transfer from the triplet state is insufficient for effective cyclisation.

Thus the following scheme may be formulated for the photochemical reaction for stilbene and its derivatives.

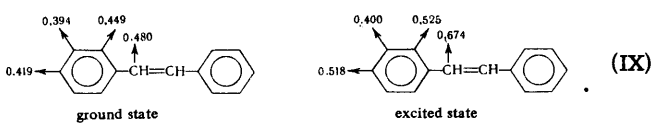


(VIII)

The symbol ~ denotes vibrational excitation.

The fact that, on pyrolysis of *cis*-stilbene, the product is also phenanthrene in a high yield[19] may be regarded as definite confirmation of the involvement of vibrationally excited stilbene molecules in the cyclisation reaction.

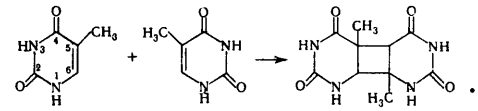
It is interesting to note that, regardless of whether electronically excited or vibrationally excited stilbene molecules are involved in the reaction, the dimerisation process which yields tetraphenylcyclobutane should compete with cyclisation to phenanthrene. The free valence indices in the ground and excited states show that the first reaction should be faster:



(IX)

Indeed, the dimerisation reaction predominates in concentrated solutions.

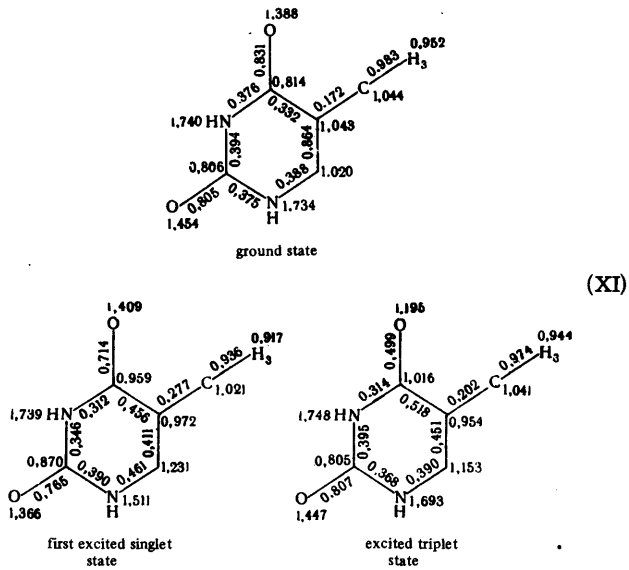
Using these simple concepts, Pullman and coworkers[20] examined the reactivities of pyrimidine rings in their photochemical dimerisation. This reaction probably plays an important role in the photochemistry of nucleic acids and in particular of DNA (nucleic acids contain pyrimidine rings as structural units). Pyrimidines are dimerised via the interaction of 5-C and 6-C atoms of two pyrimidine rings with formation of a cyclobutane ring. For example, thymine cyclises according to the mechanism:



(X)

Comparison of the electron densities and bond orders in the ground and excited states of thymine (XI) makes it clear why cyclisation takes place at the carbon atoms in the 5- and 6-positions of the thymine ring[21]†:

electron densities and bond orders of thymine



(XI)

It is noteworthy that the difference between the reactivity indices of the triplet and singlet excited states is insufficient to yield a definite conclusion about the multiplicity of the molecules involved in the reaction.

Thus simple comparison of the reactivity indices makes it possible in certain cases to obtain a definite idea about the process mechanism. However, in many instances the result is ambiguous.

A more general approach, based on the rules of conservation of orbital symmetry formulated by Woodward and Hoffmann, is possible for the interpretation of the cyclisation and cyclodecomposition reactions of symmetrical molecules.

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†The calculation was carried out by the self-consistent field method taking into account the interaction of singly excited states.

2. Reactions with Conservation of Orbital Symmetry

It was mentioned above that one of the important problems frequently encountered in the study of reactivities in photochemical reactions is whether electronically excited molecules or hot molecules in the ground electronic level are involved in such reactions. We have seen that usually an answer to this question cannot be simply obtained. However, there are many reactions, the so called concerted reactions, for which it is possible to predict, on the basis of considerations related to orbital symmetry, whether the reaction proceeds via an excited electronic state or a ground electronic level. These considerations were first put forward by Woodward and Hoffmann [22,23] and then in a more rigorous form by Longuet-Higgins and Abrahamson [24]. They are based on the symmetry of the molecular orbitals of the starting materials and reaction products and reduce to the requirement that the symmetry be retained in the course of the reaction. This can be made clear by examples discussed in the literature [22-24]—the cyclodimerisation of ethylene to cyclobutane and the cyclisation of butadiene to cyclobutene.

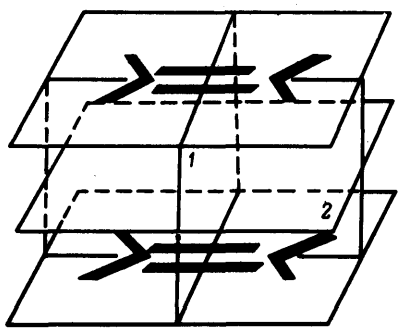


Figure 1. Mutual approach of two parallel ethylene molecules [3].

In order to form two σ bonds of cyclobutane from two π bonds of ethylene in its cyclodimerisation, it is necessary that the ethylene molecules should approach one another until the $p\pi$ electron clouds of the carbon atoms overlap. We imagine that during such approach the molecules are arranged parallel to one another and consider the symmetry of the system as a whole relative to the two planes *1* and *2* (Fig. 1).

If the ethylene molecules are in the ground state (the π bonding molecular orbital), two cases are possible: either the molecules approach one another so that components of the π-electron clouds of the same sign overlap or the approach is such that components of the π-electron clouds of opposite sign overlap (Fig. 2).

In the first case a bonding interaction takes place between the ethylene molecules—a combination of two π-electron functions of ethylene symmetrical relative to both planes *1* and *2* (such combination will be referred to as *SS*). In the second case a weak repulsion arises between the approaching molecules and the electronic combination is symmetrical relative to plane *1* and antisymmetric relative to plane *2* (*SA*). If the π-electron function of one ethylene molecule is denoted by π_1 and that of the other by π_2, the first combination may be characterised by the function $\pi_1 + \pi_2$ and the second by $\pi_1 - \pi_2$.

If we now consider what happens when two ethylene molecules in an excited electronic state (π_1^* and π_2^*) approach one another, examination of Fig. 2 readily shows that again there is a possibility of a bonding combination $\pi_1^* + \pi_2^*$ characterised by *AS* symmetry and an antibonding combination $\pi_1^* - \pi_2^*$ with *AA* symmetry.

The symmetry of the different states of cyclobutane can be treated similarly. The difference is that the carbon atoms in the cyclobutane molecule are linked by σ bonds. Here the bonding states are evidently $\sigma_1 + \sigma_2$ and $\sigma_1 - \sigma_2$ with *SS* and *AS* symmetries. The antibonding states are $\sigma_1^* + \sigma_2^*$ and $\sigma_1^* - \sigma_2^*$ with *AS* and *AA* symmetries.

We now draw lines connecting the states of cyclobutane and of the system of two ethylene molecules with the same symmetry, as in Fig. 2, and obtain a correlation diagram similar to those proposed at one time by Hund and Mulliken [25] to elucidate the relations between the molecular

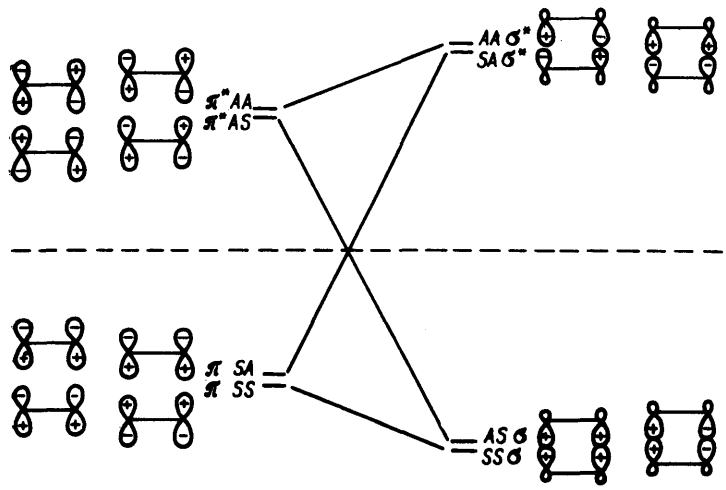


Figure 2. Correlation diagram for the formation of cyclobutane from two ethylene molecules [8].

orbitals of diatomic molecules and the atomic orbitals of their constituent atoms.

By considering the two approaching ethylene molecules as a single formation, we distribute four π electrons among its electronic orbitals in accordance with the Pauli principle. Evidently the lowest state of this system is the symmetrical (S) state $(SS)^2(SA)^2$. Similarly the lowest electronic state of isobutane should be $(SS)^2(AS)^2$ with S symmetry in which four σ electrons are located. The lowest level of a combination of two ethylene molecules should be correlated with the doubly excited cyclobutane state $(SS)^2(SA)^2$ and the lowest level of cyclobutane should be correlated with the doubly excited state $(SS)^2(AS)^2$ of the system of two ethylene molecules. However, since these states have the same symmetry, the non-crossing rule, according to which levels of the same symmetry do not intersect owing to electron repulsion, applies to them.

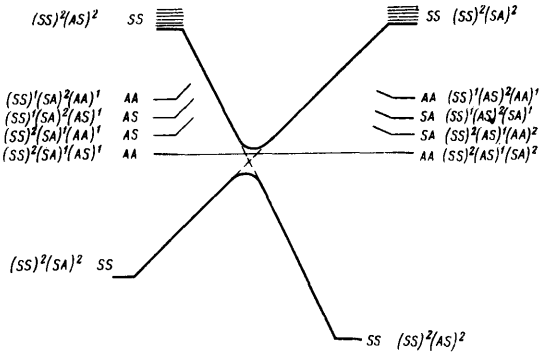


Figure 3. Diagram of electronic states for the formation of cyclobutane from two ethylene molecules. The symmetry of the states is defined by the relations[8]

$$S\times S\to S\leftarrow A\times A,$$
$$S\times A\to A\leftarrow A\times S.$$

As a result the diagram assumes the form shown in Fig. 3, where the ground level of the two ethylene molecules is seen to be correlated with the ground level of cyclobutane. The highest excited levels are also correlated with one another. It is evident from the diagram that, for the conversion of the two approaching ethylene molecules in the ground state into cyclobutane with retention of symmetry, the system must overcome an energy barrier. Therefore such a process is unlikely. In a situation where two π electrons of the ethylene molecules are promoted to excited orbitals—the state in which the conversion into cyclobutane can occur without an activation energy—is also improbable. However, the transition of one π electron of ethylene to a lower excited state yields the symmetrical function $(SS)^2(SA)^1(AS)^1$, which is correlated with the lowest excited state $(SS)^2(AS)^1(SA)^1$ of the cyclobutane molecule, corresponding to the excitation of one π electron. In other words such a transformation is allowed by symmetry and does not require an activation energy, as can be seen from the diagram. At the same time this state can be readily achieved when ethylene is subjected to the action of light [for many compounds, such an excited dimer (excimer) can be actually detected spectroscopically]. From this it follows that the dimerisation of ethylene should have a photochemical and not a thermal mechanism‡.

The correlation diagrams also make it possible to discover the relations governing the reversible cyclobutane $\rightleftharpoons$ butadiene reaction. Such reactions, which involve the formation of a σ bond from two π electrons without a change in the number of carbon atoms in the molecule, are called electrocyclic. Cyclobutene can be converted into butadiene via two pathways (Fig. 4): the dissociation of the σ bond between the C_1 and C_4 atoms in such a way that the methylene groups $H_3 \diagdown C_1 \diagup H_1$ and $C_4 \diagup H_4 \diagdown H_2$ rotate either in the same direction (Fig. 4*a*) or in the opposite directions (Fig. 4*b*). The first pathway is called conrotatory and the second disrotatory. Evidently, in conrotatory ring opening, the system retains a two-fold symmetry axis in the course of the entire reaction. In disrotatory ring opening, the system retains a plane of symmetry. This is also true of the converse reaction—the cyclisation of butadiene.

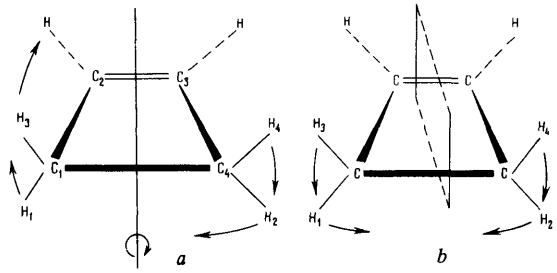


Figure 4. Symmetry of the conrotatory (*a*) and disrotatory (*b*) transformations[26].

Naturally if the polyene or the cyclic form do not contain substituents, the conrotatory and disrotatory transformations cannot be distinguished experimentally. However, if one hydrogen atom at each of the extreme carbon atoms is replaced by a substituent (as has been done in Figs. 5*a* and 5*b*), each type of rotation gives rise to different stereoisomers.

Using the same principle of the conservation of orbital symmetry, it is possible to construct correlation diagrams for these reactions[8], as was done for ethylene. The diagrams show that the conrotatory cyclobutene $\rightleftharpoons$ $\rightleftharpoons$ butadiene interconversion should have a thermal mechanism and the disrotatory interconversion should take place as a photochemical process involving the first excited states.

The same conclusions were reached in the first study by Woodward and Hoffmann[22] with the aid of simpler considerations based on the hypothesis that the nature of the electrocyclic reaction is determined by the symmetry of the highest occupied orbital of the acyclic product. For the ground state of butadiene, the ψ_2 orbital is of this kind

‡In this case thermal processes are understood as processes in which vibrationally excited molecules, formed on transition of the molecule from an excited electronic to the ground state, are involved.

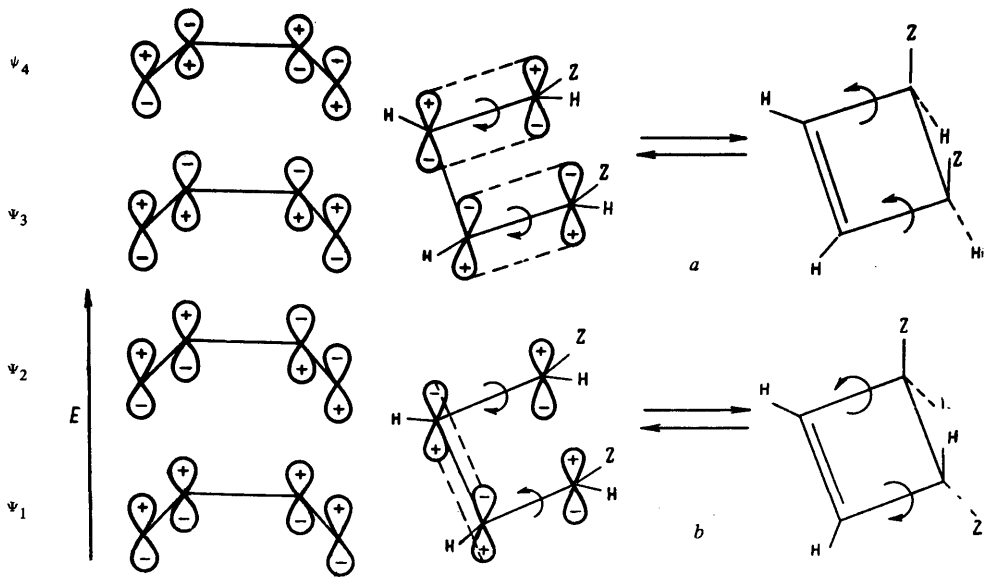
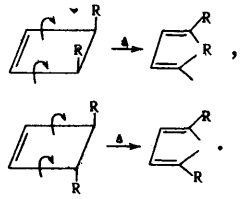


Figure 5. Schematic illustration of the butadiene ⇌ cyclobutane electrocyclic reaction[26].

(Fig. 5). Fig. 5*a* shows that the conversion of the π bond into a bonding σ linkage in the ring as well as the reverse process require a conrotatory transformation. For the photochemical reaction, where the highest occupied butadiene level is ψ_3 (Fig. 5*b*), cyclisation and ring opening are disrotatory processes. Although these considerations do in fact give rise to certain doubts[24], nevertheless they constitute a simple and convenient procedure and lead to the same conclusions as the correlation diagrams. For example, examination of the highest occupied orbitals leads to the prediction that, for the cyclopropyl cation ⇌ ⇌ allyl cation electrocyclic reaction, the thermal process should be disrotatory and the photochemical process conrotatory[22]. This is also indicated by the correlation diagram[24]. The hexatriene ⇌ cyclohexadiene reaction should also have a thermal mechanism for the disrotatory transformation and a photochemical mechanism for the conrotatory transformation.

Generalising all these results, Woodward and Hoffmann concluded that, for all systems the acyclic components of which contain $4n$ π electrons (n = 0, 1, 2, 3, ...), electrocyclic reactions involve a conrotatory thermal mechanism and a photochemical disrotatory mechanism. For a system with an acyclic component containing $4n + 2$ π electrons, the thermal and photochemical reactions take place with rotations in the opposite sense. This relation in fact constitutes one of the familiar Woodward–Hoffmann rules.

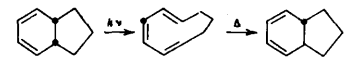
According to the Woodward–Hoffman rules, the thermal opening of the cyclobutene ring with substituents in the 1- and 4-positions leads to the formation of isomers corresponding to the conrotatory process[27–29]:



(XII)

The symbol Δ denotes heating and R = CH_3, $COOCH_3$, CH_2OTs, or Cl.

The sequence of the transformations of the *cis-cis-cis*-cyclonona-1,3,5-triene is very instructive[30,31]:



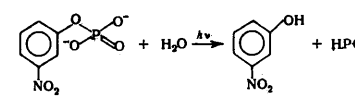
(XIII)

The principle of the retention of orbital symmetry is obeyed by all concerted organic reactions[8]. These include the Diels–Alder reaction, certain rearrangements (the Claisen, Cope, and sigmatropic rearrangements), etc. "Selection rules" have also been formulated for these reactions.

III. PHOTOCHEMICAL SUBSTITUTION REACTIONS OF AROMATIC COMPOUNDS

The scope and disadvantages of the simple molecular orbital method for the interpretation of the chemical behaviour of excited molecules can also be discovered by considering photochemical heterolytic substitution reactions involving aromatic substances.

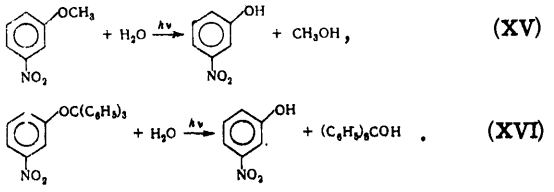
In 1956 Havinga et al.[32] observed that, when aqueous solutions of nitrophenyl phosphate and sulphate esters are illuminated, they are hydrolysed to nitrophenol and the corresponding acid. For example:



(XIV)

At the same time, in the absence of light, these substances are quite stable to water. It is particularly surprising that the photochemical hydrolysis takes place with the maximum quantum yield when the ester group is in the *meta*-position relative to the nitro-group, while the *ortho*- and *para*-derivatives are relatively inactive under the action of light. In the usual dark nucleophilic substitution reactions, the nitro-group should be *ortho*- and

para-directing regardless of whether the reaction of the substituting agent is with a fluorine (sulphur) atom or a ring carbon atom. Experiments with *m*-nitrophenyl phosphate in $H_2{}^{18}O$ showed that at pH ≤ 12 the photochemical hydrolysis involves the reaction of water with the phosphorus atom, while at pH > 12 the reaction is with a ring carbon atom[33]. Nucleophilic substitution takes place also with CH_3NH_2, CH_3OH, etc. the products being *m*-$NO_2C_6H_4NHCH_3$, *m*-$NO_2C_6H_4OCH_3$, etc. Photochemical hydrolysis has likewise been observed with *m*-nitroanisole[32,34], *m*-nitrophenyl trityl ether, and *m*-cyanophenyl trityl ether[35].

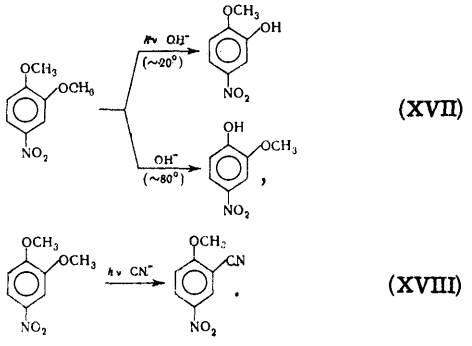


(XV)

(XVI)

The second reaction does not take place in the dark, although the corresponding *p*-isomer readily hydrolyses at 25°C.

The selectivity of the photochemical reaction is shown particularly clearly when identical substituents are present in the ring in both *m*- and *p*-positions (4-nitroveratrol)[36,37]:



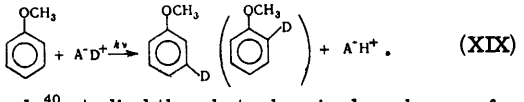
(XVII)

(XVIII)

The reaction of 4-nitroveratrol with methylamine takes place similarly[38].

Photochemical electrophilic substitution reactions include deuterium exchange in aromatic compounds, which was observed independently by de Bie and Havinga[39] and by Kuz'min, Berezin, and coworkers[40].

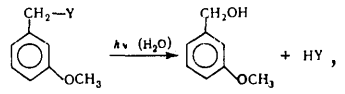
De Bie and Havinga[39] studied light-induced deuterium exchange between anisole and deuteroacetic and trifluorodeuteroacetic acid. It was found that the photochemical substitution of hydrogen in the benzene ring by deuterium takes place only in the *ortho*- and *meta*-positions, the *para*-position is almost inactive:



(XIX)

Kuz'min et al.[40] studied the photochemical exchange of deuterated naphthalene and anthracene with sulphuric acid. The rate of exchange was found to depend on the acidity of the medium, which is characteristic also of dark heterolytic substitution reactions.

Zimmerman and Sandel[41] compared the photochemical hydrolytic reactions of *m*- and *p*-methoxybenzyl acetates, 3,5-dimethoxybenzyl acetate, and *m*-methoxybenzyl chloride in aqueous dioxan solutions. In all cases when the substituted benzyl group was in the *meta*-position, photochemical hydrolysis occurred in a high yield (the presence of two methoxy-groups in the *meta*-position greatly increased the role of hydrolysis compared with homolytic radical decomposition):



(XX)

where Y = OAc or Cl. *Para*-derivatives are scarcely hydrolysed. In this case substitution takes place in the side chain although it is evident that the electron-donating substituent activates the *meta*-position with respect to the photochemical reaction, as in ring substitution.

The results have been interpreted[34,39-43], by comparing the electron densities at different atoms in the molecule. On transition of the molecule from the ground to an excited electronic state, the electron densities change, which may be illustrated for the benzyl cation and anion as examples[41]. Here the $-CH_2^+$ and $-CH_2^-$ groups play the role of electron-accepting and electron-donating substituents (Fig. 6).

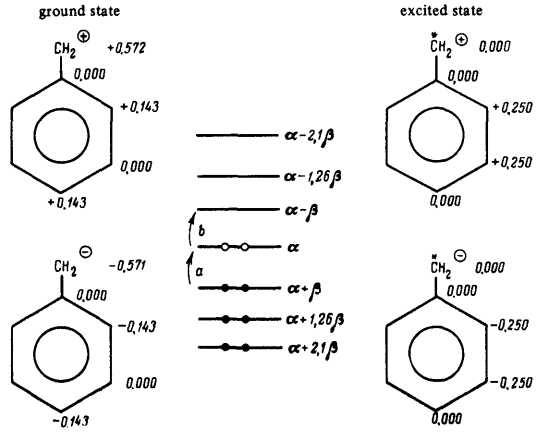
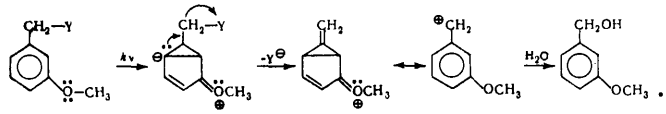


Figure 6. Charge distribution in the benzyl cation and anion[41].

Fig. 6 shows that in the ground state positive and negative charges in the cation and anion are localised in the *ortho*- and *para*-positions, while in the first excited state the charges are localised in the *ortho*- and *meta*-positions. This simple example shows that excitation of the molecule should promote both nucleophilic and electrophilic substitution in the *ortho*- and *meta*-positions. In order to account for reaction (XX) Zimmerman and Sandel[41] suggested that in the excited state of methoxybenzyl derivatives the negative charge is localised at the Y substituent with subsequent dissociation of the molecule to give the methoxybenzyl cation:



(XXI)

Similar charge distributions were obtained also by a more rigorous examination of substituted benzenes using the "molecule in molecule" method[41,43].

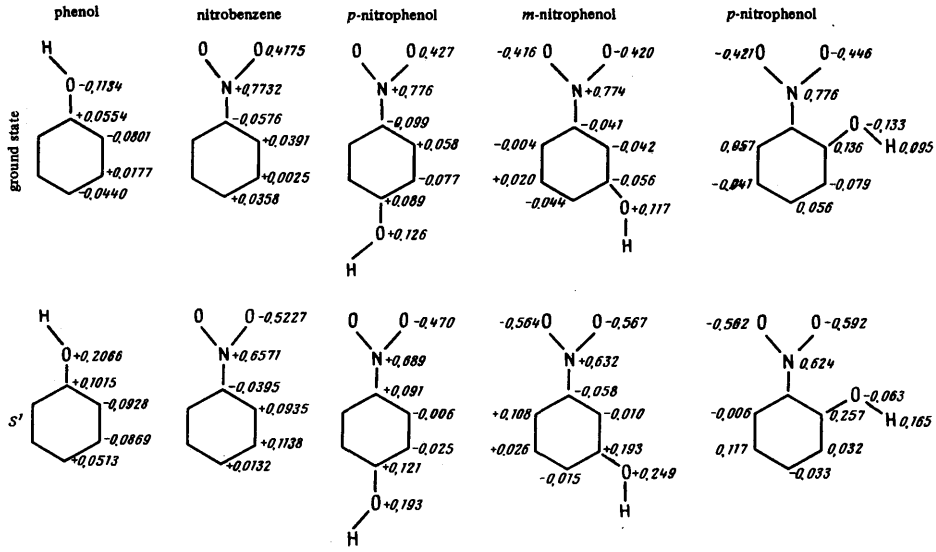


Figure 7. Charge distribution in the ground and lowest excited singlet ($\pi-\pi^*$) states of substituted benzenes[34].

Qualitatively the same redistribution of electron density on excitation of the molecule was obtained by de Bie and Havinga[39] by a calculation using the self-consistent field method for specific phenol (anisole analogue), nitrobenzene, and nitrophenol molecules (Fig. 7).

Thus the localisation of a negative or positive charge at a particular site in the excited molecule probably determines the most favourable site of attack by electrophilic or nucleophilic substituents. A number of data[34,36] clearly show that singlet molecules in the first $\pi-\pi^*$ excited state are involved in the reaction.

The above approach to the estimation of the reactivities of excited molecules in substitution reactions is quite analogous to the approaches employed for the estimation of the reactivities of molecules in the ground state in which a π complex is adopted as a model of the transition state. In this case electron density is a characteristic parameter determining the activation energy for the process. However, according to some data[34,36], the activation energy for photochemical substitution reactions is close to zero. Consequently the employment of reactivity indices such as electron density within the framework of the activated complex concept gives rise to certain doubts[44,45], as already stated. Certain qualitative considerations[34,44] reduce basically to the fact that Coulombic interaction forces arise between atoms at which positive or negative charges are located and between the substituting agents, increasing the reaction cross-section at these particular sites in the molecule. Such concepts are largely intuitive and are not related to a specific reaction model.

One can put forward also another explanation, assuming that the lower experimental activation energies for photochemical reactions are only apparent. Indeed if the substituting agent behaves as a quenching agent, it is quite likely that the quenching process follows the same pathway as the photochemical reaction[34,46]. Then both competing processes (quenching and chemical reaction) should have similar activation energies and an increase of temperature should increase the rates of both processes and should not alter their relative contributions and hence the quantum yield of the reaction. Fig. 8 illustrates a possible mechanism for the substitution reaction.

A clear representation of the intersection in space of the potential surfaces for the reactions was proposed by Kuz'min[47,48]. Like Havinga, he believes that the reaction proceeds non-adiabatically, i.e. in the course of the reaction the electronic excitation energy is degraded. In agreement with the spirit of Nagakura's idea[50], Kuz'min[47-49] believes that in the excited state too the heterolytic substitution reaction is preceded by electron transfer.

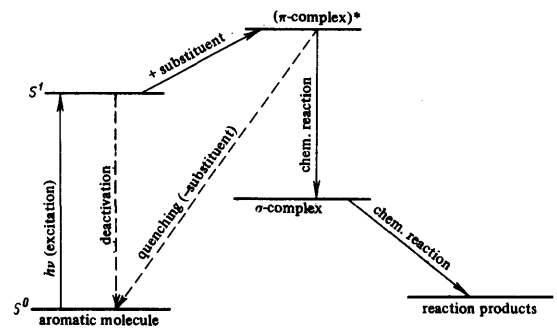
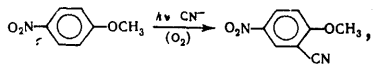


Figure 8. Schematic illustration of the elementary processes in photochemical substitution in the aromatic ring[34].

It is noteworthy that not all photochemical heterocyclic substitution reactions proceed in accordance with the distribution of electron density in the excited molecule. For example, photochemical deuteration of nitrobenzene takes place only in the *para*- and *meta*-positions[39] although the difference between the electron densities in the *meta*- and *ortho*-positions is insignificant (Fig. 7).

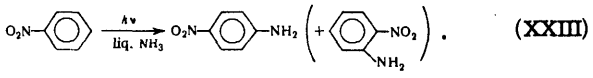
Photochemical cyanation of *p*-nitroanisole takes place in the *o*-position relative to the alkoxy-group [51]:



(XXII)

although according to Fig. 7 this position should be least favourable for nucleophilic substitution.

The position where nitrobenzene is aminated in liquid ammonia [52] is also inconsistent with charges on the ring:



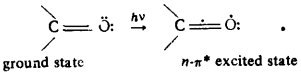
(XXIII)

Havinga and coworkers [36] explain the path of this reaction using the fact that it involves neutral ammonia molecules, and that the electron density near different carbon atoms in the ring should therefore be no longer of decisive importance. In this case a σ complex may be adopted t as a model of the transition state and the localisation energy is best employed as a reactivity index. It is also possible that reaction (XXIII) involves hot molecules (after the conversion of the molecule to the ground state). Then preferential formation of the *para*-substituted derivative is consistent with the distribution of electron density in the molecule.

IV. ABSTRACTION OF HYDROGEN BY KETONES

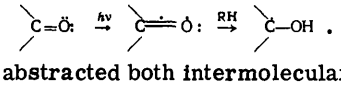
A fairly striking effect of the structure of molecules on their reactivity in the excited state is revealed by a qualitative examination of photochemical reactions of ketones. These constitute one of the most important and one of the most thoroughly investigated branches of organic photochemistry. They are considered in almost all monographs on photochemistry and in many reviews (see, for example, Refs. 1–5, 7, 53). Here we shall confine ourselves to a discussion of the relevant aspects of certain reactions involving the abstraction of hydrogen by the carbonyl group.

The specific features of the photochemical behaviour of ketones are determined by their carbonyl group C=O with an unbonded electron pair at the oxygen atom. When the molecule absorbs a light quantum, one of the electrons of this pair can pass from the non-bonding $2p_y$ orbital to the antibonding π^* orbital ($n-\pi^*$ transition).



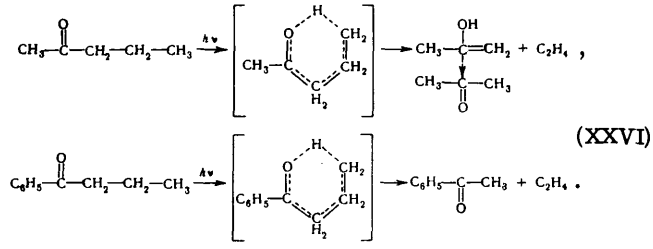
(XXIV)

This transition is forbidden by symmetry and therefore the corresponding absorption band (in the region of 300 nm) is usually weak. The $\pi-\pi^*$ and $n-\sigma^*$ transitions are of course possible, but in aliphatic and many aromatic ketones the $n-\pi^*$ state is the lowest excited electronic state of the molecule. A second important characteristic of many ketones is the comparative ease of the intercombination transition of the excited molecule from the singlet to the triplet state. Since triplet states are usually much longer-lived than singlet states, this increases the likelihood that the molecule will enter into a chemical reaction. When one of the electrons of the pair is transferred from the *n* orbital to the π^* orbital, the interaction between the electrons is weakened and a structure resembling a free radical, with a shift of the negative charge to the carbonyl carbon atom, is generated in the carbonyl group. This is probably why carbonyl compounds in the excited state readily abstract hydrogen with formation of the O–H bond:



(XXV)

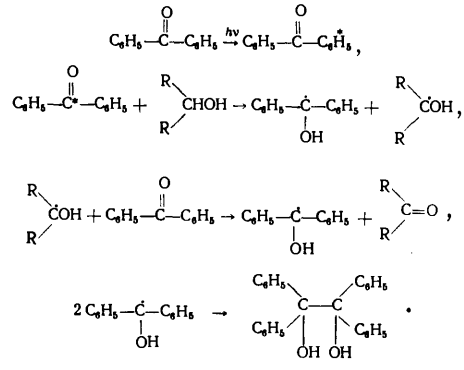
Hydrogen is abstracted both intermolecularly, for example from a solvent molecule, and intramolecularly, i.e. from a hydrogen-containing group of the ketone itself. The latter process takes place particularly readily if the ketone has an aliphatic substituent containing a hydrogen atom in the γ-position relative to the carbonyl group. Probably this proceeds via a stage involving the formation of a six-membered intermediate ring [54–56] and results in the elimination of an unsaturated compound from the ketone:



(XXVI)

Such "biting off of its own tail" by the excited ketone molecule is called Norrish type II split.

The most familiar photochemical reaction involving intermolecular abstraction of hydrogen by a ketone is the formation of benzopinacol from benzophenone, discovered by Ciamician and Silber [57] at the beginning of this century. Pitts and coworkers showed that reactions of this type involve the mechanism [58]



(XXVII)

The maximum possible quantum yield of the disappearance of the ketone in this reaction is 2.

Since the triplet $n-\pi^*$ state of benzophenone, which is the lowest excited electronic state, is involved in this reaction [59–62], it is important to consider to what extent the multiplicity and the nature of the state ($n-\pi^*$ or $\pi-\pi^*$) and the energy of excited molecules determine its capacity to enter into the hydrogen abstraction reaction.

The literature data [62] suggest that the involvement of excited singlet benzophenone molecules in the hydrogen abstraction reaction should be limited primarily by the short lifetime of these molecules [60]. This should be shown particularly clearly in cases where the rate of abstraction of hydrogen (k_r) is low compared with the rate of diffusion. Indeed the quantum yield of the abstraction of hydrogen is given in the simplest case by the expression

$$\varphi = \frac{k_r[B^*][RH]}{k_r[B^*][RH] + 1/\tau[B^*]}, \qquad \text{(XXVIII)}$$

where k_r is the rate constant for the abstraction of hydrogen, [B*] and [RH] are the concentrations of the excited benzophenone and hydrogen donor molecules and τ is the natural lifetime of B*. If it is supposed that the reactivities of excited singlet and triplet ketone molecules in the $n-\pi^*$ state are approximately the same, i.e. $k_r^{S_1} = k_r^T \simeq 10^6$ litre mole^{-1} s^{-1} [63] and $\tau_{S_1} \leq 10^{-9}$ s, then even for the reaction in pure alcohol $\{[RH] \simeq 10$ M$\}$, φ for singlet molecules should be $\leq 10^{-2}$ while for triplet molecules $\varphi \simeq 1$ ($\tau_T \simeq 10^{-5}$ s). One should remember that the quantum yield of the singlet–triplet conversion is close to unity for benzophenone. Hence it is clear that virtually only the triplet benzophenone molecules should be involved in the reaction even if their reactivity is somewhat lower than that of the excited singlet molecules. The report that excited singlet molecules can also participate in hydrogen abstraction [64] was not confirmed [65].

We shall now consider to what extent the $n-\pi^*$ state determines the reactivity of ketones. As already mentioned, owing to the weak interaction between the n and π^* orbitals, the carbonyl group excited to the $n-\pi^*$ state behaves like a free radical. Walling and Gibian [66,67] compared the reactivities of the excited benzophenone molecule and the tetrabutoxy-radical with respect to different hydrogen donors (alcohols, unsaturated hydrocarbons, alkylbenzenes) and showed that the reactivities of the alkoxy-radical and the excited benzophenone molecule vary in parallel for the series of donors investigated, although the sensitivity of the excited molecule to the strength of the C–H bond of the donor is somewhat higher than that of the radical.

Ketones usually react in the lowest excited fairly long-lived triplet state. Therefore, as a result of a decrease of the $\pi-\pi^*$ excitation energy or an increase of the $n-\pi^*$ excitation energy, the $\pi-\pi^*$ state may become the lowest excited state or its contribution to the lowest excited state increases appreciably. Comparison of the decay times and the phosphorescence spectra of acetophenone and its mono- and di-methyl derivatives in different solvents leads to the conclusion that, with increase of the number of methyl groups in the benzene ring, the triplet level of the $n-\pi^*$ state becomes higher and that of the $\pi-\pi^*$ state becomes lower [68]. Accordingly, there is a sharp decrease also in the quantum yields of the reduction of ketones in 2-propanol and cyclohexane. However, one should note that, although the lowest triplet level in dimethylacetophenone is the $\pi-\pi^*$ state, pinacol is nevertheless formed with an appreciable quantum yield.

The same behaviour is observed on passing from acetophenone to acetonaphthone, i.e. when the benzene ring is replaced by a naphthalene ring [69]. In acetonaphthone the lowest triplet state is the $\pi-\pi^*$ state, which is not sufficiently reactive to abstract hydrogen from the alcohol. However, the reaction proceeds fairly readily with a stronger reducing agent—tri-n-butyl stannate.

Thus we see that transition from the $n-\pi^*$ to the $\pi-\pi^*$ state reduces significantly the reactivity of the excited ketone molecules in the hydrogen abstraction reaction, although the latter is not fully suppressed. This finding can probably be explained by the fact that in the $\pi-\pi^*$ excited state of the ketone there is always some contribution by the $n-\pi^*$ state.

Porter and Suppan [70] believe that the $\pi-\pi^*$ state "itself" has a definite reactivity in the photochemical reduction reaction. They believe that the experiment on the sensitised photochemical reduction of α-naphthaldehyde confirms this. The lowest triplet level of this substance is the $\pi-\pi^*$ state (19 900 cm^{-1}), which lies below the triplet $n-\pi^*$ level by more than 3000 cm^{-1}. The lowest $\pi-\pi^*$ level was populated by the transfer of excitation energy from 4,4′-$[N(CH_3)_2PhCO]_2$, the lowest triplet level of which is near 21 700 cm^{-1}. It was found that with such selective population of the triplet $\pi-\pi^*$ state of α-naphthaldehyde, the quantum yield of the photochemical reduction is appreciably higher than on direct excitation of the aldehyde. However, it is then evidently difficult to assert that the lowest level is a "pure" $\pi-\pi^*$ level.

When electron-donating substituents [NH_2, $N(CH_3)_2$, OH] are introduced into the *para*-position of the benzene ring of benzophenone, the quantum yield of the photochemical reduction decreases sharply [26]. Porter and coworkers [65,70] showed that this is caused by the generation of a charge-transfer state (CTS), which leads to the disappearance of the electron density deficit at the carbonyl oxygen in the excited state. Moreover, in these excited molecules the negative charge is displaced towards the carbonyl oxygen:

(XXIX)

This leads to a sharp decrease of the reactivity of these molecules in electrophilic attack (the abstraction of the hydrogen atom may be regarded as successive removal of an electron and then a proton from the hydrogen donor [65]).

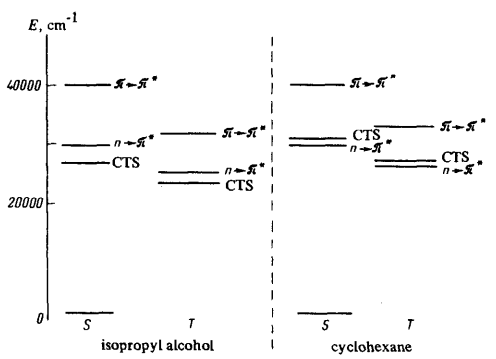


Figure 9. Energy levels of *p*-aminobenzophenone in isopropyl alcohol and cyclohexane [65].

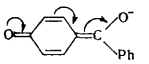
Porter [65,70] regards the $\pi-\pi^*$, $n-\pi^*$, and charge-transfer states in compounds of the type of *p*-aminobenzophenone as separate excited levels with different reactivities. On passing from a polar solvent (isopropyl alcohol) to a non-polar solvent (cyclohexane), the polarising influence of the solvent diminishes and the lowest triplet state becomes $n-\pi^*$ and not the charge-transfer state (see scheme in Fig. 9). The quantum yield of the disappearance of aminobenzophenone increases accordingly from zero in isopropyl alcohol to 0.2 in cyclohexane.

The comparison of hydroxy- and methoxy-benzophenones is extremely interesting. The complete similarity of the spectra of these compounds suggests that they have approximately the same distribution of levels and the short phosphorescence decay times in hydrocarbon and alcoholic matrices indicate that the lowest triplet level in both substances is the $n-\pi^*$ state. Nevertheless methoxybenzophenone reacts in isopropyl alcohol with a quantum yield $\varphi \simeq 1$ and hydroxybenzophenone reacts with $\varphi = 0.02$.

Porter and Suppan [70] believe that hydroxybenzophenone exhibits acidic properties in the excited state:

$$H—O—Ph_2CO \rightleftharpoons {}^{-}O—Ph_2CO + H^{+} .$$

The anion formed is unreactive in isopropyl alcohol since now the lowest triplet level is the charge-transfer state.



(XXX)

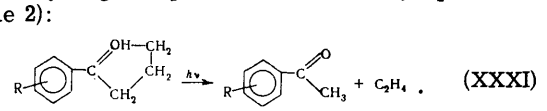
In cyclohexane, where there is no stabilisation of the charge-transfer state by the solvent, hydroxybenzophenone reacts with a quantum yield close to unity.

The properties of various excited states of the benzophenones studied by Porter and Suppan are summaried in Table 1.

Table 1. The properties of the $n-\pi^*$, $\pi-\pi^*$, and charge-transfer states of benzophenone derivatives.

States	Intensity of light absorption, lg ε	Energy range (cm^{-1} in *para*-derivatives)	Shift of absorption band by solvent, cm^{-1}	T-S splitting, cm^{-1}	Reactivity φ	Lifetime in triplet level, ms	Distribution of electrons in carbonyl group
$n-\pi^*$	2	30 000	−800	<3000	1	< 20	$C=O^{\delta+}$
$\pi-\pi^*$	4	40 000	+600	10 000	0.1	>100	C=O
CTS	3—4	30 000	+2500	>3000	0.01	>100	$C=O^{\delta-}$

Pitts and coworkers [62,71,72] believe that the unreactive state in the *para*-substituted benzophenones discussed is the triplet $\pi-\pi^*$ state (the charge-transfer state is not considered as such, as it is believed that it only makes a contribution to the $\pi-\pi^*$ state). Baum et al. [71] compared the quantum yields of the intramolecular photochemical abstraction of hydrogen in *para*-substituted butyrophenones (Table 2):



(XXXI)

Table 2. The quantum yields (φ_{II}) of the Norrish type II photochemical cleavage in benzene solutions at 25°C and 313 nm.

Butyrophenone derivatives substituted in the *para*-position	φ_{II}	Triplet level, kcal	Butyrophenone derivatives substituted in the *para*-position	φ_{II}	Triplet level, kcal
p-Cl	0.43	72.4	*p*-OH	0.00	71.0
p-$OCOCH_3$	0.42	74.3	*p*-NH_2	0.00	64.5
p-H	0.42	74.7	*p*-$NHCOCH_3$	0.00	69.9
p-CH_3	0.39	73.7	*p*-C_6H_5	0.00	not established
p-F	0.29	72.9	*p*-Br	0.00	72.9
p-OCH_3	0.10	73.3			

The data in Table 2 agree with data for the intermolecular photochemical reduction of benzophenone: as the electron-donating properties of the substituent become more pronounced, the reactivity diminishes. As before, this can be explained by a transition from the lowest $n-\pi^*$ state to the $\pi-\pi^*$ state, which involves an increase of the negative charge at the carbonyl oxygen.

It is interesting that, on passing from isopropyl alcohol to cyclohexane, there is no significant change of φ_{II}. The solvent behaves merely as a medium and its polarity evidently does not influence the rate of reaction. Clearly this result is inconsistent with Porter's data. (Pitts [71,73] notes that pinacol could not be detected at all in the photochemical reaction of *p*-aminobenzophenone in cyclohexane.)

Yang and Dusenbery [74] compared the rate constants for the photochemical abstraction of hydrogen by acetophenone and its derivatives [*p*-CH_3, *p*-CF_3, 3,4-$(CH_3)_2$] with the positions of the $[\pi-\pi^*]^1$, $[\pi-\pi^*]^3$, $[n-\pi^*]^1$, and $[n-\pi^*]^3$ levels in these compounds. It was found that the introduction of the electron accepting *p*-CF_3 group into acetophenone increases the distance between the $[\pi-\pi^*]^1$ and $[n-\pi^*]^3$ levels, which reduces the contribution of the $[\pi-\eta^*]^1$ state to the lowest state $[\pi-\eta^*]^3$ and increases the rate of photochemical abstraction of hydrogen. Introduction of the electron-donating CH_3 groups decreases the vibronic interaction of the $[\pi-\pi^*]^3$ level (which in this case is the lowest excited level) with the $[n-\pi^*]^3$ level and thereby reduces its reactivity.

In many compounds the $n-\pi^*$ and $\pi-\pi^*$ levels are so close that it is difficult to tell which of them in fact reacts.

In a study of the photochemical cleavage of substituted butyrophenones, Pitts and coworkers [75] compared the φ_{II} for these substances with their phosphorescence decay times in a solid matrix and found that for certain compounds, for example for *ortho*- and *para*-acetoxy-derivatives, the phosphorescence decay time and hence the contribution of the $[\pi-\pi^*]^3$ state to the lowest $[n-\pi^*]^3$ state increase sharply. At the same time the φ_{II} for these compounds have the same value as for the unsubstituted ketone (~ 0.4). This contradiction may arise because, for a constant quantum yield, the photochemical reaction rate constants may diminish significantly, as was shown for substituted valerophenones [76,77]. In this connection one must emphasise yet again that a simple comparison of the reaction quantum yields can lead to incorrect conclusions, since the quantum yield is not determined solely by the photochemical reaction rate constant but also by the lifetime of the excited molecule. It has been shown that in many cases [78,79] an increase of the contribution of the charge-transfer state to the excited state entails a decrease of the lifetime of the excited molecules.

In a discussion of the mechanism of hydrogen abstraction by ketones, the problem arises whether this reaction should be regarded as a two-stage process (electron and then proton transfer from the alcohol) or a single-stage process (radical abstraction of the hydrogen atom). In the first case heterolytic electrophilic substitution is evidently the rate-limiting stage, while in the second stage the reaction is homolytic. The available experimental data are insufficient to resolve this problem, which is important for the construction of a model of the transition state in the reaction.

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Study of Tautomerism by Nuclear Magnetic Resonance Spectroscopy

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The present review describes the contribution of NMR to the study of prototropic tautomerism of various types, with the exception of keto-enol tautomerism, which was dealt with in an earlier review[1]. The bibliography contains 221 references.

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I. IMINE-ENAMINE TAUTOMERISM

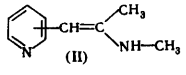
As with keto-enol tautomerism, the tautomeric change takes place slowly, and it is possible to observe separately the PMR spectra of the two forms:

(A) (B)

Ahlbrecht and coworkers[2] obtained the imine (IA) by condensing α-phenylpropionaldehyde with methylamine. Equilibrium with the enamine form (IB) is gradually established. The quantity of the enamine form increases with decrease in temperature and with increase in the polarity of the medium. The same picture is observed for non-chelate enol forms[1]. At 50° the equilibrium mixture contains 72% of the imine (IA) in chloroform and 32% in DMSO†. The amine tautomer (IB) consists of a mixture of the *cis*- and *trans*-isomers. *cis*-*trans*-Isomerisation takes place in the tautomeric change.

(IA) (IB)

The same authors[3] subsequently studied the influence of substituents on the imine-enamine equilibrium. For example, it was shown that the concentration of the enamine form (II) depends markedly on the position at which the acyclic residue is attached to the pyridine ring (100% enamine in the α- and γ-positions, and 61% in the β-position in DMSO). This result is apparently related to the deficit of electrons in the α- and γ-positions of the heterocyclic ring.



(II)

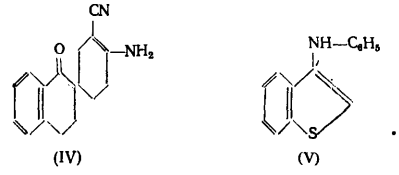
†Dimethyl sulphoxide.

Colvin and coworkers[4] observed the tautomerism of the iminourethanes (III)

(IIIA) (IIIB)

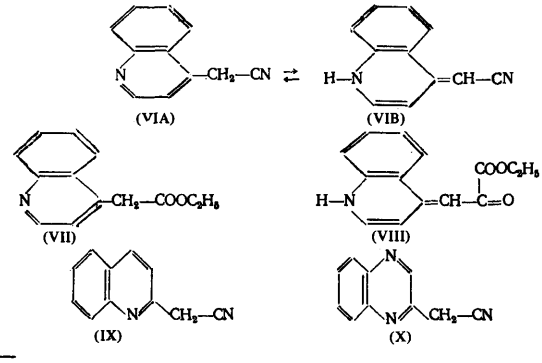
and detected forms (IIIA) and (IIIB) in comparable amounts. The broadened PMR signals of the amino-group lay in the range 3–4 p.p.m. ‡

Compound (IV) exists entirely in the enamine form[5]:



(IV) (V)

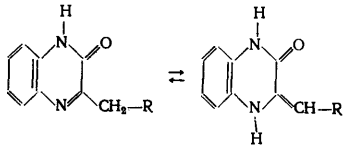
The amine form of the 3-phenylamino thianaphthene (V) predominates in neutral solvents[6]. In DMSO, 25% of 4-quinolylacetonitrile is present as the enamine form (VIB), whereas for the ester (VII) the enamine form is not observed, and for the pyruvate (VIII) the enamine form is the chief form[7]. This is apparently due to the stabilisation of the enamine as a result of conjugation between the nitrogen atom of the ring and the functional group of the side chain, which compensates the dearomatization of the heterocyclic ring. The enamine forms of 2-quinolylacetonitrile (IX) and 2-quinoxalylacetonitrile (X) are not detected[7].



(VIA) (VIB) (VII) (VIII) (IX) (X)

‡In this review the chemical shifts are given in the τ scale.

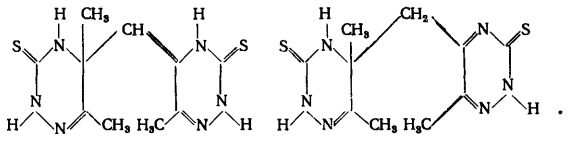
For the oxo-derivatives (XI), in which the aromaticity of the heterocyclic ring is destroyed, however, the enamine form (XIB) predominates in various solvents[7,8]:



(XIA) (XIB)

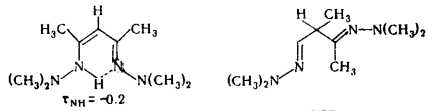
(100% for R = C_6H_5 and 70% for R = CN). The concentration of form (XIB, R = CN) decreases with increase in temperature[8].

For the dimers (XII) in DMSO, the A ⇌ B equilibrium is observed[9]:



(XIIA) (XIIB)

The tautomerism of bis-dialkylhydrazones can be regarded as imine-enamine tautomerism[10]. Acetylacetone bis-dialkylhydrazone exists entirely in the hydrazone-hydrazine form (XIII), whereas the corresponding α-methylacetylacetone derivative exists as 100% dihydrazone (XIV); this is attributed to the instability of the planar chelate structure, resulting from the spatial interaction of the methyl groups:



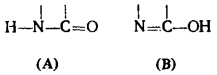
(XIII) (XIV)

For compounds of type (XIII), intra-chelate tautomerism takes place. The rapid migration of the proton between the nitrogen atoms and the consequent effective equivalence of the C–CH_3 groups is indicated by their single PMR signal in the spectrum of compound (XIII).[10]

The imine-enamine tautomerism of *o*-ethylvalerolactam[11] and *N*-isopropylideneisopropylamine[12] has been confirmed by deuteration of the protons on the carbon atoms.

II. AMIDE-IMIDOL TAUTOMERISM

The width and CS§ of the PMR signal of the mobile protons are not reliable criteria for choosing between the amide (A) and imidol (B) forms. The CS of the nitrogen and oxygen (^{17}O) nuclei and the SSCC¶ between these nuclei and the protons are more informative. The more readily available data on the CS of the stable protons of the molecule and, where possible, on the SSCC between these protons and the mobile protons are more frequently used, however.



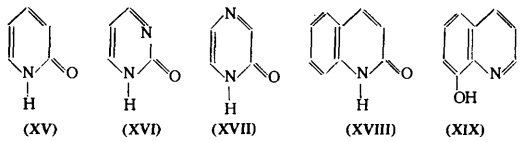
(A) (B)

§Chemical shifts.

¶Spin-spin coupling constants (J).

The absence of the imidol form (B) in simple amides† was confirmed by the PMR spectra. In all secondary amides studied, SSC between the α-protons of the substituent and the amide protons (J = 5 Hz) is observed[14,15]. The ^{15}N–H SSCC in formamide is close to 90 Hz.[16] The existence of the imidol form in the amides and hydrazides of phosphorylated carboxylic acids has been reported[17]. The imidol form is more probable for heterocyclic compounds, where it may be stabilised as a result of the formation of a heteroaromatic system. The results of NMR studies of a number of heteroaromatic compounds for which rapid tautomerism of only the amide-imidol type is possible are examined below.

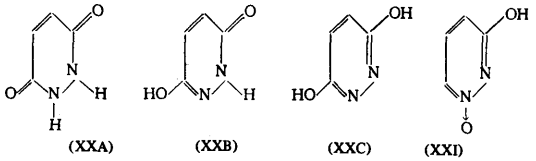
The 2-oxo-derivatives of pyridine (XV),[18] pyrimidine (XVI),[19] pyrazine (XVII),[20] and quinoline (XVIII)[21] exist in the amide form (A). For compound (XV) in non-polar media, ^{15}N–H SSC (90 Hz) is observed at low temperatures. The low values of τ_{NH} (–3.6) are attributed to the formation of dimers with strong InterMHB‡:



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

The amide structure of compounds (XVI) and (XVII) was demonstrated by comparing the CS of the stable protons of the tautomeric and fixed (O- and N-methylated) compounds. These CS were found to be sensitive to the breakdown of the aromaticity of the heterocyclic ring on production of form (A). For compound (XVIII), the ^{14}N CS was measured (235 p.p.m. relative to NO_3^-). This value is typical for amides and differs sharply from the value for 8-quinolinol (XIX) (90 p.p.m.) with sp^2-hybridisation of the nitrogen atom.

Of the three tautomeric forms of 3,6-dioxopyridazine (XX), the symmetrical form (XXA) was first proposed as the predominant form, since the spectrum shows a common signal for the protons in positions 4 and 5§.[21] These protons may also become effectively equivalent, however, if there is rapid exchange between two equivalent forms (XXB). Later, evidence in support of the oxo-hydroxy-structure (XXB) was obtained from the PMR spectra of model compounds[23,24], in agreement with the infrared and ultraviolet spectra[25-27].



(XXA) (XXB) (XXC) (XXI)

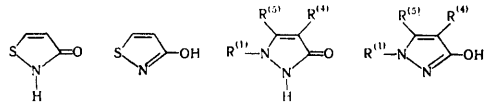
According to the PMR data, and in agreement with the infrared and ultraviolet spectra, 3-hydroxypyridazine-*N*-oxide and its methyl derivatives exist chiefly in the imidol form (XXI).[28]

†Form (B) was erroneously assumed to be present in benzoyl-α-aminoethylbenzene on the basis of optical rotatory dispersion data[13].

‡Intermolecular hydrogen bonding.

§The infrared and ultraviolet spectra indicate that the symmetric dioxo-form (XXC) is unlikely.

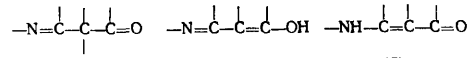
Of the two rapidly interconvertible tautomeric forms of 3-hydroxyisothiazole (XXII), the form (XXIIB) predominates in $CDCl_3$ (100%) and also in DMSO and methanol (~75%).[29]



(XXIIA) (XXIIB) (XXIIIA) (XXIIIB)

Tautomerism of the amide-imidol type is observed in *N*-substituted pyrazol-3-ones (XXIII, $R^{(1)} = CH_3$, C_6H_5; $R^{(4)}$, $R^{(5)} = H$, CH_3).[30,31] The PMR, infrared, and ultraviolet spectra indicate that in pyridine, these compounds exist chiefly in the hydroxy-form (XXIIIB), whereas in aqueous-alcoholic solutions, appreciable quantities of the oxo-form (XXIIIA) are observed[30,31].

III. KETOAMINE-ENOLIMINE TAUTOMERISM

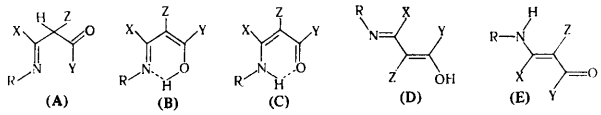


(A) (B) (C)

Like the amide form of the simple amides, the keto-amine form (C) of the vinylogous amides examined below is the most stable. The change to the enolimine form (B) generally takes place if this is accompanied by a significant gain in the energy of conjugation of the molecule as a whole (for example the formation of an aromatic ring). The keto-imine form (A) usually exists in sterically hindered systems.

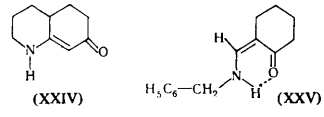
1. Schiff's Bases–Derivatives of β-Dicarbonyl Compounds

The possible tautomeric forms of the Schiff's bases (SB) (A–E) examined here are analogous to the tautomeric forms of the corresponding β-dicarbonyl compounds[1]. The SB usually exist in the stable ketoamine chelate form (C) and in some instances in the non-chelate form E¶ (Table 1).



(A) (B) (C) (D) (E)

The suggestion, based on the ultraviolet spectra[34], that the enol-imine tautomers (B) and (D) exist is refuted by PMR data[32,35]†. The PMR spectra show low-field signals due to the chelate protons ($\tau_{NH} < 1.4$), which are split in the spectra of the compounds containing ^{15}N, with SSCC 88–95 Hz. Moreover, SSC with the protons of the amino-group leads to splitting of the signals of the substituents R = Alk and X = H with SSCC 4.5–8.0 Hz and 12–14 Hz respectively. The keto-amine form also predominates in compounds (XXIV) and (XXV).[39,40]



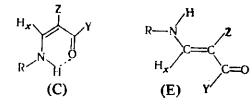
(XXIV) (XXV)

¶The presence of traces of the keto-imine form (A) in some compounds is indicated by deuterium exchange of the α-protons (Z = H) in D_2O.[36,37]

†The enol-imine structure has been assigned to the product of the monocondensation of 4,5-diaminopyrimidine with acetylacetone[38].

The *trans*-isomers (E, Z = H) of the keto-amine tautomer, detected for a number of amino-derivatives of β-aldoketones (Table 1) and acetoacetic ester[41], are characterised by high values of τ_{NH} (> 3.3) and the SSCC between the vinyl protons ($J_{HC=CH}$ = 12–13.5 Hz). For the *cis*-forms (C, Z = H) $J_{HC=CH}$ = 7–8 Hz, and the α-protons are less shielded in view of the proximity of the carbonyl oxygen atom[32] (Table 1). The SSCC with the amine protons are the same for the *cis*- and *trans*-isomers.

Table 1. *cis*-*trans* Isomerism of Schiff's base derivatives of β-ketoaldehydes[32]:



(C) (E)

Compounds			Medium	Concn., M	Concn. of tautomers, %		τ_{NH}		τ_Z		J_{H_X-Z}, Hz	
R	Z	Y			C	E	C	E	C	E	C	E
H	H	CH_3	—[a]	—			0.9	3.3	4.97	4.58	7.5	12,8
			$CDCl_3$	2,0	90	10	0.3	3.3	4.95	4.61	7.9	13,2
H	CH_3	CH_3	$CDCl_3$		25	75	b	4.8	8.18	8.33		
CH_3	H	CH_3	—[a]	—	0	100	—	b	—	4.87	—	13.3
			$CDCl_3$	1.9	64	36	0.3	b	5.01	4.84	7.3	13.1
			$CDCl_3$	1.0	75	25	0.4	b	5.02	4.81	7.4	13.3
CH_3	CH_3	CH_3	$CDCl_3$	1.6	43	57	0.4	4.9	8.20	8.35	—	—
$CH_2C_6H_5$	H	CH_3	[a]	—	90	10	0.1	—	5.03	4.72	7.4	11.8
			$CDCl_3$		100	0	0.1	—	4.97	—	7.5	—
CH_3	H	C_6H_5	$CDCl_3$		100	0	—0.2	—	4.32	—	7.4	—
C_2H_5	H	C_6H_5	$CDCl_3$		100	0	—0.3	—	4.31	—	7.6	—
C_6H_5	H	CH_3[c]	CCl_4		100	0	—2.77	—				

[a] Pure liquids.
[b] Very broad signals.
[c] Ref. 33.

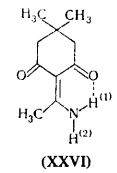
The concentration of the *trans*-isomer increases when the α-hydrogen atom (Z) is replaced by a methyl group and decreases when the methyl groups on the nitrogen atom and the carbonyl group (R and Y) are replaced by phenyl or benzyl groups (Table 1). These effects are related to the steric interactions of the substituents in the isomers (C) and (E).[32] Dilution in inert solvents decreases the proportion of the *trans*-isomer as a consequence of the rupture of the IntraMHB, which stabilises form (E).[32]

trans-Isomers were not detected in the SB derivatives of acyclic β-diketones[36,42].

The chelate amine protons of the SB are more shielded than the protons in the chelates of the corresponding β-dicarbonyl compounds, but the nature of the dependence of τ_{NH} and τ_{OH} on the substituents X and Y is the same[32,36,41,42]. τ_{NH} decreases by almost 3 p.p.m. on going from R = H to R = C_6H_5 (Table 1). Low values of τ_{NH}, indicating strong IntraMHB‡, are characteristic of the SB derivatives of the 2-acyldimedones (XXVI)[41] and (XXVII).[33] As in the β-keto-esters, the replacement of the COOAlk group in the SB by the CSSAlk group leads to a sharp decrease (by ~4 p.p.m.) in the shielding of the chelate proton of compound (XXVIII).[43] The medium and

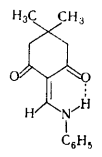
‡Intramolecular hydrogen bonding.

the temperature have little influence on τ_{NH} and the SSCC for the SB, indicating fairly strong IntraMHB and the stability of the keto-amine form (C).



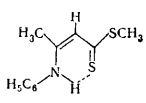
(XXVI)

$\tau_{NH}^{(1)} = -2{,}10$, $\tau_{NH}^{(2)} = +2{,}60$ $(CDCl_3)$



(XXVII)

$\tau_{NH} = -6{,}45\ (CCl_4)$

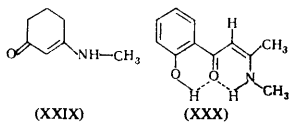


(XXVIII)

$\tau_{NH} = -4{,}88\ (CCl_4)$

A significant decrease in τ_{NH} for the chelate forms (C) is observed with increase in the electron-accepting properties of the substituent R.[36]

In the non-chelate keto-amine forms (acyclic *trans*-isomers and compounds of the type (XXIX)), an increase in τ_{NH} is observed with increase in temperature and on dilution in inert solvents. The SSCC with the amine protons remain unchanged[42].

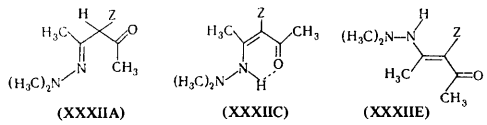


(XXIX) (XXX) (XXXI)

$\tau_{NH} = -0{,}80\ (CDCl_3)$ $\tau_{NH} = -1{,}31\ (CDCl_3)$

As in the β-dicarbonyl compounds, the IntraMHB in the corresponding SB with a carbonyl group involved in other hydrogen bonding (XXX)[45] is slightly weaker than ordinary IntraMHB (XXXI).[42]

Domnin and Yakimovich[10] demonstrated the presence of three tautomeric forms in the products of the monocondensation of β-diketones with dimethylhydrazine (XXXII, Z = Alk). The concentration of the chelate form (C) decreases with increase in the polarity of the medium and the size of the substituent Z. For compound (XXXII, Z = H), only the chelate keto-hydrazine form (C) was detected. The corresponding derivatives of 2-acetyl-2-benzoylcyclohexanones also exist in a chelate form of type (C) (τ_{NH} = –0.5).



(XXXIIA) (XXXIIC) (XXXIIE)

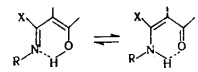
2. Schiff's Bases—Derivatives of *o*-Acylphenols and *o*-Acylnaphthols

In these compounds, which form condensed systems of chelate and aromatic rings, conjugation has a significant influence on the imine-amine equilibrium B ⇌ C (Table 2). The existence of the amine form, which predominates in all SB previously described, is possible in this instance only when the aromatic character of the rings is destroyed; this requires the expenditure of large quantities of energy (tens of kcal mole^{-1}).[46] Nevertheless, the existence of considerable quantities of the amine form in many instances has been demonstrated by means of the NMR spectra§ (see Table 2).

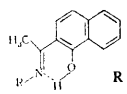
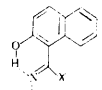
§The amine form of compounds of this type was previously detected by ultraviolet spectroscopy[47].

Measurement of the $^{15}N-H$ SSCC made it possible to determine fairly accurately the constant for the amine-imine equilibrium at various temperatures, and other thermodynamic constants (Table 2).

Table 2. Concentrations and differences in the enthalpies of the tautomers of aromatic Schiff's bases, and the CS and SSCC of the chelate protons (concentration 0.2 M):



(B) (C)

Compound	Medium	T, °C	τ,	SSCC, Hz			Concn. of tautomers, %		$-\Delta H$, kcal mole^{-1}	References
				$^{15}N-H$	HN—CH	NH—R	B	C		
X=H, R-iso-C_3H_7[a]	CCl_4	20	–2.73	—	0	0	100	0		45
X=H, R=$CH_2C_6H_5$	$CDCl_3$	30	–2.70	—	0	0	100	0		46
X=H, R=C_6H_5	$CDCl_3$	30	–3.22	0	0	—	100	0		48
	$CDCl_3$	–50	–3.61	0	0	—	100	0		
	C_2H_5OH	0	–5.02	13.1		—	85.5	14.5		
X=CH_3, R=CH_3	$CDCl_3$	20	–6.50	17	—		81	19	1.5	49
	$CDCl_3$	–50		32.4	—		64	36		
	CH_3OH	–50		68.2	—		24.2	75.8		
X=CH_3, R=C_6H_5	$CDCl_3$	30	–4.59	0	—	—	100	0		48,49
	$CDCl_3$	–40	–5.01	0	—	—	100	0		
 R = CH_3										
	$CDCl_3$	50	–5.92	76.9	—	4.6	14.6	85.4	2.3	42,44
	$CDCl_3$	15	–5.79	80.3	—	4.8	10.8	89.2		
R=$CH_2C_6H_5$	$CDCl_3$	30	–6.14	—	—	4.8				46,50
R=C_6H_5	$CDCl_3$	30	–6.99	27.5	—	—	69.4	30.6	1.1[b]	48
	$CDCl_3$	–30	–7.41	36.5	—	—	59.4	40.6		
										
X=H, R=CH_3	$CDCl_3$	30	–4.29	64.5			28.3	71.7	2.7	42,46
	$CDCl_3$	0	–4.20	72.3	9.8	4.6	19.7	80.3		
	$CDCl_3$	–45	–4.02	81.4	11.2	5.1	9.6	90.4		
	pyridine	31	–4.78	58.2			35.3	64.7	1.8	
X=H, R=t-C_4H_9	$CDCl_3$	30	–4.70	—	10.5	—	20	80		36
X=H, R=$CH_2C_6H_5$	$CDCl_3$	30	–4.80	—	6.4	3.0	50	50		36
	CCl_4	30	–4.70	—	5.9					46
X=H, R=C_6H_5	$CDCl_3$	30	–5.44	33.0		—	63.3	36.7	1.5	48
	$CDCl_3$	15	–5.51	36.1	5.2	—	59.9	40.1		
	$CDCl_3$	–40	–5.69	49.4	6.9	—	44.1	54.9		
	CCl_4	30	–4.95	12.3		—	86.3	13.7	0.4	
X=CH_3, R=CH_3	$CDCl_3$	30	–3.80	—	—	0	100	0		50
X=CH_3, R=$CH_2C_6H_5$	$CDCl_3$	30	–6.30	—	—	0	100	0		

[a]Concentration 0.02 M.
[b]0.1 in CH_3CN.

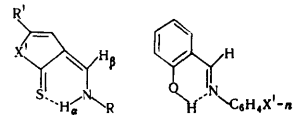
According to the results in Table 2, the concentration of the amine form (C) in α-naphthol derivatives is much greater than that in the analogous derivatives of β-naphthol and phenol. The replacement of an alkyl substituent on the nitrogen atom in α-naphthol derivatives by an aryl substituent leads to a decrease in the percentage of the amine

form. The percentage of the amine form is greater in the SB derivatives of 1-formyl-2-naphthol than in the 1-acetyl-2-naphthol derivatives.

With increase in the polarity of the medium in the order CCl_4, $CHCl_3$, and CH_3OH, the concentration of the keto-amine form increases considerably. Decrease in temperature has the same effect.

The introduction of different substituents into the benzene ring of the SB derivative of 2-hydroxyl-1-naphthaldehyde and aniline has little influence on the concentration of the intrachelate tautomers. In almost all compounds of this type, the SSCC for the chelate and aldehyde protons have values of 3–5 Hz (25–40% of the amine form) [36].

The SB derivatives of 2-thiol-3-formylfurans and 2-thiol-3-formylthiophens (XXXIII) (X′ = O, S; R, R′ = H, Alk, Ar) exist chiefly in the chelate amine form in different solvents. This is indicated by the SSCC values:



(XXXIII) (XXXIV)

$^{15}N-H_\alpha$ = 86 Hz, $H_\alpha-H_\beta$ = 13–15 Hz, and τ_{NH} has values between −2 and −5. [51]

For derivatives of salicylaldehyde (XXXIV), which exist entirely in the enol-imine form, the dependence of τ_{OH} on the substituent X′ (−3.45, −3.25, and −2.58 Ψ for X′ = OCH_3, H, and NO_2 [30]) is the opposite of that observed for τ_{NH} in aliphatic keto-amines. In the naphthol derivatives, the CS of the chelate proton is determined not only by the shielding action of the substituent R, but also by the concentration of intrachelate tautomers (XXX) (Table 2).

3. α-Azaheterocyclic Ketones, Esters, and Pyruvates

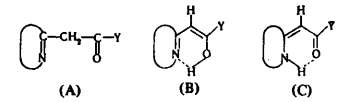
For these compounds, three tautomeric forms are possible (Table 3). The chelate forms (B) and (C), stabilised by IntraMHB, are similar to those for the SB considered above. The existence of form (C) is possible only with breakdown of the aromaticity of the heterocyclic ring. The marked tendency for the keto-amine form (C) to be produced is realised more readily in these compounds than in the SB-derivatives of phenol and naphthol, since the breakdown of the aromaticity of the heterocyclic ring takes place more readily [59].

For the esters (Y = OAlk), form (B) is not observed, and the A ⇌ C equilibrium is displaced considerably towards (A) for pyridine, quinoline, and quinoxaline, and towards (C) for cyclic amides and esters, when the aromaticity of the heterocyclic ring is decreased (see Table 3).

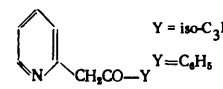
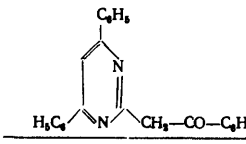
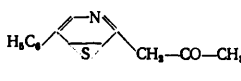
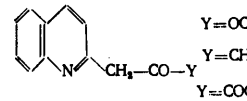
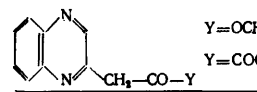
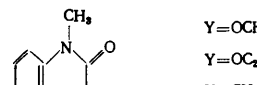
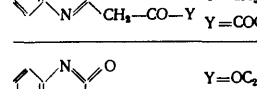
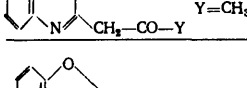
In the ketones (Y = Alk, Ar) and more particularly the pyruvates (Y = COOAlk), the concentration of the keto-imine form (A) is much smaller than for the corresponding esters, and the B ⇌ C equilibrium is determined by the nature of the heterocyclic ring.

For pyridine [52,53], the phenol form (B) is produced, and form (C) is not observed, since $^{15}N-H$ SSC is not observed. With increase in temperature, form (B) for a number of compounds is converted into form (A). [52,53] For the ketones and pyruvates derived from quinoline, quinoxaline, 2-oxo-1,2-dehydroquinoxaline, and other compounds, Mondelli and Merlini [7] detected form (C), in a number of instances in equilibrium with form (A). Form (B) was regarded as unlikely, because of the absence of the marked SSC of the vinyl and methyl protons (Y = CH_3), characteristic of form (B) with $J \simeq 1$ Hz. This conclusion was confirmed by the ultraviolet and infrared spectra [52,53].

Table 3. Tautomeric composition and shielding of the acidic proton for a series of α-azaheterocyclic ketones, esters, and pyruvates.



(A) (B) (C)

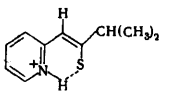
Compound	Medium	Concn. of tautomers, % (A)	(B)	(C)	$\tau_{NH(OH)}$	References
 Y = iso-C_3H_7	CS_2	10	90	0	−4.0	52,53
Y = C_6H_5	CS_2	15	85	0		52,53
	$CDCl_3$	33	67	0	−4.5	54
	CCl_4	70	30	0		55
	DMSO	88	12	0		
 Y = OC_2H_5	$CDCl_3$	100[a]	0	0	—	7
Y = CH_3	$CDCl_3$	25	0	75	−5.0	7
	DMSO	35	0	65	−4.8	7
Y = $COOC_2H_5$	$CDCl_3$	0	0	100[a,b]	−5.7	7
 Y = OCH_3	$CDCl_3$	100[a]	0	0	—	7
Y = $COOC_2H_5$	$CDCl_3$	0	0	100[a]	−3.8	7
 Y = OCH_3	$CDCl_3$	30	0	70		56
Y = OC_2H_5	$CDCl_3$	0	0	100	−1,20	7,56
Y = CH_3	$CDCl_3$	0	0	100[a]	−3,30	7
Y = $COOC_2H_5$	$CDCl_3$	0	0	100[a]	−4,0	7
 Y = OC_2H_5	$CDCl_3$	0	0	100[a]	−0.7	7,57
Y = CH_3	$CDCl_3$	0	0	100[a]	−2,4	7,8,56
	DMSO	0	100	—	−0,37	58

[a] Same concentration in DMSO.
[b] The analogous *para*-derivative likewise does not contain form A.

The preference for a given chelate form (B or C) is apparently determined by the energy of dearomatization of the heterocyclic ring.

The marked downfield shift of the chelate proton and the fact that it depends little on concentration [7] indicate strong IntraMHB. The CS increases in the order: esters,

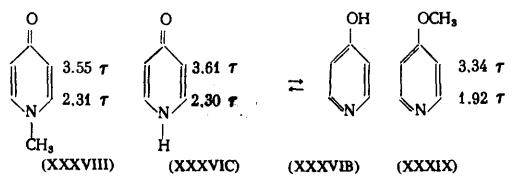
ketones, pyruvates (Table 2). The same picture is observed for the β-dicarbonyl compounds[1]. A noteworthy feature is the very strong downfield shift for 2-picolinyl isopropyl thioketone (τ = −8.60) compared with its oxygen analogue (τ = −4.0). This is attributed[60] to the participation of the bipolar form (XXXV) in the tautomeric equilibrium.



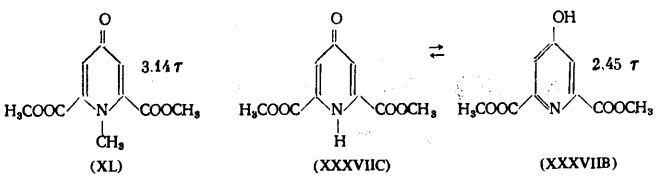
(XXXV)

4. Derivatives of 4-Hydroxypyridine

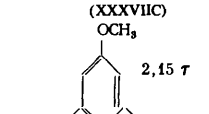
4-Hydroxypyridine (XXXVI) and its 3,5-disubstituted derivatives exist in the keto-amine form (pyridones-4) (XXXVIC),[61] whereas for various 2,6-disubstituted 4-hydroxypyridines, in particular compound (XXXVII), the enolimine hydroxy-form (XXXVIIB) predominates. These data were obtained by comparing the CS of the stable protons¶ of the tautomeric and model compounds (XXXVIII–XLI).[62,63] The pyridone-4 (XXXVI) is characterised by a low value for τ_{NH} (−3.92 in $CDCl_3$).[64]



(XXXVIII) (XXXVIC) (XXXVIB) (XXXIX)

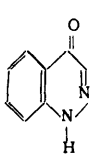


(XL) (XXXVIIC) (XXXVIIB)



(XLI)

4-Cinnolone (XLII) and its derivatives exist in the oxo-form[65,66].



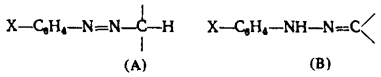
(XLII)

¶In water for 4-hydroxypyridine and in $CDCl_3$ for its 2,6-disubstituted derivatives.

IV. AZO-HYDRAZONE TAUTOMERISM

1. Arylhydrazones and Similar Compounds

For the phenylhydrazones of aldehydes and ketones, two tautomeric forms are possible:



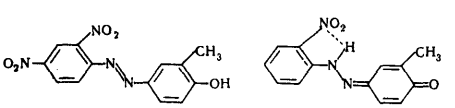
(A) (B)

The PMR spectra of freshly prepared solutions of phenylhydrazones in various solvents, and also of semicarbazones and thiosemicarbazones, contain lines due to only the hydrazone form (B).[67-69] With the passage of time, solutions of some phenylhydrazones become yellow, and the PMR spectra, instead of the signals of the –NH– (τ_{NH} = 2–3) and =CH– groups, show the signals of the protons on saturated carbon atoms, characteristic of the azo-form (A).[67] In inert media, the transformation B → A proceeds to completion in several minutes or tens of minutes, whereas in polar media the transformation is not complete even after several hours. InterMHB with the solvent molecules apparently stabilises form (B). In a number of instances the PMR spectra reveal *cis-trans*-isomerism of tautomer (B).[67,68]

2. Azophenols and Heterocyclic Azo-compounds

In contrast to the situation for the hydrazones examined above, the tautomerism of azophenols and similar compounds involves the transfer of protons between nitrogen and oxygen atoms. The PMR CS of the –NH– and –OH groups in general are not characteristic, so that information on the tautomeric composition is usually obtained from the CS of the stable protons of the ring, and also from the ^{14}N and ^{17}O CS. The *ortho*-protons of the aromatic ring of the azo-form (Ar–N=N–) absorb in lower fields (1.9–2.2 τ) than the corresponding protons of the hydrazone form (Ar–NH–N=) ($\tau > 2.5$). Moreover, the breakdown of the aromaticity on going from the phenolic to the quinone ring structure produces an upfield shift of the signals of the corresponding protons[70].

The PMR spectra of 4-hydroxy-3-methyl-2,4-dinitroazobenzene in $CDCl_3$ showed the signals of both the azophenol (XLIIIA) and quinone-hydrazone (XLIIIB) tautomers. Instead of the singlet signal of the methyl group[7,68] of form (XLIIIA), the spectrum of form (XLIIIB) shows two doublets (7.79 and 7.88 τ; $J_{HC=C-CH_3}$ = 1.4 Hz), which apparently belong to two stereo-isomers.

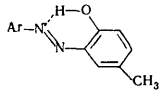


(XLIIIA) (XLIIIB)

The low value of τ_{NH} (−2.33) indicates IntraMHB for compound (XLIIIB).[70] Polar solvents bring about a marked displacement of the equilibrium towards the azo-form. In dimethylacetamide, the signals of form (XLIIIB) were not detected.

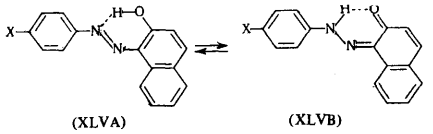
Derivatives of 2-hydroxy-5-methylazobenzene (XLIV), where Ar = nitro- and methoxy-derivatives of benzene, exist completely in the azo-form. The *ortho*-protons of

the substituent Ar absorb in the range 1.9–2.4 τ, and the values of τ_{OH} lie between −2.5 and −3.5 τ. [70,71]



(XLIV)

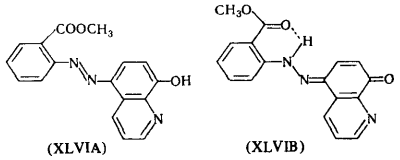
Derivatives of 1-phenylazo-2-naphthol (XLV) give an NMR spectrum which is averaged as a result of rapid intrachelate tautomeric transformations:



(XLVA) (XLVB)

Berrie and coworkers [72] compared the CS of ^{14}N in the α-position relative to the benzene ring (XLV, X = H) (111 τ) with that for compounds which are models of form (A) (−129 τ) and form (B) (175 τ) and found that $CDCl_3$ contains 21% of form (A). The concentration of form (XLV) is decreased to 3% for X = CN, and increased to 48% for X = OCH_3. This tendency was confirmed by the PMR data [70] and also by the infrared and ultraviolet spectra [70]. The *meta*-substituents have a weaker influence on the tautomeric equilibrium [72]. The percentage of the azo-form is greatest in inert media (62% for compound (XLV, X = H) in hexane) and smallest in aqueous-alcohol solution [72]. The values of τ for the chelate protons of compound (XLV) are extremely low: between −5.6 and −6.1. [71,72]

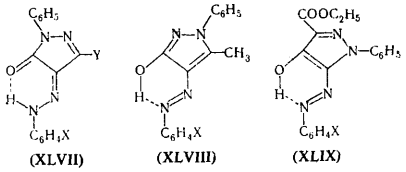
2-Phenylazo-1-naphthol exists in the hydrazone and azo-forms, and the PMR data [70] and the ^{17}O CS [73] indicate that the former predominates in $CDCl_3$. On the other hand, for 2-phenylazo-3-naphthol the equilibrium is displaced towards the azo-form [70]. The azo-form has also been assumed for 4-phenylazo-1-naphthol [70], for which, in contrast to the other phenylazonaphthols, IntraMHB is impossible. The same paper gives PMR data supporting the hydrazone structure for 1-phenylazo-2-anthrol. The spectrum of 5-*o*-carbomethoxyphenylazo-8-quinolinol in $CDCl_3$ shows the individual signals of the azophenol form (XLVIA) and the quinone hydrazone form (XLVIB) (33% and 67%). The spectra of the tautomers differ primarily in the values for the mobile protons (τ_{OH} = 4.6; τ_{NH} = −2.7).



(XLVIA) (XLVIB)

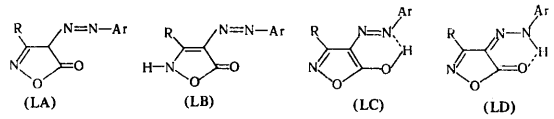
Moreover, the protons in position 4 of the quinoline ring are more shielded in form (XLVIB), in which the aromaticity is destroyed [70].

3-Substituted 1-phenyl-4-arylazopyrazol-5-ones (XLVII, Y = CH_3 or C_6H_5) in $CDCl_3$ exist in the hydrazone form, irrespective of the nature of the substituent X [70,71,74]. The spectra of the compounds with the ^{15}N isotope in the α-position relative to the benzene ring show doublet signals in weak fields (τ_{NH} lies between −3 and 3.5 τ; J_{NH} = 96 Hz). In DMSO and pyridine, compound (XLVII, Y = CH_3) apparently exists as a mixture of the hydrazone and azo-forms [74]. For the azo-derivatives of pyrazol-3-ones (XLVIII) and pyrazol-4-ones (XLIX), however, the azo-form predominates, with higher values of τ_{OH} (0–1.6) (XLVII). For compounds (XLVII–XLIX) it was impossible to detect the oxo-form, in which the mobile proton is joined to the nitrogen or carbon atoms of the ring. These results agree with the infrared spectra [71].



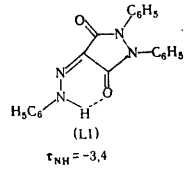
(XLVII) (XLVIII) (XLIX)

For 4-arylazoisooxazol-5-ones (L) in $CDCl_3$, the hydroxy-azo-form (C) and the hydrazone form (D) are not observed, and of the two remaining forms, form (B) predominates:



(LA) (LB) (LC) (LD)

irrespective of the substituents R (H, CH_3, C_6H_5, *p*-$NO_2C_6H_4$) and Ar (C_6H_5, CH_3O–C_6H_4). [75]



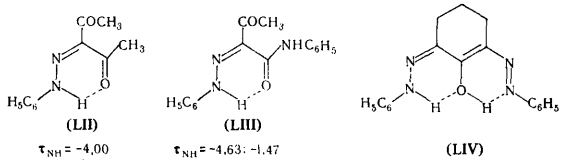
(LI)

τ_{NH} = −3,4

Of the three possible forms of 4-phenylazo-1,2-diphenyl-3,5-dioxopyrazolidine, the chelate hydrazone form (LI) is realised in various solvents [76].

3. Azoketones, Formazans, and Osazones

Phenylazo-derivatives of acetylacetone and acetoacetanilide exist in the chelate hydrazone forms (LII) and (LIII) respectively [70].



(LII) (LIII) (LIV)

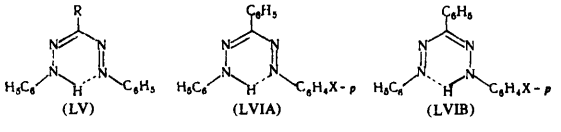
τ_{NH} = −4,00 τ_{NH} = −4,63; −1,47

Cyclohexanone-2,1,3-dihydrazone can exist in two forms: a red form, to which the chelate enol phenylhydrazone-phenylazo-structure (LIV) was assigned, and a yellow ketohydrazone form [77]. The hydrazone form, which exists as the hydrate, is converted into the red azo-form on dehydration. Two analogous forms were also found for other hydrazones of 1,2,3-tricarbonyl compounds.

The existence of tautomerism in formazans was clearly demonstrated by Mester and coworkers [78]. The PMR spectrum of the formazan of *D*-galactose penta-acetate (LV, R = monosaccharide residue) with one ^{15}N α-atom (relative to C_6H_5) (Fig. 1) shows an NH signal, split to form a doublet (J_{NH} = 46.5 Hz), expected for rapid intrachelate† migration of the proton between equivalent positions. When both α-nitrogen atoms are ^{15}N isotopes, the NH signal is split to form a triplet with component ratio 1 : 2 : 1 and J_{NH} = 46.5 Hz, since in the migration

†τ_{NH} depends little on temperature and the medium.

process the proton interacts (alternately) with two ^{15}N atoms.



(LV) (LVIA) (LVIB)

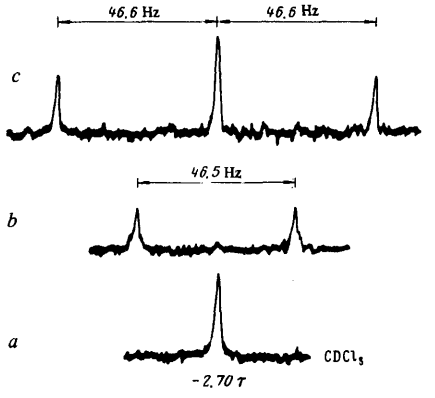
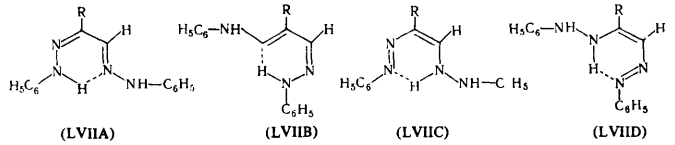


Figure 1. *a*) Low-field part of the PMR spectrum of the formazan of *D*-galactose penta-acetate in dioxan (60 MHz); *b*) the same with one ^{15}N atom; *c*) the same with two ^{15}N atoms [78].

Qualitatively similar PMR spectra should also be observed for a mesomeric structure with symmetrically arranged mobile protons, but this possibility was excluded on the basis of theory [79] and the infrared spectra [80]. In the nonsymmetrical formazans (LVI) the position of the tautomeric equilibrium depends markedly on the nature of the substituent X. When X = OCH_3, the magnitude of the splitting of the (NH...N=) PMR signal is 86.5 Hz, which corresponds to 4% of form A and 86% of form B. For compound (LVI, X = NO_2), form (A) predominates (100%), since splitting is not observed. In the symmetrical structure (LVI, X = H), the splitting is equal to 45 Hz, which is half J_{NH} = 90 Hz. In compounds (LVI), τ_{NH} varies between −4.6 and −5.7 (in $CDCl_3$). [81]

The PMR spectra of the osazones of monosaccharides in dioxan (LVII, R = monosaccharide residue) with two ^{15}N atoms in the α-positions relative to C_6H_5 show two signals due to mobile protons: the chelate proton (τ_{NH} = −2.20) and the non-chelate proton (τ_{NH} = 0.79). Both signals are split to form doublets (J_{NH} = 94.5 Hz and 93 Hz). [82] Thus both protons are joined directly to ^{15}N atoms; this agrees with the previously proposed [83] bis-phenylhydrazone



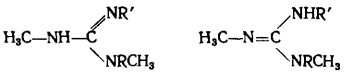
(LVIIA) (LVIIB) (LVIIC) (LVIID)

structure (LVII, A or B) and excludes the azo-form (LVII, C and D). The tautomerism of 1,2,3-tris-phenylhydrazone derivatives of propane, cyclopentane, and cyclohexane have been studied [77].

V. AMINE-IMINE TAUTOMERISM

In the amine-imine tautomeric transformation, the mobile proton moves from one nitrogen atom to another. The corresponding PMR signals are not always observed separately and usually are not characteristic. In such instances, the CS of the stable protons of tautomeric and model compounds are compared.

The splitting of the PMR signals of the methyl groups as a result of SSC with the protons on the nitrogen atoms (J = 5 Hz) made it possible to determine the structure of the predominant tautomer (A) of guanidine derivatives (LVIII, R = H, R′ = Cl, and R = Cl, R′ = H). [84]



(LVIIIA) (LVIIIB)

Of the two possible tautomeric forms of the amidoximes (LIX, R = C_6H_5, $COOC_2H_5$, $CH_2C_6H_5$, or $C(NH_2)$=NOH), the amino-oxime-form (A) is realised in various solvents [57,85].

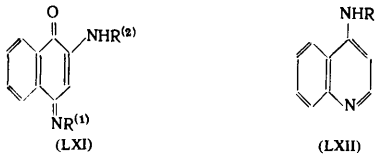
(LIXA) (LIXB)

The spectra show the signals of the amine and oxime groups (τ_{NH_2} = 4–5.5; τ_{OH} = 0–1), with intensity ratio 2:1. The PMR of the broad lines was used to determine the tautomeric form of cyanoguanidine (LX) in the crystalline state. Kotera and coworkers [86] compared with experimental value of the second moment of the PMR line with the calculated values for the two possible forms, and concluded that cyanoguanidine has the diamino-structure (LXA).

(LXA) (LXB)

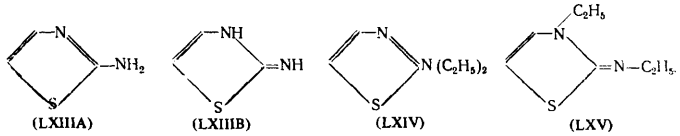
The NMR spectrum of 2-amino-1,4-naphthoquinonimine (LXI) showed that at room temperature an equilibrium between the *o*- and *p*-quinonimines is established [87].

4-Aminoquinolines exist in the amino-form (LXII) in various solvents [88,99].



(LXI) (LXII)

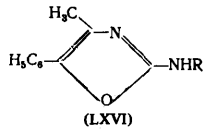
In $CDCl_3$, the CS of the vinyl protons of the potentially tautomeric 2-aminothiazole (LXIII) and the model compound (LXIV) almost coincide (2.86 and 3.52 τ) and differ sharply from the corresponding values for compound (LXV) (3.45 and 4.20 τ). This provides evidence in support of the amino-form (LXIIIA). [90]



(LXIIIA) (LXIIIB) (LXIV) (LXV)

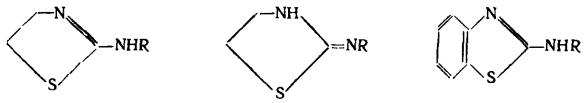
The same result was obtained for 4-phenyl-2-aminothiazole derivatives [91].

In the same way it was found [92] that 2-amino-5-phenyl-4-methyl-2-oxazolines (LXVI, R = H, CH_3, or C_6H_5) exist in the amino-form. It was pointed out [90,92] that the ultraviolet spectra do not give clear-cut information on the structure of these compounds.



(LXVI)

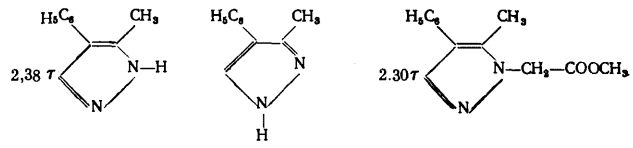
Sheinker and coworkers [93,94] showed that derivatives of 2-aminothiazoline (LXVII) exist in $CDCl_3$ in the amino-form (LXVIIA) if R = H, $CH_2C_6H_5$, or $COCH_3$, and in the imino-form (LXVIIB) if R = COC_6H_5, $COOCH_3$, or $COCCl_3$. In the derivatives with structure (A), the methylene protons in position 4 absorb in the range 6.0–6.1 τ, whereas in the tautomeric and fixed compounds with structure (B) they absorb in the range 6.3–6.5 τ. This effect is due to the deshielding influence of the neighbouring unsaturated nitrogen atom.



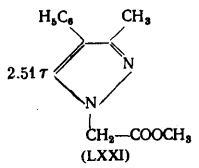
(LXVIIA) (LXVIIB) (LXVIII)

The amino-structure was also assigned to 2-aminobenzothiazoles (LXVIII) on the basis of the CS of the exocyclic nitrogen (310–320 τ). [95]

Comparison of the CS of the vinyl protons of 3-methyl-4-phenylpyrazole (LXIX) and its non-tautomeric derivatives (LXX) and (LXXI) leads to the conclusion that the form (LXIXA) predominates [96].

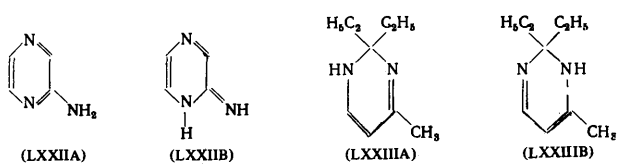


(LXIXA) (LXIXB) (LXX)



(LXXI)

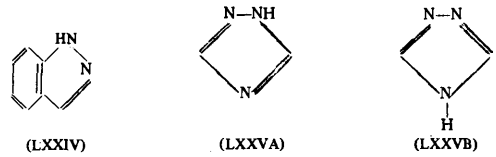
Aminopyrazine in various solvents exists in the amino-form (LXXIIA). This is indicated by the change in the CS and SSCC of the stable protons on breakdown of the aromaticity characteristic of the imino-form (LXXIIB). [20] 1,2-Dihydropyrimidine (LXXIII) in DMSO exists as a mixture of forms A and B in the ratio 2:1. [97]



(LXXIIA) (LXXIIB) (LXXIIIA) (LXXIIIB)

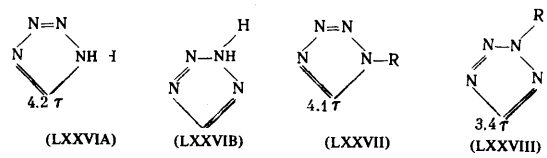
For indazole and its derivatives, the structure (LXXIV) shows best agreement with the PMR spectra [98].

The two signals of the vinyl protons in the spectrum of non-substituted 1,2,4-triazole in hexamethylphosphoramide at −34° indicate that under these conditions the unsymmetrical (1-H)-form (LXXVA) predominates [99].



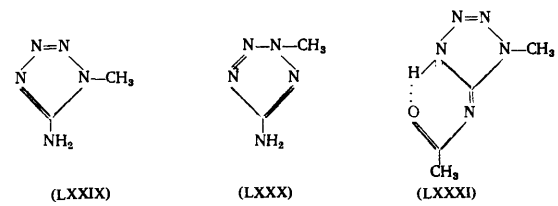
(LXXIV) (LXXVA) (LXXVB)

Benzotriazole exists in the 1-H-form. At room temperature, rapid exchange of protons between positions 1 and 3 is observed, as indicated by the symmetrical spectrum of the aromatic protons [100]. The similarity in the CS of the C–H protons of tetrazole (LXXVI) and its 1-alkyl-derivatives (LXXVII) confirms that in DMPA the tetrazole exists chiefly in the (1-H)-form [101].



(LXXVIA) (LXXVIB) (LXXVII) (LXXVIII)

5-Amino-1-methyl- and 5-amino-2-methyltetrazoles exist in the amino-forms (LXXIX) and (LXXX), but for 5-acetamido-1-methyltetrazole the imino-form (LXXXI), stabilised by IntraMHB, was detected [102].

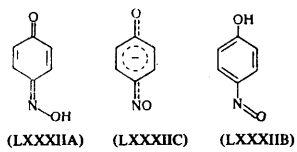


(LXXIX) (LXXX) (LXXXI)

PMR data have demonstrated the equivalence of the four pyrrole rings in various porphyrin derivatives; this is attributed to rapid tautomerism of the amine-imine type [103].

VI. NITROSO-OXIME TAUTOMERISM

Three groups of authors [104–106] have used PMR together with infrared and ultraviolet spectroscopy to study the tautomerism of *p*-nitrosophenols.



(LXXXIIA) (LXXXIIC) (LXXXIIB)

The PMR spectra of 4-nitrosophenol (LXXXII) in DMSO, D_2O acetone, tetrahydrofuran, and other organic solvents indicate that the protons in positions 2 and 6 and 3 and 5 are equivalent. On this basis, Fischer and coworkers [104] concluded that the nitroso-form (B) predominates, with rapid rotation about the C–N bond. Other workers [105,106], however, correctly point to rapid A ⇌ B transformation via the mesomeric anion (C).

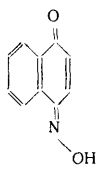
The PMR spectra of form (A), unlike those of form (B), are in fact characterised by different CS for the protons of the ring situated in the *syn*- and *anti*-positions relative

to the oxime group‡. The fact that the CS of the signals of the protons in positions 3 and 5 (and also 2 and 6) coincide, however, does not prove that form (B) predominates, since the same picture will be observed for rapid exchange of (A) with even a small quantity of (B). In the process there is rapid interconversion of equivalent stereo-isomers of form (A).

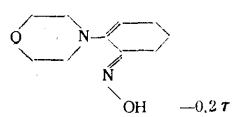
The correct conclusions[105,106] are confirmed by the fact that the values of the CS and SSCC of the nitrosophenol are intermediate between the corresponding values for the model compounds 4-nitrosoanisole and 1,4-benzoquinone-monoxime methyl ether. The addition of a small quantity of HCl or trifluoroacetic acid (TFA) suppresses the ionisation and leads to a sharp decrease in the rate of the tautomeric transformation. This is revealed by a broadening of the PMR signals in these solvents, and in dioxan containing a trace of HCl or TFA it is possible to observe separately the spectra of both tautomers, the concentrations of which correspond to 83–86% of the oxime form and 17–14% of the nitroso-form. An analogous picture is observed in pure dibutyl and dipropyl ethers, in which ionisation is unlikely. These conclusions agree with the ultraviolet spectra in the same solvents.

2-Methyl-, 3-methyl-, 2,6-dimethyl-, and 3,6-dimethyl-derivatives of 4-nitrosophenol, and also 2-chloro-4-nitrosophenol, exist to the extent of more than 95% in the benzoquinonemonoxime form. It has been shown that 3-substituted 1,4-benzoquinonemonoximes exist only in the *anti*-form[106].

Fischer and coworkers[104] compared the PMR spectra of 4-nitroso-1-naphthol and 1,4-naphthoquinonemonoxime methyl ether, and concluded that in DMSO the quinone-oxime form (LXXXIII) predominates.



(LXXXIII)

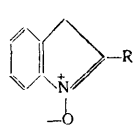


(LXXXIV)

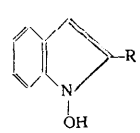
According to PMR data[107], the nitroso-derivative of 1-morpholinecyclohexane in deuterochloroform is present entirely in the form of the oxime (LXXXIV).

VII. NITRONE-HYDROXYLAMINE TAUTOMERISM

Mousseron-Canet and Boca[108,109] showed that the position of the A ⇌ B equilibrium for *N*-hydroxyindoles (LXXXV) depends markedly on the proton-donating properties of the solvent (0% of form A in pyridine and in DMSO, 33% in CCl_4, and 100% in phenol). It was suggested that in neutral solvents and in the absence of a solvent, the tautomers (A) and (B) are combined in associates by InterMHB.



(LXXXVA)

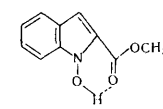


(LXXXVB)

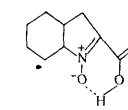
‡Moreover, form (A) should show stronger SSC through the −C=C− bond.

On dilution with proton-donating or proton-accepting solvents, the associates break down and form new InterMHB, which stabilises the corresponding tautomeric form. Since the tautomeric transformation is slow (the proton migrates between the carbon atoms and the hetero-atom[1]), the spectra of tautomers (A) and (B) are observed separately. The spectrum of the nitrone (A) contains the signal of the methylene group (6–7 τ) and the spectrum of the enhydroxylamine (B) contains the signals of the *N*-hydroxyl (3.9–4.3 τ) and vinyl protons. It should be noted that the positive charge on the nitrogen atom decreases the value of the CS of the protons of the condensed aromatic ring (by 0.2–0.3 τ) and, more particularly, of the methyl group in position 2 (by 0.8 to 1.1 τ) in the nitrone form, compared with the enhydroxylamine form.

Methyl *N*-hydroxyindolecarboxylate in chloroform is present almost entirely in the hydroxylamine form[110]. The low value of the CS of the hydroxyl proton indicates the chelate structure (LXXXVI).



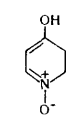
−0,03 τ
(LXXXVI)



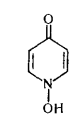
−0,40 τ
(LXXXVII)

On the other hand, with 4-bromo-1-hydroxyindole-2-carboxylic acid the chelate stabilises the nitrone form (LXXXVII).[110]

Nitrone-hydroxylamine tautomerism is observed for 4-hydroxypyridine-*N*-oxide (LXXXVIII). In contrast to the tautomerism of the *N*-hydroxyindoles, however, in this instance the proton migrates rapidly between the oxygen atoms, and the overall PMR spectrum of the two tautomeric forms is observed.



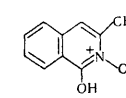
(LXXXVIIIA)



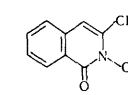
(LXXXVIIIB)

Using models of the tautomeric forms, Katritzky and coworkers[111] found that in aqueous solutions the tautomers (LXXXVIII A and B) are present in the ratio 3 : 2.

On the basis of ultraviolet and PMR spectroscopy, it was concluded[112] that the equilibrium (LXXXIXA ⇌ LXXXIXB) is displaced towards the hydroxylamine form (LXXXIXB).



(LXXXIXA)



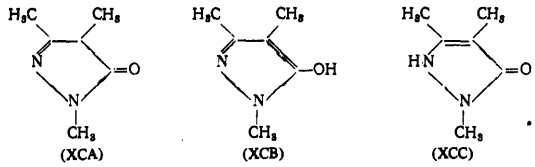
(LXXXIXB)

VIII. COMPLEX TAUTOMERISM OF HETEROCYCLIC COMPOUNDS

This section gives the results of studies of the tautomeric composition of five- and six-membered heterocyclic rings which can exist in more than the two tautomeric forms. Simpler examples were examined above.

1. Five-membered Heterocyclic Rings

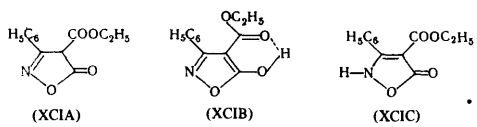
1,3,4-Trimethylpyrazolone-5 (XC), like other 1-substituted pyrazol-5-ones, may exist in three tautomeric forms:



(XCA) (XCB) (XCC)

The PMR spectrum of this compound in chloroform [113], in addition to the intense signals of form (A), shows signals characteristic of forms (B) and (C), or one of them (C(4)–CH_3 8.27; N–CH_3 6.60; NH and (or) OH 1.07 τ). These CS coincide with those for the *N*-methylated derivative, which is a model of form (XCC) and differ from those for the model of form (XCB) (C(4)–CH_3 8.06 τ; N–CH_3 6.46 τ). Thus the pyrazolone (XC) contains form (A) and a smaller quantity of form (C).

3-Phenyl-4-carbethoxyisoxazol-5-one (XCI) can also exist in three tautomeric forms:



(XCIA) (XCIB) (XCIC)

Table 4. Tautomeric composition of derivatives of pyrazol-5-one [30] and isoxazol-5-one [114].

Compound	Chloroform	Methanol	Water	Pyridine
Pyrazol-5-one				
3-Methyl-	A[a]	60%B + 40%C	10%B + 90%C	B
4-Methyl-	A	70%B + 30%C	15%B + 85%C	B
3,4-Dimethyl-	A	35%B + 65%C	C	B
1,3-Dimethyl-	A	25%B + 75%C	C[b]	B
1,4-Dimethyl-	C > A	20%B + 80%C	C	B
1,3,4-Trimethyl-	A > C	C	C	B > C > A
1-Phenyl	A	—	—	—
1-Phenyl-3-methyl	A	C	C[b]	—
1-Phenyl-3,4-dimethyl	50%A + 50%C	C	90%C + 10%A[c]	—
1,3-Diphenyl	A	—	—	—
1-Methyl-3-phenyl	A	—	—	—
Isoxazol-5-one				
3-Methyl-	A[d]	—	—	—
3-Phenyl	A[d]	—	—	—
3-Phenyl-4-methyl	40%A + 60%C	—	—	—
3,4-Tetramethylene-	80%A + 20%C	—	—	—
3-Phenyl-4-carbethoxy-	Bf	—	—	—
3,4-Dimethyl-	70%A[e]	0%A[e]	0%A[e]	30%A[e]

[a] A, B, and C represent the CH-, OH-, and NH-forms respectively (see compounds XC and XCI); [b] 10% A according to ultraviolet spectra [113]; [c] according to Ref. 112; [d] in CCl_4; [e] according to Ref. 115.

The PMR spectrum of its solution in $CHCl_3$ [114] does not contain the signal of a methine proton, and this eliminates the CH-form (A). The mobile proton absorbs in very weak fields (–2.25 τ). This value is much lower than the CS of the group in the NH-form (C) of other isoxazolones (between 0 and +1 τ) [113] and shows good agreement with the chelate structure (B). The tautomeric compositions of other pyrazol-5-ones and isoxazol-5-ones are given in Table 4.

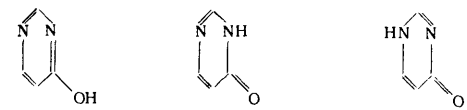
The results in Table 4, obtained by PMR spectroscopy, show that methylation of the nitrogen atom of the pyrazolones increases the concentration of the NH-form (C) at the expense of the CH- and OH-forms (A) and (B). The introduction of an alkyl group in position 4 also displaces the equilibrium considerably towards the NH-form (C) in both pyrazolones and isoxazolones. The CH-form, which predominates in CCl_4 and $CHCl_3$ (particularly in dilute solutions) is almost absent in polar media, in which the NH- and OH-forms are stabilised by InterMHB. The concentration of the OH-form increases with increase in the proton-accepting power of the solvent.

In latter work, the magnetic resonance of the protons [116] and ^{13}C nuclei [117] gave additional information on the tautomerism of 1-phenylpyrazol-5-ones. Electron-donating substituents in position 3 of the ring displace the equilibrium considerably towards the CH-form in various solvents, and electronegative substituents stabilise the OH-form. The influence of substituents and the medium on the keto-enol equilibrium of 2-phenylthiazolin-4-one [118] and 2-phenylthiazolin-5-one [119] has been studied. In the latter instance it was suggested that dilute solutions in polar solvents contain an appreciable quantity of the mesoionic form in addition to the CH- and OH-forms.

Studies of the tautomerism of five-membered heterocyclic compounds by various methods were briefly reviewed in a paper by Elguero and coworkers [30].

2. Six-membered Heterocyclic Rings

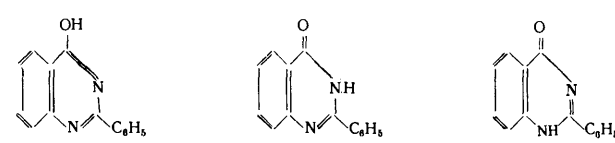
4-Hydroxypyrimidine (XCII) can exist in three tautomeric forms:



(XCIIA) (XCIIB) (XCIIC)

Comparison of the CS and SSCC for 4-hydroxypyrimidine and its methylated derivatives (Table 5), which provide models of the three tautomeric forms, indicates that the predominant form is the quasi-*o*-quinone form (B) in DMSO [120] and in water [121]§. To choose between (B) and (C) it is first of all necessary to compare the CS of the C_5–H signals, which show smaller changes than the others on *N*-methylation [121]. For the SSCC J_{56}, a linear correlation with the bond order is observed (calculation by the MO method for structures A, B, and C [121]). The same method was used to show that a form of type (B) predominates for 4-thiopyrimidine [120].

2-Phenyl-4-hydroxyquinazoline (XCIII) can exist in three analogous tautomeric forms:



(XCIIIA) (XCIIIB) (XCIIIC)

§In agreement with the infrared and Raman spectra [122,123]. According to ultraviolet spectroscopy, tautomers (B) and (C) are present in water in the ratio 2 : 1. [124]

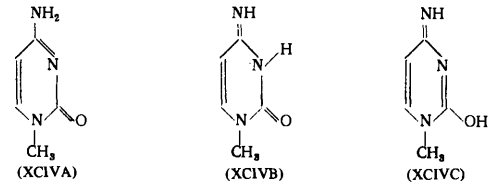
In aromatic dicyclic compounds the signal of the proton in the *peri*-position relative to a carbonyl group lies at lower fields (1.7–1.9 τ) than the other aromatic protons ($\tau > 2.0$), because of the deshielding action of the C=O bond [70,125]. The fact that the PMR spectrum of compound (XCIII) in DMSO contains a low-field doublet signal of the aromatic proton C_5–H (1.87 τ) reduces the problem to the choice between the two oxo-forms (B) and (C). In the *N*-methylated derivatives which are models of forms (B) and (C) the *peri*-proton absorbs at 1.90 τ and 1.77 τ respectively, provinding evidence in support of the amide form (B), in agreement with the infrared and ultraviolet spectra [126].

Table 5. Parameters of the PMR spectra of 4-hydroxypyrimidine and its methylated derivatives [120,121].

Compound	Medium	CSτ,			SSCC, Hz			Model form
		H_2	H_5	H_6	H_2–H_5	H_2–H_6	H_5–H_6	
4-Hydroxypyrimidine	DMSO [a]	1.80	3.63	2.05	1.0	0.5	6.3	—
	D_2O	1.63	3.49	2.02	1.0	1.2	7.15	
3-Methyl-4-pyrimidone	DMSO	1.50	3.58	2.05	0.85	—	6.0	B
	D_2O	1.58	3.45	2.01	0.80	0.6	6.8	
1-Methyl-4-pyrimidone	DMSO	1.70	3.98	2.28	0.5	2.5	7.0	C
	D_2O	1.64	3.67	2.21	0.6	2.5	7.5	
4-Methoxypyrimidine	DMSO	1.27	3.03	1.45	1.1	0.4	5.4	A
	D_2O	1.32	3.05	1.55	1.2	0.8	6.2	

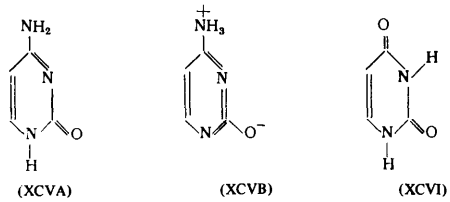
[a] The parameters of the spectra agree with earlier data [19].

The PMR spectrum of 1-methylcytosine (XCIV) with a ^{15}N atom in the amino-group shows splitting (J_{NH} = 90 Hz) of the signal, the intensity of which corresponds to two protons. This provides unambiguous evidence in support of the amino-form (A). [127]



(XCIVA) (XCIVB) (XCIVC)

Analysis of the PMR spectra of cytosine (XCV), for which seven tautomeric forms are possible, confirms the generally accepted form (XCVA) in DMSO and D_2O. [128]



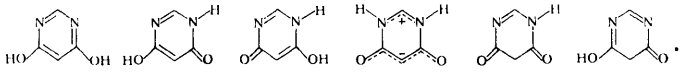
(XCVA) (XCVB) (XCVI)

The CS and SSCC (J_{56}) of cytosine and *N*-methylcytosine (XCIV) almost coincide, and the values differ considerably from those predicted for the bipolar form (XCVB), which was erroneously assumed in earlier work [129]. The tautomerism of cytosine nucleosides has been studied [127, 130,131].

PMR spectroscopy has confirmed the diamide structure of uracil (XCVI), for which six tautomeric forms are possible [19,129]. The PMR spectrum of uracil is shown in Fig. 2. The components of the C_6–H doublet (J_{56} = 7.6 Hz) are split as a result of SSC with the amide proton (J_{61} = 5.7 Hz), and the components of the C_5–H doublet are split to form a triplet, as a consequence of SSC with the two amide protons ($J_{51} = J_{53}$ = 1.4 Hz). On heating, the splitting due to the amide protons disappears as a consequence of their rapid intermolecular exchange, leaving only the splitting due to the SSC of the C_5–H and C_6–H protons. The PMR method has also been used to study many potentially tautomeric derivatives of uracil and thiouracil [132,133]. It has been concluded that the diamide form is preferred.

Figure 2. PMR spectrum of uracil in DMSO (40 MHz). [19]

For 4,6-dihydroxypyrimidine (XCVII), which is an isomer of uracil, six tautomeric forms (A–F) are possible:



(XCVIIA) (XCVIIB) (XCVIIC) (XCVIID) (XCIIE) (XCVIIF)

Table 6. Chemical shifts of the PMR of 4,6-dihydroxypyrimidine and its methylated derivatives [134].

Compound	Medium	CSτ,			Model form
		C_5–H	C_5–H	OH or H	
4,6-Dihydroxypyrimidine (XCVII)	DMSO	1.90	4.85[a]	–1.60[b]	—
	D_2O	1.60	—	—	
N-Methyl derivative (CII)	DMSO	1.76	4.75	–1.30	—
	D_2O	1.46	4.90	—	
O-Methyl derivative (CI)		2.00	2.00	4.56	–2.20	—
		2.07	2.07	4.46	—	
3-Methyl-6-methoxypyrimidone-4- (XCVIII)		1.62	1.62	4.40	—	B
		1.76	1.76	4.42	—	
4,6-Dimethoxypyrimidine (XCIX)	DMSO	1.63	3.85	—	A
Mesomeric betaine (C)	DMSO[c]	—	—	—	D
	D_2O	0.95	4.9	—	

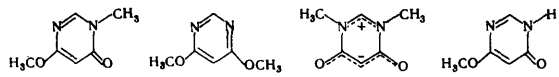
[a] Soluble on heating, C_5–H proton then replaced by deuterium; [b] overall signal of the NH and OH protons; [c] sparingly soluble in DMSO.

Comparison¶ of the CS of 4,6-dihydroxypyrimidine and its *O*- and *N*-methylated derivatives with completely (XCVIII–C) and partly† (CI and CII) fixed structures (Table 6) led to the following conclusion [134]: 1) the mono-*O*-methyl-derivative in aqueous solutions and in DMSO

¶ With allowance for the influence on the CS of the C_2–H and C_5–H protons of the neighbouring OCH_3 and N–CH_3 groups.

† For compound (CI) tautomeric forms of types A, B, C, and F are possible, and for compound (CII) forms of types B, C, D, and E are possible.

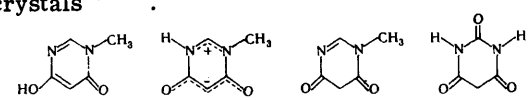
exists in the oxo-hydroxy-form (CI); 2) the mono-*N*-methyl-derivative and 4,6-dihydroxypyrimidine itself exist in DMSO in the oxo-hydroxy-form (CIIB) and (XCVIIB) respectively, whereas in water they exist chiefly in the bipolar ionic form (CIID) and (XCVIID) in equilibrium with a very small quantity of the dioxo-form‡ (CIIE) and (XCVIIE).



(XCVIII) (XCIX) (C) (CI)

The PMR data agree with the results obtained by ultraviolet [135,136] and infrared [137] spectroscopy.

NMR data indicate [134] that barbituric acid in DMSO exists in the trioxo-form (CIII), as in aqueous solutions [139] and crystals [139-141].



(CIIB) (CIID) (CIIE) (CIII)

IX. RING-CHAIN TAUTOMERISM

Ring-chain tautomerism (R-CT) of the electrophilic type (in Jones' terminology [142]) is accompanied in the great majority of examples by the migration of a proton. It can therefore undoubtedly be regarded as a form of prototropic tautomerism§.

In an examination of physical methods used to study R-CT, Jones points out that NMR is becoming one of the most valuable methods used for this purpose [142].

Because of lack of space, we cannot examine the work on R-CT carried out by means of NMR, but the following list, which illustrates Jones' prediction, may to some extent provide a useful supplement to his review.

NMR spectra have been used to study the mutarotation of sugars [144-149], aminosugars [150], and osazones of ascorbic acid [151], and the temperature dependence of the formation of hemiacetals of hydroxyketones [152] and lactones of laevulinic acid [153]. The R-CT of *o*-acylcarboxylic acids [154-159] and the similar transformation of the hemialdehydes of carboxylic acids of the benzene, pyridine, and thiophene series [157,158] have been studied. NMR has been used to study the R-CT of oxazolidines [159,160], various oxadiazines [161-165], thiazolidine- [166] and thiadiazolidine-2-thiones [167], dihydrobenzothiazoles [168], tetrahydropyrimido-4,5-*d*-pyrimidines [169], and the products of the condensation of *o*-hydroxybenzylamine with aldehydes and ketones [170]. R-CT has also been studied in alkaloids which are derivatives of indole [171].

X. DETERMINATION OF THE POINT OF PROTONATION OF UNCHARGED MOLECULES WITH TWO OR MORE PROTON-ACCEPTING CENTRES

Neutral tautomeric forms are the products of the protonation of a mesomeric anion at a given proton-accepting centre. Analogously, the protonation of neutral molecules with two or more proton-accepting centres may lead to the formation of cations with different structures in a state of dynamic equilibrium, which can be regarded as prototropic tautomerism.

The methods examined above are fully applicable to the study of tautomeric equilibrium in these systems by NMR spectroscopy.

Here, as in paragraph IX, we shall restrict ourselves to giving a list (which does not claim to be complete) of papers dealing with NMR studies of the protonation of compounds of various classes: the saturated amides of carboxylic [172-177] and sulphonic [176,178] acids, nitrosoamines [179], phenol and aromatic ethers [180-183], α-diazoketones [184], α,β-unsaturated β-aminocarbonyl compounds [185,189], guanidine [86], nitroguanidine [187], and biguanide [188], 4-dimethylaminoazobenzene [189], pyrroles [190,191] and pyrrolethiazoles [192], thiophenes [193], indoles [194], and indolizines [195,196], imidazoles [197,198] and imidazopyridines [199], pyrazolines [200], various benzazoles [201], 2- [202,203] and 4-pyridones [111,204,205] and their thio-analogues [206], aminopyridines [206], *N*-hydroxypyridine [207], and aminoquinolines [89], 4-phenylpyrimidine [208], and various amino- and hydroxypyrimidines [209], 4,6-dihydroxypyrimidine and its derivatives [134], 1-methylcytosine [127,210], caffeine [211], *s*-triazolo-(1,5*a*)-pyrimidines [212], cinnolines [213], and pteridines [214], nitro- [215,216] and acylazulenes [217] and pseudoazulenes [218], and 3-phenylsydnone [219]. NMR has also been used to study the structures of salts of heterocyclic enamines [220,221].

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‡On the basis of a study of the kinetics of C_5–H deuterium exchange.

§R-CT of the non-prototropic type is regarded as a particular case of valency isomerisation [143].

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Study of the Location of Transition Metal Cations in Synthetic Zeolites Using Electron Paramagnetic Resonance and Optical Spectroscopy

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The application of EPR and optical reflection spectroscopy to the study of zeolites containing first-row transition metal cations is discussed. A qualitative theoretical analysis of the optical and magnetic properties of some ions with an unfilled $(d)^n$ electron shell is given. The most important results of EPR and reflection spectroscopic studies of the behaviour of transition metal cations in synthetic zeolites are presented. 80 references

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I. INTRODUCTION

Synthetic zeolites are widely used for the separation of hydrocarbons by adsorption, for drying gases, and in petroleum refining. The last application is particularly important, because zeolites containing bi- and trivalent metal cations (introduced by cation exchange) are much more active catalysts than the amorphous aluminosilicates previously used. Most workers ascribe the catalytic properties of cation-exchanged zeolites to the polyvalent ions themselves, or to acidic centres formed by the introduction of these ions into the crystal lattice. Hence, location studies of polyvalent metal ions in synthetic zeolite structures are of fundamental importance in understanding their catalytic properties.

Because of the large volume of publications on various properties of zeolites, including a number of contradictory statements, special review articles have been written on the catalytic activity of zeolites[1-4], on the state of water and other molecules adsorbed by zeolites[5], and other similar topics. Some of these reviews discuss the location of polyvalent cations within the lattice, mainly on the basis of structural studies of zeolites containing alkali, alkaline-earth, and rare-earth metal ions.

An attempt is made here to systematise the published results of work on the structure of zeolites containing transition-metal ions. The number of such publications is not large, but it is sufficient to show that zeolites containing transition-metal cations have catalytic properties essentially different from those of zeolites containing alkali or alkaline-earth metal ions. A special feature of the present review is that conclusions regarding the sites occupied by transition-metal cations are drawn entirely from the results of optical and EPR spectral studies of the zeolites. The discussion will be largely confined to zeolites containing cations of the first transition group (ions with an unfilled $3d$ electron shell). The theory of the EPR and optical spectra of these ions is sufficiently well understood, and the spectral results can be interpreted with confidence in the light of the wealth of experimental information on homogeneous complexes. Zeolites containing cations of other transition metals have not so far been investigated by EPR and optical spectroscopy.

1. General Discussion of Synthetic Zeolites and Cation Localisation Sites in their Crystal Lattices

Zeolites, both naturally occurring and synthetic, are crystalline aluminosilicates†. The various forms of zeolites have been described in detail elsewhere, and we shall therefore only briefly consider the properties of zeolites with a three-dimensional skeletal structure, which have the highest adsorption capacity and thermal stability and therefore offer the greatest promise in the field of catalysis. Among the three-dimensional skeletal zeolites, we shall be concerned in particular with the recently developed and widely used synthetic zeolites of types A, X, and Y. The skeleton of these zeolites consists of aluminium–oxygen and silicon–oxygen tetrahedra. Twenty-four of these tetrahedra are joined to form a polyhedron (cubo-octahedron), and the cubo-octahedra are joined by oxygen bridges into the crystalline skeleton of the zeolite. Depending on the aluminium to silicon ratio, these zeolites fall into three types: A ($SiO_2/Al_2O_3 = 2$), X ($SiO_2/Al_2O_3 = 2.2-3$), and Y ($SiO_2/Al_2O_3 = 3.2-5.0$).

In type A zeolites the cubo-octahedra form a simple cubic lattice, similar to the rocksalt structure, but with each ion replaced by a cubo-octahedron. The cubo-octahedra are connected by four-membered oxygen bridges (see Fig. 1*a*). In zeolites of types X and Y the cubo-octahedra are arranged in a lattice of the diamond type, and the bridges connecting the cubo-octahedra consist of six oxygen atoms (see Fig. 1*b*).

Because of their skeletal structure, the zeolites contain holes which are interconnected by windows of well defined sizes. The holes within the cubo-octahedra are termed small holes, and their size is practically the same in zeolites A, X, and Y ($v = 150$ Å^3, $d = 6.5$ Å). The hollows bounded by the outer surfaces of the cubo-octahedra and of the oxygen bridges are termed large zeolite holes. Their diameter in A, X, and Y zeolites is ~ 11.5Å,

† Zeolites have been synthesised in which the aluminium is replaced by gallium[6,7], or chromium[8,9], and the silicon is replaced by germanium[6], beryllium, or magnesium[10].

and their volume is of the order of 800 Å^3.[11] The diameter of the six-membered oxygen windows leading from the small to the large holes is approximately 2 Å. In type-A zeolites the large holes are interconnected by 8-membered oxygen windows ($d \simeq 4.2$ Å), and in zeolites of types X and Y by 12-membered oxygen windows 8–9 Å in diameter.

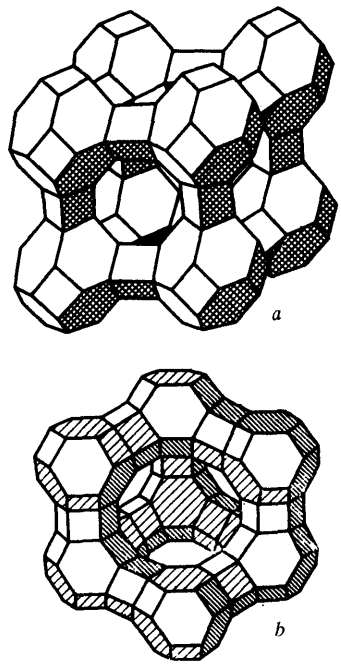

Figure 1. Three-dimensional model of the alumina–silica lattice of zeolites (*a*) of type A and (*b*) of types X and Y.

Since the aluminium–oxygen tetrahedra carry an excess of negative charge, the zeolite structure must include an equivalent amount of metal cations (usually Na^+ or Ca^{2+}). These ions can readily be exchanged[12] by other ions, and therefore a great variety of cationic forms of zeolite can be prepared. Without discussing cation exchange in detail, we note in passing that the process is determined by the nature of the metal ions, their size and charge, the pH of the medium, the temperature, and the structure of the zeolite[13–19]. The crystal lattice parameters of the zeolite are not significantly altered by cation exchange, up to the point where the crystal lattice breaks down. The stability of the zeolite structure towards exchange is determined mainly by the pH of the medium, the extent of exchange, and the zeolite type.

One of the most important problems in the structure of cationic zeolite forms concerns the sites occupied by the metal ions which compensate the charge on the aluminium–oxygen tetrahedra. In zeolites of types X and Y, three types of cation site are usually distinguished[20]: *S*I sites are the centres of the hexagonal prisms formed by the oxygen connecting links between cubo-octahedra (16 sites per unit cell); *S*II sites are the hexagonal oxygen windows which connect the large and the small holes (32 sites per unit cell); *S*III sites are the walls of the channels interconnecting the large holes (48 sites per unit cell). In type-A zeolites the *S*I sites are absent. The differences between the sites which can be occupied by cations have recently been identified in greater detail. Sites in the six-membered oxygen windows adjacent to a large hole have been designated *S*II, those adjacent to a small hole *S*II′. The location of an ion within a small zeolite hole near a six-membered oxygen window leading to the cavity of a hexagonal oxygen prism (*S*I site) is referred to as an *S*I′ site. Some characteristics of the sodium forms of synthetic type A, X, and Y zeolites are listed in Table 1.

Table 1. Some characteristics of the Na-forms of synthetic zeolites (types A, X, Y).

Zeolite type	Composition of the elementary cell of the hydrated zeolite	Size of windows, Å	Population of sites by univalent cations			Lattice parameters, Å	Adsorption capacity for water of 1 g of dehydrated zeolite
			I	II	III		
A	$Na_{12}[(AlO_2)_{12}(SiO_2)_{12}]\cdot 27H_2O$	4.2	—	8	4	12.32	0.30
X	$Na_{86}[(AlO_2)_{86}(SiO_2)_{106}]\cdot 264H_2O$	8.0	16	32	38	24.95	0.36
Y	$Na_{56}[(AlO_2)_{56}(SiO_2)_{136}]\cdot 264H_2O$	8.0	16	32	8	24.70	0.35

The sites available for cations in zeolites of types X and Y are shown schematically in Fig. 2. Depending on the symmetry of the surroundings, two types of site can be distinguished: those with C_{4v} and those with C_{3v} symmetry.

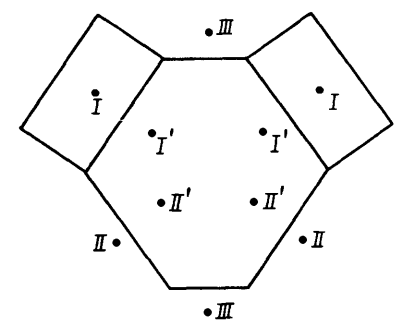

Figure 2. Structure of type X and Y zeolites (diagrammatic). The points show possible localisation sites for ions.

We know from X-ray diffraction studies of zeolites that the hexagonal oxygen windows of the cubo-octahedra are trigonally distorted. They consist of two unequal equilateral triangles, rotated by 60°, formed by the oxygen atoms of the lattice. The interplanar spacing of these triangles is several tens of angstroms.

As a result, the electrical ligand field for cations in *S*I′, *S*II′, and *S*II sites has C_{3v} symmetry (trigonal, compressed or extended along the trigonal axis of the tetrahedron depending on the conditions of the particular

system). The three planar ligands, in this case, are the oxygen atoms of the lattice, and the fourth ligand could be either a residual water molecule (or its fragments O^{2-} or OH^-), or any other adsorbate molecule. When a cation is localised in the plane of the six-membered oxygen window it experiences a ligand field with D_{3h} symmetry (special case of C_{3v}). However, an environment corresponding to a trigonally distorted octahedron can be realised also by the adsorption of three fairly small molecules on a cation in an *S*II position (see below).

The ligand field surrounding *S*I and *S*II sites has a distorted octahedral symmetry. In the former, the ligands are 6 negatively charged oxygen atoms from the zeolite lattice, which form a fairly regular octahedron. (These sites are not accessible to adsorbed molecules.) When a cation is localised on the surface of a large zeolite hole (site *S*III), one or more (up to 4) of the ligands can be provided by the lattice oxygen atoms, and the remainder may be residual water molecules, or other molecules. As will be shown below, the environment of delocalised cations ("floating" in the large holes) of fully hydrated zeolites is almost perfectly octahedral.

2. Basic Physicochemical Methods of Studying Zeolite Structure. Application of EPR and Reflection Optical Spectroscopy to the Study of Zeolites Containing Cations of the First Transition Series

Almost all the physicochemical methods used in the study of heterogeneous catalysts have been applied to the study of zeolite structures. X-ray diffraction and infrared spectroscopy are the most widely used spectroscopic methods. Other methods include chemical analysis, calorimetry, thermogravimetry, differential thermal analysis, electrical and dielectric measurements, tracer studies, measurements of static magnetism, etc. Some problems have been studied by a combination of these methods, with satisfactory results.

X-ray analysis gives the most direct indication of the sites in which metal cations are localised in zeolites, but the results are difficult to interpret because sufficiently large single crystals are not yet available, and powder patterns are exceedingly complicated. Furthermore, the method becomes unreliable at relatively low concentrations of added cations, when these do not give rise to a distinct sublattice. Adsorption and desorption phenomena on cationated zeolite forms are not easily studied by X-ray diffraction. Hence, the usefulness of the X-ray method is limited essentially to studies of the distribution of cations in zeolites.

I. r. spectroscopy is used in the main to study the nature of the acidic centres and the state of the surface hydroxyl groups in zeolites. Its relevance to studies of cation localisation sites stems from the perturbation of the vibrational spectra of adsorbed molecules (e.g. CO) by interaction with cations[21]; this provides information on the accessibility to adsorbed molecules of cations on various sites.

When the zeolite contains ions of transition metals, which are usually paramagnetic and absorb in the u.v. and visible regions of the spectrum, the combined application of EPR and reflection spectroscopy has given very promising results. The EPR and the optical spectra of transition-metal ions are very sensitive to the symmetry of their immediate environment. Hence, the localisation of ions in various crystal lattice sites can be identified, since these sites can be distinguished by the symmetry of their surroundings.

The EPR and optical spectroscopy methods are to some extent complementary, since the splitting of the electronic levels of the ions by the crystal field can easily be determined by the optical method, and the parameters of the EPR spectra are dependent on this splitting. It should be noted, however, that the EPR method gives best results with magnetically dilute samples, containing low concentrations of paramagnetic ions. On the other hand, the optical spectra of such samples tend to be insufficiently intense, owing to the low extinction coefficients of the transition-metal ions. Hence, combined EPR–optical spectral measurements is far from universally applicable.

The interpretation of optical and EPR spectra for transition-metal ions requires a knowledge of the energy levels of the ions and of the corresponding electronic wave functions in ligand fields of different symmetries. Qualitative and semi-quantitative interpretations of EPR and optical effects are usually attempted with the help of ligand-field theory, whose limitations and methods are discussed in detail elsewhere (see, for example, Refs. 22 and 23).

Most of the problems, however, concern small distortions of octahedral and tetrahedral fields, and their solution relies on the application of perturbation theory. Large distortions, e.g. the removal of an entire ligand from the coordination sphere, are not considered as a rule. Therefore, before reviewing the published data, we shall briefly summarise the results of our calculations of the electronic levels and spin-Hamiltonian constants for ions with a $(3d)^n$ electron shell in low-symmetry ligand fields. These calculations allow us to interpret more reliably the EPR and optical spectra of transition-metal cations in zeolites, and they can also be applied to the interpretation of corresponding data for oxide catalysts, on whose surface the coordination of ions may be abnormal[24]. The calculations are directly relevant, also, to the structure of "atypical" complexes of transition metals with structurally complex ligands. For example, in the bivalent copper complex $[Cu(tren)OH]^+$, studied in our laboratory[25], the ligand field has C_3 symmetry, whereas weakly distorted octahedral and tetrahedral structures are more usual for copper.

II. CALCULATIONS OF THE OPTICAL AND MAGNETIC PROPERTIES OF FIRST-ROW TRANSITION METAL IONS IN LOW-SYMMETRY LIGAND FIELDS

A full account of our qualitative evaluation of energy levels and spin-Hamiltonian constants for ions with a $(3d)^n$ electronic configuration in low-symmetry ligand fields lies beyond the scope of the present review. However, our subsequent discussion of experimental results by EPR and optical spectroscopy methods for zeolites containing first-row transition metal cations will be made more meaningful by a brief examination of the following types of ligand field distortion, which (as already stated) are found in zeolites:

1. Tetragonal distortions of a ligand field with O_h symmetry (regular octahedron), including the transition to a square planar symmetry by gradual removal of the two ligands on one of the tetrad axes, and also to axial symmetry by gradual removal of the 4 ligands in the plane perpendicular to the tetrad axis (Fig. 3*a*).

2. Distortions of a trigonal bipyramid, analogous to the above (Fig. 3*b*).

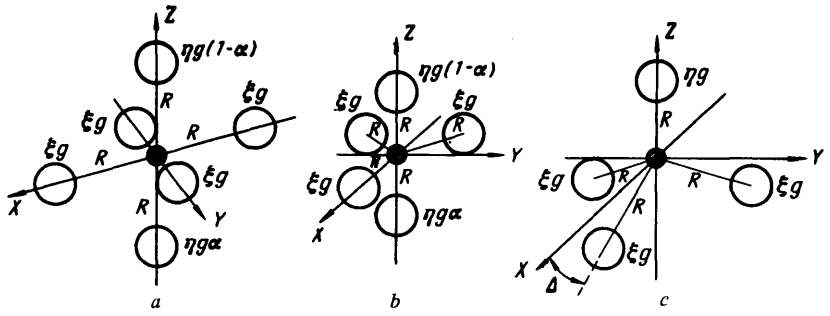

Figure 3. Models of complexes with different symmetry: (*a*) C_{4v}, (*b*) C_{3v} pyram, and (*c*) C_{3v} tetr. ξg is the effective charge on the ligands in the plane; $\eta g(1-\alpha)$ and $\eta g\alpha$ $(0 \leqslant \alpha \leqslant 1)$ are the effective charges on the ligands located on the Z axis.

3. Distortions of a tetrahedron (type C_{3v}), including the continuous transition from a planar triangular configuration to a tetrahedron compressed along the trigonal axis (Fig. 3*c*).

These distortions in the ligand field are modelled by varying the charges on the ligands located on the z-axis $[\eta q(1-\alpha)$ and $\eta q\alpha]$ or in the xy plane $[\xi q]$, and also by varying the angle Δ between the planar ligand M and the xy plane (see Fig. 3). The distances between the central ion and all the ligands are assumed to be identical and equal to R.

We shall consider only the special cases of strong and weak ligand field, because the intermediate field approximation requires electronic computation and is usually confined to specific ions in fields of known symmetry.

Ligand fields are termed weak if they split the ground state by an amount smaller than the distance to the nearest excited state but greater than the spin–orbital interaction constant λ for the corresponding ions.

Tables 2 and 3 show the angular components of the electronic wave functions, and expressions for the corresponding eigenvalues of the energy, for the strong and the weak field case respectively, calculated by the ligand field theory[22,23]. The parameters ξ, η, and $\sin^2\Delta$ have already been defined (see Fig. 3); the quantities F_2 and F_4 are the coulombic interaction integrals between an electron localised at the central ion and the spherical harmonics of a ligand field of the second and the fourth order respectively (see Ref. 23 for a more detailed discussion).

The electronic energy levels of ions in the above fields are shown in Figs. 4 and 5. The plots are constructed for $F_4/F_2 = 0.15$ because this case exemplifies nearly all possible intersections of the resulting electronic levels. Similar plots for different values of the ratio F_4/F_2 can easily be made by reference to Tables 2 and 3.

The $(3d)^n$ electron configuration (n = 2, 3, ..., 9) in a strong crystal field is obtained by progressive population of the states derived by us for a single $3d$ electron, with account being taken of Pauli's principle.

The energy levels of transition-metal ions in the free state follow Hund's rule, and therefore the following high-spin states are chosen as the initial levels in the weak field approximation of the ligand field theory:

Configuration	Ground state	Spin	Angular Momentum	Ion
d^1, d^9	^2D	$^1/_2$	2	Ti^{+3}, V^{4+}, Cr^{5+}, Cu^{2+}, Mn^{6+}
d^4, d^6	^5D	2	2	Cr^{2+}, Fe^{2+}, Co^{3+}, Mn^{3+}
d^3, d^7	^4F	$^3/_2$	3	Cr^{3+}, Co^{2+}, V^{2+}
d^2, d^8	^3F	1	3	Cr^{4+}, Ni^{2+}, Co^{+}, V^{3+}
d^5	^6S	$^5/_2$	0	Mn^{2+}, Fe^{3+}

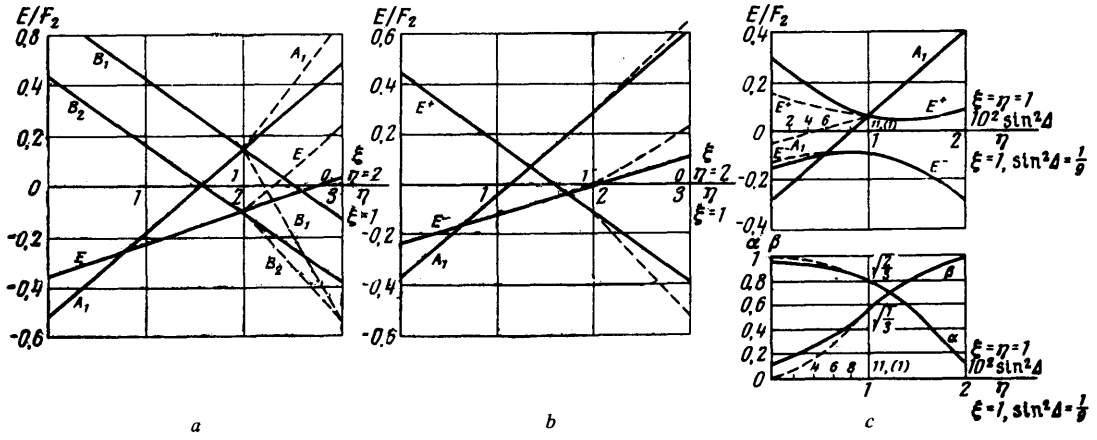

Figure 4. Energy levels of one $3d$ electron in ligand fields of symmetry (*a*) C_{4v}, (*b*) C_{3v} pyram, and (*c*) C_{3v} tetr in units of F_2 $(F_4/F_2 = 0.15)$. Plots of the coefficients in the wave functions are also shown in Fig. 4*c*. The full lines refer to changes in the parameter η at constant $\xi = 1$ (*a*, *b*) or $\xi = 1$, $\Delta = \Delta_{tetr}$; the broken lines refer to changes in the parameter ξ at constant $\eta = 2$ (*a*, *b*) or to changes in the parameter $\sin^2\Delta$ at constant $\xi = \eta = 1$ (*c*).

Table 2. Angular components of the wave functions and corresponding eigenvalues of the energy for one $3d$ electron in electrical ligand fields of symmetry C_{4v}, C_{3v} pyram, and C_{3v} tetr.

C_{4v}			C_{3v} pyram			C_{3v} tetr		
Symbol	Ψ	E	Symbol	Ψ	E	Symbol	Ψ	E
A_1	Y_2^0	$2a_2+2a_4$	A_1	Y_2^0	$2a_2+2a_4$	A_1	Y_2^0	$2a_2+2a_4$
B_1	$\frac{1}{\sqrt{2}}\left(Y_2^2+Y_2^{-2}\right)$	$-2a_2+\frac{1}{3}a_4+b$	E^-	$\frac{1}{\sqrt{2}}\left(Y_2^1\pm Y_2^{-1}\right)$	$a_2-\frac{4}{3}a_4$	E^-	$\beta Y_2^2+\alpha Y_2^{-1}$ $\beta Y_2^{-2}-\alpha Y_2^1$	$-\frac{a_2+a_4}{2}-\sqrt{h}$
B_2	$\frac{1}{\sqrt{2}}\left(Y_2^2-Y_2^{-2}\right)$	$-2a_2+\frac{1}{3}a_4-b$	E^+	$\frac{1}{\sqrt{2}}\left(Y_2^2\pm Y_2^{-2}\right)$	$-2a_2+\frac{1}{3}a_4$	E^+	$\alpha Y_2^2-\beta Y_2^{-1}$ $\alpha Y_2^{-2}+\beta Y_2^1$	$-\frac{a_2+a_4}{2}+\sqrt{h}$
E	$\frac{1}{\sqrt{2}}\left(Y_2^1\pm Y_2^{-1}\right)$	$a_2-\frac{4}{3}a_4$						

$a_2=\frac{1}{7}F_2(-2\xi+\eta)$; $b=\frac{5}{6}F_4\xi$;
$a_4=\frac{1}{7}F_4\left(\frac{3}{2}\xi+\eta\right)$.

$a_2=\frac{1}{7}F_2\left(-\frac{3}{2}\xi+\eta\right)$;
$a_4=\frac{1}{7}F_4\left(\frac{9}{8}\xi+\eta\right)$.

$a_2=\frac{1}{7}F_2\left[\left(-\frac{3}{2}+\frac{9}{2}\sin^2\Delta\right)\xi+\eta\right]$;
$a_4=\frac{1}{7}F_4\left[(35\sin^4\Delta-30\sin^2\Delta+3)\frac{3}{8}\xi+\eta\right]$;
$h=\left(\frac{a_2+a_4}{2}\right)^2+c^2+2a_2^2+\frac{4}{9}a_4^2-3a_2a_4$;
$c^2=\frac{25}{16}\sin^2\Delta\cdot\cos^2\Delta\cdot F_4^2\xi^2$.

*In Tables 2 and 3 the quantities F_2 and F_4 are taken to be positive. The sign of the product of the unit electronic charge and of unit charge on the ligand is included in the tabulated values of F_2 and F_4.

Table 3. Angular components of the wave functions and corresponding eigenvalues of the energy of ions with d^2 and d^7 electronic configuration in weak ligand fields of symmetry C_{4v}, C_{3v} pyram, and C_{3v} tetr.

C_{4v}			C_{3v} pyram			C_{3v} tetr		
Symbol	Ψ	E	Symbol	Ψ	E	Symbol	Ψ	E
A_1	Y_3^0	$\frac{4}{5}a_2-2a_4$	A_1^-	Y_3^0	$\frac{4}{5}a_2-2a_4$	A_1^-	$\alpha'Y_3^0+\beta'\frac{(Y_3^3-Y_3^{-3})}{\sqrt{2}}$	$-\left[\frac{1}{10}a_2+\frac{3}{2}a_4+\sqrt{g}\right]$
B_1	$\frac{1}{\sqrt{2}}(Y_3^2-Y_3^{-2})$	$\frac{7}{3}a_4-b$	A_1^+	$\frac{1}{\sqrt{2}}(Y_3^3-Y_3^{-3})$	$-a_2-a_4$	A_1^+	$\beta'Y_3^0-\alpha'\frac{(Y_3^3-Y_3^{-3})}{\sqrt{2}}$	$-\left[\frac{1}{10}a_2+\frac{3}{2}a_4-\sqrt{g}\right]$
B_2	$\frac{1}{\sqrt{2}}(Y_3^2+Y_3^{-2})$	$\frac{7}{3}a_4+b$	A_2	$\frac{1}{\sqrt{2}}(Y_3^3+Y_3^{-3})$	$-a_2-a_4$	A_2	$\frac{1}{\sqrt{2}}(Y_3^3+Y_3^{-3})$	$-a_2-a_4$
E^-	$\alpha(Y_3^{-3}\pm Y_3^3)+$ $+\beta(Y_3^1\pm Y_3^{-1})$	$-\frac{1}{5}a_2-\frac{2}{3}a_4-\sqrt{h}$	E^-	$\frac{1}{\sqrt{2}}(Y_3^1\pm Y_3^{-1})$	$\frac{3}{5}a_2-\frac{1}{3}a_4$	E^-	$\alpha Y_3^{-2}-\beta Y_3^1$ $\alpha Y_3^2+\beta Y_3^{-1}$	$\frac{3}{10}a_2+a_4-\sqrt{h}$
E^+	$\beta(Y_3^{-3}\pm Y_3^3)-$ $-\alpha(Y_3^1\pm Y_3^{-1})$	$-\frac{1}{5}a_2-\frac{2}{3}a_4+\sqrt{h}$	E^+	$\frac{1}{\sqrt{2}}(Y_3^3\pm Y_3^{-3})$	$\frac{7}{3}a_4$	E^+	$\beta Y_3^{-2}+\alpha Y_3^1$ $\beta Y_3^2-\alpha Y_3^{-1}$	$\frac{3}{10}a_2+a_4+\sqrt{h}$

$a_2=\frac{1}{7}F_2(-2\xi+\eta)$;
$a_4=\frac{1}{7}F_4\left(\frac{3}{2}\xi+\eta\right)$; $b=\frac{5}{6}F_4\xi$
$h=\left(\frac{1}{5}a_2+\frac{2}{3}a_4\right)^2+\frac{3}{5}b^2-(a_2+a_4)\times$
$\times\left(-\frac{2}{5}a_2+\frac{1}{3}a_4\right)$.

$a_2=\frac{1}{7}F_2\left(-\frac{3}{2}\xi+\eta\right)$;
$a_4=\frac{1}{7}F_4\left(\frac{9}{8}\xi+\eta\right)$.

a_2, a_4 — see Table 2
$g=\left(\frac{1}{10}a_2+\frac{3}{2}a_4\right)^2+c_{A_1}^2-\left(-\frac{4}{5}a_2+2a_4\right)(a_2+a_4)$;
$h=\left(\frac{3}{10}a_2+a_4\right)^2+c_E^2+\frac{3}{7}a_4\left(-\frac{3}{5}a_2+\frac{1}{3}a_4\right)$;
$c_{A_1}^2=\frac{90}{112}F_4^2\xi^2\sin^2\Delta\cos^2\Delta$; $c_E^2=\frac{10}{16}F_4^2\xi^2\sin^2\Delta\times\cos^2\Delta$.

Since the splitting of high-spin levels which weak ligand fields induce in the $(3d)^6$ and $(3d)^4$ electronic configurations is similar to the splitting in strong ligand fields of the $(3d)^1$ and $(3d)^9$ configurations respectively, it can be discussed by reference to the results given in Table 2 and Fig. 4.[22,23]

We shall not be concerned with the behaviour of ^6S high-spin levels in weak ligand fields for $(3d)^5$ electronic configurations. The optical spectra of these ions are relatively insensitive to changes in the symmetry of the external field, and their intensity is extremely low (spin-forbidden transitions). Because of the absence of an

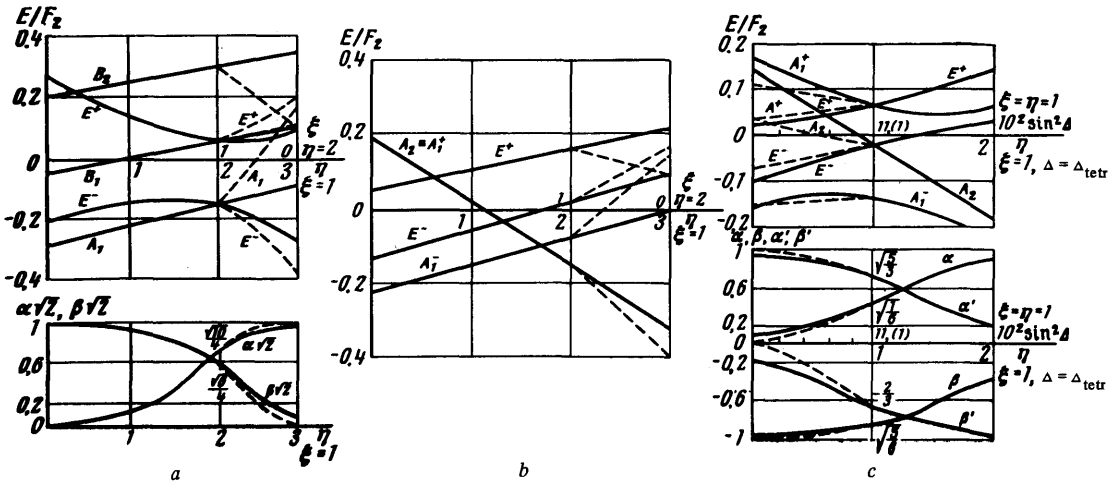

Figure 5. Splitting of the high-spin F-levels arising from the electronic configurations d^2 and d^7 in units of F_2 ($F_4/F_2 = 0.15$) in weak ligand field of symmetry (*a*) C_{4v}, (*b*) C_{3v} pyram, and (*c*) C_{3v} tetr. Figs. 5*a* and 5*b* also show plots of the coefficients in the wave functions. (The significance of the full and the broken lines is defined in the caption to Fig. 4.)

Table 4. Expressions for the spin-Hamiltonian constants of the Cu^{2+} and Co^{2+} ions in different ligand fields.

Ion	n	Ligand field symmetry	$g_\parallel$	$g_\perp$	D	Remarks
Cu^{2+}	9	C_{4v}, stretched octahedron ($\xi = 1; \eta < 2$)	$2+\frac{8\lambda}{\Delta_{B_1B_2}}$	$2+\frac{2\lambda}{\Delta_{B_1E}}$	—	$\lambda>0;\ \Delta_{ij}>0$
		C_{4v}, compressed octahedron ($\xi<1, \eta=2$) ($\xi=1, \eta>2$)	2	$2+\frac{6\lambda}{\Delta_{A_1E}}$	—	$\lambda>0;\ \Delta_{ij}>0$
		C_{3v}, compressed bipyramid ($\xi=1; \eta>1,4$) ($\xi=0\div1; \eta=1$)	2	$2+\frac{6\lambda}{\Delta_{A_1E^-}}$	—	$\lambda>0;\ \Delta_{ij}>0$
		C_{3v}, compressed tetrahedron ($\eta>1; \sin^2\Delta=1/9$)	2	$*2+6\lambda$	$(\alpha^2/\Delta_{A_1E^-}+\beta^2/\Delta_{A_1E^+})$	$\lambda>0;\ \Delta_{ij}>0$
		Compressed tetrahedron C_{3v}	$**g_\parallel>g_\perp>2$		$D<0$	spin ground state $\pm3/2$
		Regular tetrahedron d	$2-\frac{8\lambda}{\Delta_{A_1^-A_2}}$	$2-\frac{8\lambda}{\Delta_{A_1^-A_2}}$	$D=0$	$\lambda<0;\ \Delta_{ij}>0$
		Stretched tetrahedron C_{3v}	$**2<g_\parallel<g_\perp$		$D>0$	spin ground state $\pm1/2$
Co^{2+}	7	Trigonal pyramid C_{3v}	2	$2-12\lambda/\Delta_{A_1^-E^-}$	$D=\frac{6\lambda^2}{\Delta_{A_1^-E^-}}$	spin ground state $\pm1/2$ $\lambda<0;\ \Delta_{ij}>0$
		Planar triangle D_{3h}	2	$2-\frac{12\lambda}{\Delta_{A_1^-E_2^-}}$	$D=\frac{6\lambda^2}{\Delta_{A_1^-E^-}}$	spin ground state $\pm1/2$ $\lambda>0;\ \Delta_{ij}>0$

* The coefficients α and β are presented graphically in Fig. 4*c*.

** Only the analytical results are presented because the expressions are too complicated.

orbital angular momentum, the g-factor of the EPR spectrum is close to the free-electron value (*a*), and the hyperfine coupling constants are insensitive to the symmetry of the surroundings.

Table 4 lists the expressions for the spin-Hamiltonian constants of the Cu^{2+} and Co^{2+} ions in different ligand fields, needed for our subsequent discussion, and obtained from the data in Tables 2 and 3 by the method of Abragam and Pryce[26]. These expressions include the spin–orbital interaction constant (λ) of the corresponding ion and the splitting constant of its i and j electronic levels in the ligand field (Δ_{ij}).

III. RESULTS OF STUDIES ON ZEOLITES CONTAINING METAL IONS OF THE FIRST TRANSITION ROW

We shall consider the results of recent studies on zeolites containing first-row transition metal cations with a charge not greater than three, because no zeolite has yet been synthesised in which the charge of the alumina–silica lattice is compensated by cations in a still higher valency state. The results are best discussed in the order of increasing atomic number of the element introduced into the zeolite.

Scandium. The electronic configuration of the ground state of the scandium atom is $[A](3d)^1(4s)^2$, where [A] denotes the electronic structure of the argon atom. Doubly charged Sc^{2+}, with the electronic configuration $[A](3d)^1$, can be observed in principle by EPR and optical spectroscopy, but there are no references in the literature to zeolites containing bivalent scandium ions. A zeolite of type Y containing tervalent scandium ions with the [A] electronic configuration has been investigated[27] as a cumene cracking catalyst. In the same work it was shown by X-ray diffraction that extensive exchange of Na^+ ions by Sc^{3+} ions tends to disrupt the zeolite lattice.

Titanium. The electronic configuration of the ground state of the free titanium atom is $[A](3d)^2(4s)^2$. No work on zeolites containing Ti^{2+} or Ti^{3+} ions has come to our notice, probably because of the difficulty of preparing these zeolite forms.

Vanadium. The electronic configuration of the ground state of the free vanadium atom is $[A](3d)^3(4s)^2$.

Vanadium has been introduced into zeolites only as the doubly charged vanadyl cation $[VO]^{2+}$. The EPR spectra of these zeolites are reported[28] to be identical to the EPR spectrum of vanadyl in solution. No other information concerning the behaviour of vanadyl in the zeolite lattice is available. A strong internal ligand field is known to exist in the vanadyl ion: this field is mainly responsible for the optical and paramagnetic properties of the ion. The spectral parameters of the vanadyl ion are relatively insensitive to the coordination of the cation, and therefore a detailed description of the behaviour of vanadyl in zeolites cannot be expected from EPR and optical spectral studies. This conclusion, however, is not indisputable.

Zeolites containing vanadium ions in other valency states have not been prepared or investigated. An optical study of zeolites containing V^{3+} cations would be very interesting.

Chromium. The electronic configuration of the ground state of the free chromium atom is $[A](3d)^5(4s)^1$. Only zeolites containing tervalent chromium ions have so far been prepared.

We shall consider the effects which can be expected in the optical spectra of zeolites containing Cr^{3+} ions.

The spectrum of the octahedral $[Cr(H_2O)_6]^{3+}$ complex has been discussed fully[29]. The splitting diagram of the ^4F level of the ground state of the free Cr^{3+} ion in fields of C_{4v} symmetry (distorted along the four-fold octahedral axis) is shown in Fig. 5*a* with the sign of the vertical axis reversed. The optical spectra of aqueous solutions of tervalent chromium salts reveal two optical transitions within the ^4F level ($^4A_2 \rightarrow {}^4T_1$; $^4A_2 \rightarrow {}^4T_2$). It is evident from Fig. 5*a* that for a ligand field corresponding to an octahedron stretched along its four-fold axis (case of $\eta < 2$, $\xi = 1$) the absorption bands of the optical spectrum should split into two, the transitions $B_2 \rightarrow B_1$ and $B_2 \rightarrow A_1$ remaining approximately in the original positions and the transitions $B_2 \rightarrow E^-$ and $B_2 \rightarrow E^+$ undergoing a shift towards the red end of the spectrum. If the absorption bands are sufficiently broad, this effect manifests itself as a broadening of the bands accompanied by a displacement of their centre of gravity towards longer wavelengths. The same shift, but without band broadening, is produced by a weakening of the ligand field whilst retaining the octahedral symmetry.

If the octahedron surrounding the ion is compressed along its four-fold axis, the absorption bands of the Cr^{3+} ions are again broadened, but the shift is towards the blue end of the spectrum.

The optical reflectance spectra in diffuse scattered light of A, X, and Y zeolites containing tervalent chromium ions have been investigated by the present writers together with Minachev and others[30]. Since all the spectra (after cation exchange) consisted of three absorption maxima at 285, 425, and 625 nm, i.e. in the same positions as those in the optical spectra of Cr^{3+} solutions, it was concluded that the chromium ions exist as hexaquo complexes $[Cr(H_2O)_6]^{3+}$ in the zeolite structure. After vacuum heat treatment at 200–250° the samples lost most of the adsorbed water, and the absorption bands of the optical spectrum became broader and were shifted towards the red. This effect was explained by assuming that the ligand field had been weakened by the removal of the water from the second coordination sphere of the chromium ion. It follows from the above discussion that the replacement of one water molecule in the first coordination sphere of the Cr^{3+} ion by a weaker ligand (e.g. oxygen from the zeolite lattice) should lead to the same result. Both the two proposed band-broadening and band-shift mechanisms probably operate in the present system.

In zeolites of types A and X these changes in the optical spectrum were found to be irreversible, since the original spectrum of the hexaquo complex could not be reproduced by hydrating the samples at room temperature. This effect was ascribed to incipient breakdown of the zeolite lattice of CrNaX and CrNaA upon vacuum heat treatment at temperatures above 200°, which had been demonstrated independently by differential thermal analysis and thermovolumetric analysis. In contrast, with CrNaY zeolite (known to be stable up to 700°) the reflectance spectrum after water adsorption at room temperature was found to be practically identical to the spectrum recorded on the initial sample after cation exchange.

After vacuum heat treatment at 400° the optical spectrum of CrNaY zeolite showed some radical changes: the sample developed a grey colour and began to absorb over practically the whole of the visible region of the spectrum, suggesting complete breakdown of the hydration shell of the Cr^{3+} ions. The spectral changes were irreversible towards water adsorption, despite the evidence (from differential thermal and thermovolumetric analyses) that the zeolite crystal structure had survived the heat treatment. This observation was interpreted by assuming that the dehydrated Cr^{3+} ions at high temperatures can penetrate within the sodalite cells, where they experience a ligand field with a lower symmetry (probably on *SI'* sites). These holes are too small to accommodate the hexaquochromium complexes, and therefore the optical spectra after exposure to water do not revert to their original form (though some minor changes can be seen). This interpretation, which is consistent with the demonstration[31] by X-ray diffraction analysis that tervalent lanthanum cations penetrate into the small holes of LaNaY zeolite after dehydration, was further confirmed by studies of the adsorption of ethanol and diethyl ether.

Tsitsishvili and Urushadze[32] have reported an EPR study of magnetically concentrated samples of CrNaA zeolite. They observed the EPR spectra of samples, both hydrated and vacuum-dehydrated at room temperature, and found in every case a single broad line (up to 500 G) with a g-factor close to 2, which they ascribed to the octahedral hexaquocomplex $[Cr(H_2O)_6]^{3+}$. After dehydration at room temperature the lines became slightly broader.

Chromium-containing zeolites dehydrated at higher temperatures have not been studied by EPR, because the thermally stable CrNaY zeolites tend to contain iron impurities which give a broad and strong EPR signal[33], and interfere with the study of other paramagnetic ions with broad signals‡.

Before examining in detail the results of EPR measurements, we shall consider some effects which may be present in the EPR spectra of Cr^{3+} ions localised in *SI'* sites. As stated above, the ligand field in this case has the symmetry of a tetrahedron distorted along a trigonal axis. It is evident from Fig. 5*c* that the ground state of a Cr^{3+} ion in a tetrahedron extended along a trigonal axis is not orbitally degenerate, and could give rise to an EPR

‡ A sample of CrNaY zeolite in which 27% of the Na^+ had been exchanged by Cr^{3+}, and which gave no EPR signal in its sodium form, was kindly provided for our EPR measurements by No. 20 Laboratory of the Institute of Organic Chemistry of the USSR Academy of Sciences (Kh. M. Minachev's Industrial Laboratory).

signal at low enough temperatures. An analogous situation involving the Cr^{3+} ion was reported by Henning and coworkers [34]. In a tetrahedron compressed along the trigonal axis the ground state of the Cr^{3+} ion is doubly orbitally degenerate, and the spin–orbital interaction λLS splits it into four doublets which are described by the following wave functions (including the spin variables):

E (energy)	Ψ
$9/4\,\lambda$	$\Psi_1\chi(-3/2)$; $\Psi_2\chi(3/2)$;
$3/4\,\lambda$	$\Psi_1\chi(-1/2)$; $\Psi_2\chi(1/2)$;
$-3/4\,\lambda$	$\Psi_1\chi(1/2)$; $\Psi_2\chi(-1/2)$;
$-9/4\,\lambda$	$\Psi_1\chi(3/2)$; $\Psi_2\chi(-3/2)$;

$$\Psi_1 = -\sqrt{\frac{5}{6}}Y_3^{-2} + \sqrt{\frac{1}{6}}Y_3^1; \qquad \Psi_2 = -\sqrt{\frac{5}{6}}Y_3^2 - \sqrt{\frac{1}{6}}Y_3^{-1};$$

where $\chi(m)$ is the spin wave function for the spin $S = 3/2$ with a projection m on the z axis.

It can easily be shown that none of these doublets can give an EPR signal.

We have shown experimentally [35] that the EPR spectra of CrNaY samples measured at 4.2, 77, and 300°K become gradually weaker as the dehydration temperature is increased, and are practically undetectable after vacuum dehydration above 450°. This confirms our earlier conclusion [30] that after dehydration the Cr^{3+} ions penetrate into small holes and become localised at *SI'* sites. It may be argued that one water molecule (or its fragments O^{2-} or OH^-) is retained in the coordination sphere of the Cr^{3+} ion after heat treatment, and gives rise to the observed compression of the tetrahedron along its trigonal axis. This suggestion is consistent with the conclusion [31] that cation pairs of the type $M^{3+}_{SI'}...O^{2-}...M^{3+}_{SI'}$ are formed.

An effect of the zeolite crystal structure on the mechanism of cation exchange has also been reported [30]. By comparing the amount of chromium introduced into zeolites of different types under otherwise identical conditions with the amount of exchangeable sodium ions it was concluded that exchange in type A zeolites occurs only in the near-surface regions of the microcrystallites. (It should be noted that the hexaquo complexes are larger than the diameter of the windows leading into the structural pores of this type of zeolite.) Exchange does not proceed to completion even in type X zeolites, suggesting partial blocking of the windows leading into the large holes by the hexaquo complexes in the *SIII* position. This blocking effect does not take place in type Y zeolites, evidently because only a small fraction of the exchangeable Na^+ ions is in the *SIII* position (see Table 1).

Manganese. The electronic configuration of the ground state of the free manganese atom is $[A](3d)^5(4s)^2$. Only Mn^{2+} ions have been introduced into zeolites by cation exchange. The optical spectra of bivalent manganese have a very low intensity, because the transitions are spin-forbidden: this may be the reason for the lack of publications describing optical investigations of manganese zeolites.

On the other hand, a considerable volume of work on these zeolites using EPR has been published. The reason may be that in weak ligand fields the ^6S level of the Mn^{2+} ion has no closely spaced excited states, and therefore the EPR signals can be observed over a wide range of temperature and of ligand field symmetry. The experimental results are interpreted, on the whole, with the help of the theoretical concepts developed by Bleaney and Rubins [36–38]. However, the spectra of polycrystalline samples are very difficult to interpret: although the EPR spectra of Mn^{2+} ions retain their fine structure in weakly distorted octahedral and tetrahedral ligand fields, powders usually show only the ±1/2 transition because the strong angular dependence of the lines corresponding to the residual transitions give rise to fine structure. At low D values ($D/g\beta H \ll 1$), typical of the Mn^{2+} ion, the position of the lines corresponding to this transition is insensitive to the symmetry of the ligand field, and only the shape and width of some of the components of the hyperfine structure are affected (as a result of second-order effects) by changes in the surroundings of the ion. However, the hyperfine parameters, which are easily observed for the Mn^{2+} ion, are determined essentially by the degree of covalency of the bonds between the central ion and the ligands, and to a much lesser extent by the symmetry of the surroundings.

The first attempt to investigate zeolites of types X and Y containing Mn^{2+} ions by the EPR method was made by Ursu and Nicula [39] in 1964. These workers found that the resolution of the hyperfine structure of EPR spectra measured at 9 300 MHz depended on the high-temperature dehydration treatment to which the sample had been exposed. The effect was ascribed to changes in ligand-field symmetry arising from the removal of water molecules, but no attempt was made to propose a concrete model of the location of the ions in the zeolite structure.

The next series of publications, also involving EPR measurements at 9 300 MHz, was due to Barry and Lay [33,40,41]. These workers studied zeolites of types X and Y containing manganese ions in combination with the diamagnetic ions Li^+, Na^+, K^+, Cs^+, Mg^{2+}, Ca^{2+}, Zn^{2+}, and La^{3+}. Using the Mn^{2+} ions as a "paramagnetic probe", they tried to explain some features of the distribution, in zeolites, of cations devoid of paramagnetism.

The complex and poorly resolved experimental spectra, varying with sample treatment, were ascribed to Mn^{2+} ions in different states, giving rise to their individual spectra with the following parameters:

A: $g = 2.000$; $A = 97 \pm 3.5$ G;
I: $g = 2.001$; $A = 95 \pm 1.5$ G; $D = 54 \pm 18$ G;
II: $g = 2.001$; $A = 95 \pm 1.5$ G; $D = 131 \pm 3.5$ G (occasionally $D = 100$ G);
(*i*): $g = 1.996$; $A = 76.5 \pm 2$ G; $D = 65 \pm 35$ G
(*ii*): $g = 1.995$; $A = 88.5 \pm 3$G; $D < 130$G.

The states were assigned by the authors as follows: *A*—hydrated $(Mn \cdot nH_2O)^{2+}$ ions; I—Mn^{2+} ions localised on *SI* sites; II—Mn^{2+} ions localised on *SI'*, *SII'*, or *SII* sites; (*i*), (*ii*)—Mn^{2+} ions localised on *SI'* sites with a strong covalent bond to hydroxyl (OH^-) or O^{2-} ions respectively.

However, none of the spectra (with the exception of the hydrated sample) was observed in a pure form, and the spectral assignments to manganese ions in different lattice positions are not entirely convincing because they are not supported by serious arguments based on the structure of the paramagnetic centres. For example, the observed D values vary between 0.50×10^{-2} and 1.3×10^{-2} cm^{-1} and therefore correspond to a weakly distorted cubic field: they can hardly be quoted as evidence for any particular mode of stabilisation of the Mn^{2+} ion. The hyperfine coupling constants also did not vary over a wide range, with the exception of spectrum (*i*), ascribed to tetrahedral Mn^{2+} ions containing a hydroxyl group in the coordination sphere. Lastly, Barry and Lay's interpretation was not confirmed by the more recent work of Tikhomirova and coworkers [42] at a frequency of 35 000 MHz.

Because of the EPR spectrum of Mn^{2+} ions in a low-symmetry ligand field is greatly complicated by second-order effects, resulting in overlap of the hyperfine components and in the appearance of nuclear-spin-forbidden transitions, these workers carried out their measurements in an apparatus working at a shorter wave-length. They showed[42] that by working at a higher frequency ($\lambda \simeq 8$ mm, $\nu \simeq 37\,500$ MHz) the EPR spectra of Mn^{2+} ions in hydrated MnNaA, MnNaX, and MnNaY zeolites become much simpler and consist of well resolved sextets. From the intensity ratios of forbidden and allowed transitions they obtained a D value close to 106 G. They subsequently published a more detailed study of the behaviour of Mn^{2+} ions in the sodium forms of A, X, and Y zeolites during dehydration and adsorption of water vapour[43,44]. However, their conclusions rely exclusively on changes in the hyperfine coupling constants of the EPR spectra.

Since the EPR spectra of the Mn^{2+} ions in the initial samples of A, X, and Y zeolites have parameters almost identical to those of the EPR spectra of aqueous solutions ($A = 96$ G), the authors assume that the Mn^{2+} ions in this case are present in the form of aquo complexes. Dehydration at temperatures up to 150° gives EPR spectra with a hyperfine splitting constant of 87 G for all types of zeolite, which is ascribed to partially dehydrated Mn^{2+} ions. It is also pointed out that the electronic state of partially dehydrated Mn^{2+} ions is unaffected by the charge on the zeolite lattice or by the geometry of its framework.

If the dehydration temperature is raised above 150°, three types of spectrum are observed in X and Y zeolites ($A = 99$ G, $g = 2.000$; $A = 87$ G, $g = 2.000$; $A = 87$ G, $g = 2.007$), and two types of spectrum in type A zeolite ($A = 87$ G, $g = 2.000$; $A = 73$ G, $g = 2.000$). After dehydration at 300–400°, X and Y zeolites give only one EPR signal ($A = 99$ G, $g = 2.000$), and the spectra of type-A zeolites remain practically unchanged. The authors point out that the total intensity of all the spectra for a given sample remains constant.

By analogy with the interpretation of the spectra of Mn^{2+} ions in spinels[45], it is suggested that the EPR signal in a type-A zeolite with a hyperfine splitting of 73 G arises from ions localised in the neighbourhood of a six-membered oxygen ring and on the side of a small hole (site *SII'*, see Fig. 2), within which a residual water molecule is assumed to remain even after high-temperature vacuum treatment. In this case, the Mn^{2+} ion is tetrahedrally surrounded by oxygen atoms from the lattice (at 3 corners) and water (at 1 corner). This interpretation, with the Mn^{2+} ion in an *SII'* site rather than an *SII* site, is supported by the observation that water vapour adsorption must be carried out at a relatively high temperature (~ 80°) in order to reproduce the EPR spectrum with a splitting of 87 G characteristic of the partially hydrated Mn^{2+} ion.

The EPR spectra of fully dehydrated X and Y zeolites, with a hyperfine splitting of 99 G, are assigned to Mn^{2+} ions in *SI* sites, where the ligand field is octahedral. An alternative explanation is also discussed: localisation of Mn^{2+} within a small zeolite hole, since the adsorption of water and ammonia vapour gradually yields EPR spectra corresponding to the fully hydrated initial samples.

No attempt was made to interpret the EPR spectrum of Mn^{2+} ions with a splitting of 87 G and a g-factor of 2.007.

The results obtained for MnNaY zeolites by Barry and Lay are compared with those of Tikhomirova and coworkers in Table 5. Except for the data relating to the initial samples, substantial differences in experimental results and in their interpretation are evident. The discrepancy is due partly to differences in dehydration conditions, and partly to incorrect treatment of the results obtained at 9 300 MHz from poorly resolved spectra. However, the remaining doubt will not be fully removed until EPR measurements are carried out at both radio frequencies simultaneously, under standard conditions of heat treatment and with standard control of the residual water.

It may be concluded from the above review of published EPR work on synthetic zeolites containing bivalent manganese ions that the existence of Mn^{2+} in various states within the zeolite structure has been proved beyond doubt. However, because of the spectroscopic peculiarities of this ion, the detailed interpretation of the results is still tentative.

Table 5. Results obtained by different workers for type-Y zeolites containing Mn^{2+} ions.

	Initial	Partly dehydrated	Fully hydrated	References
Hyperfine splitting constant, A	96 G	99 G 87 G 87 G	99 G	42—44
Interpretation	$[Mn(H_2O)_6]^{2+}$, large hole *SIII*	*SII*, *SI*? $(Mn \cdot n\,H_2O)^{2+}$ not interpreted	*SII*, *SI*?	
Hyperfine splitting constant, A	97 G	95 G, 76 G	95 G	33,40,41
Interpretation	$(Mn \cdot n\,H_2O)^{2+}$	*SII*, *SI'* $[MnOH]^+$ *SII'*?	*SI'*, *SII*, *SII'*?	

Iron. The electronic configuration of the ground state of the free iron atom is $[A](3d)^6(4s)^2$. Tervalent iron ions can give rise to EPR spectra. However, we have been unable to find any reference to structural studies of zeolites containing ferric ions by EPR or by optical spectroscopy. Such zeolites have been synthesised, and are being intensively studied by gamma-resonance spectroscopy[46–50]. The main results, formulated by Delgass and coworkers[50], indicate that the Fe^{2+} cations in dehydrated type-Y zeolite are in a high-spin state, and occupy two types of site: *SI* (inaccessible to adsorbed molecules) and *SII* (accessible to adsorbed molecules). It is shown[44] that zeolites of types X and A are broken down by the introduction of iron ions.

The absence of EPR studies is probably due to the complexity of the EPR spectra of Fe^{2+} and Fe^{3+} ions in surroundings of low symmetry, making interpretation impossible without a special theoretical study. Not the least of the difficulties is the presence of iron impurities in the sodium forms of zeolites even before exchange, already mentioned above, which complicates the application of EPR to these systems[33]. It should not be concluded, however, that the EPR method will not be used in future to study zeolites containing iron ions.

Difficulties may arise also in the interpretation of the optical spectra of zeolites containing Fe^{3+} ions. Having an electronic structure similar to that of the Mn^{2+} ion, the Fe^{3+} ion gives strong charge-transfer bands in the near u.v. region (see Ref. 51, p. 276), with fairly strong "shoulders" in the visible region of the spectrum which tend to mask the weak, spin-forbidden d–d transitions. Optical studies of zeolites containing Fe^{2+} $(3d)^6$ ions could give very interesting results, but the d–d transitions for

the high-spin Fe^{2+} ion lie in the near i.r. region: the $^5T_{2g} \rightarrow {}^5E_g$ transition for the hexaquo Fe^{2+} ion is observed at ~ 10 000 cm^{-1} (p. 271 of Ref. 51).

Cobalt. The electronic configuration of the ground state of the free cobalt atom is $[A](3d)^7(4s)^2$. Only zeolites containing bivalent cobalt ions have so far been synthesised and investigated.

There are many references in the literature to the splitting of the energy levels of the bivalent cobalt ion, and to its magnetic properties, in the weak ligand fields corresponding to a distorted octahedron (see, for example, Ref. 52). We shall therefore confine this review to a qualitative discussion of the optical and magnetic properties of the Co^{2+} ion in weak ligand fields of symmetry C_{3v} and C_{3v} tetr. In these cases the ground state of the Co^{2+} ion ($S = 3/2$) is described by a wave function with an angular component which gives rise to an irreducible representation A_1 of the group C_{3v} (see Table 3 and Figs. 5*b* and 5*c*). Since the transitions between the levels of the split ^4F level lie in the i.r. region and are relatively weak, only the strong transition to the excited ^4P level is usually observed in the optical spectrum (see, for example, Ref. 51). Changes in ligand-field symmetry from a tetrahedron compressed along the trigonal axis to an extended tetrahedron, a trigonal pyramid, of a planar triangle should not significantly affect the spectral position of this optical transition, since the main contribution to its energy comes from the energy difference between the ground ^4F level and the excited ^4P level of the free Co^{2+} ion.

However, fairly substantial changes in the EPR spectra can be expected to result from these changes in ligand field. Table 4 shows the results of an analysis of the expressions for the g and D tensors of the Co^{2+} ion in fields of T_d, C_{3v} tetr, C_{3v} pyram, and D_{3h} symmetry, and also lists the spin ground states in a zero magnetic field.

In a tetrahedron compressed along the trigonal axis the constant D for this interaction is negative for the Co^{2+} ion (see Table 4). Since the EPR signals of Co^{2+} are usually observed at $T = 4.2°K$ ($kT \simeq 3$ cm^{-1}) because of the short relaxation times, the population of the $\pm 1/2$ spin doublet, which gives rise to the EPR signal, can be very small for $D < 0$ and $|D| \gg kT$. Hence it is obvious that the EPR signals of polycrystalline samples are difficult to observe when the surroundings of the Co^{2+} ion correspond to a tetrahedron highly compressed along the trigonal axis ($D < 0$). For example, Owen and Bowers[53] find $D = -4.5$ cm^{-1}, so that the population of the $s = \pm 1/2$ spin doublet is only $-2|D|/ekT \simeq 0.05$. Little gain in the intensity of the EPR signal can be expected from carrying out the measurement at liquid-nitrogen temperature, because the 10-fold increase in the population of the $\pm 1/2$ doublet (to 0.5) is compensated by a decrease in the difference of the populations within the doublet by a factor of $77°/2.4° = 18$. Line broadening may also appear as a result of relaxation.

On changing from compression to extension of the tetrahedron along the trigonal axis the hyperfine interaction constant changes sign, and remains positive throughout further changes in the coordination of the ion (up to the coordination of a planar triangle). Under these conditions the population of the $\pm 1/2$ spin doublet is close to 1: evidently, this should lead to a sharp increase in the strength of the EPR signal as compared with the case discussed above.

It follows that differences in the relative intensity of the EPR spectra of Co^{2+} ions in different samples can be used as a criterion of the presence of distortions in the tetrahedral ligand field, which (as stated above) do not materially affect the optical properties.

The position of the components of the fine structure of EPR spectra for a spin of 3/2 and $|D| \gg g\beta H$ has been fully discussed[54].

The most significant structural data on cobalt-containing zeolites, published up to 1970, were obtained by optical reflectance spectroscopy in the visible and near u.v. regions of the spectrum.

It has been shown[55] that the adsorption of substances such as H_2O, NH_3, CH_3OH, etc. on dehydrated CoNaA zeolites is accompanied by a colour change, which suggests that molecules of these compounds can enter the coordination sphere of Co^{2+} ions.

A recent paper by Klier[56] shows, on the basis of optical data, that the Co^{2+} ion in dehydrated type-A zeolite is localised in the plane of the six-membered oxygen window, whereas after adsorption of N_2O molecules its coordination increases to the tetrahedral configuration. Klier stresses the reversibility of this process upon outgassing the sample at 50°, but at 150° the nitrous oxide decomposes catalytically into molecular nitrogen and oxygen.

Barry and Lay[41] observed, in their study by reflection spectroscopy of CoNa13X zeolite dehydrated at 300°, that the Co^{2+} ions are located in a tetrahedral ligand field. Hence they suggested that the ions are localised in *SI'* sites in this zeolite. Three of the planar ligands are lattice oxygen atoms, and the fourth ligand is a residual water fragment (OH^- or O^{2-}). It is not clear, however, why *SI'* sites are chosen in preference to *SII'* or *SII* sites, since measurements of the specific adsorption of nitrous oxide[40] have shown that the Co^{2+} ions can be localised also in sites accessible to the molecules of adsorbate.

Until recently there were no published references to EPR studies of cobalt-containing zeolites, evidently because of the need to work at liquid-helium temperatures. We have recently reported[57] an investigation of this type on X and Y zeolites, carried out in cooperation with Brotikovskii. Since no significant difference could be found between the spectra (either optical, or ESR) of these two types, we shall confine the following discussion to the results obtained for the zeolite of type Y.

EPR and optical spectra were recorded before and after dehydration by vacuum baking. (The dehydration–rehydration cycle was found to be fully reversible.) The spectra were practically identical to those of aqueous solutions of Co^{2+} salts, suggesting that the cobalt ions after exchange (and rehydration) exist as $[Co(H_2O)_6]^{2+}$ aquo-complexes, located in large zeolite holes.

Vacuum baking at 100° removes only some of the water from the zeolite, and the Co^{2+} ions retain their hexaquo coordination. This is confirmed by the optical reflectance spectra, in which the absorption bands are only slightly displaced towards the red (from 19 000 to 17 000 cm^{-1}), with a somewhat increased intensity, after vacuum baking.

Dehydration at 200–500° produces a blue colour in the samples, characteristic of the tetrahedral compounds of bivalent cobalt, and strong, overlapping bands appear in the optical spectra at 18 500, 17 000, and 15 100 cm^{-1}. Since, as already stated, the position of these bands is relatively insensitive to distortions of the tetrahedral surroundings of Co^{2+}, it is not easy to assign the localisation of the cobalt ions to *SI'*, *SII'*, or *SII* sites.

On the other hand, we can deduce from the EPR spectra of samples dehydrated at 200–500° that after this treatment the Co^{2+} ions exist in two different states within the zeolite. For dehydration temperatures of 200–350° they

lie on SII sites, with the coordination of a tetrahedron compressed along its trigonal axis. The fourth (axial) ligand is assumed to consist of residual water molecules or water fragments (OH^- or O^{2-}). As stated above, polycrystalline samples may fail to give an EPR signal under these conditions because the ±1/2 spin doublet is lightly populated ($D < 0$). The EPR signal disappears completely[57], and reappears ($g_\parallel \simeq 2.00$; $g_\perp \simeq 2.75$) only after heating the sample at higher temperatures (400–500°). We have ascribed the spectra observed under these conditions to Co^{2+} ions localised in the plane of the six-membered oxygen window (between SII′ and SII sites). As Table 4 shows, $g_\parallel$ should be approximately 2 in this case, and $g_\perp > 2$, as observed experimentally. We have not considered the possibility of localisation of Co^{2+} ions in SI′ sites, because the adsorption of tertiary pentanol molecules on a dehydrated sample is known to alter the EPR spectrum, suggesting that quite large molecules can enter the coordination sphere of the Co^{2+} ion.

Summing up all that has been said on zeolites containing Co^{2+} ions, we stress that these cations can be introduced by exchange into zeolites of type X and Y in the form of octahedral aquo-complexes $[Co(H_2O)_6]^{2+}$, which "float" in the large holes of the zeolite lattice. As the samples are dehydrated, the cobalt ions are transferred initially to SII sites, where they retain a water molecule or fragment (OH^- or O^{2-}) in the first coordination sphere, and finally to the six-membered windows of the sodalite cells, where they remain accessible to adsorption of various molecules.

In conclusion, we note that Co^{2+} ions can be reduced if the host zeolite is dehydrated under reducing conditions. Thus, reproducible results on water adsorption at room temperature can be obtained only if the sample is carefully protected from the vapours of vacuum grease and other organic materials[57].

Nickel. The electronic configuration of the ground state of the free nickel atom is $[A](3d)^8(4s)^2$. One of the first papers describing optical and EPR studies of nickel-containing X and Y zeolites is due to Rabo and coworkers[58], who used EPR to observe the Ni^{1+} ion (electronic structure $[A](3d)^9$), obtained by reducing the samples in alkali metal vapours or in hydrogen, and also the signal from ferromagnetic metallic nickel. On the assumption that reduction of the ions does not cause them to migrate to new sites, the authors conclude that for 5–75% exchange of Na^+ by Ni^{2+} ions in dehydrated X and Y zeolites the ions occupy SII as well as SI sites. The EPR spectrum with $g_\parallel = 2.30 + 2.40$ and $g_\perp = 2.096$ is ascribed to Ni^{1+} cations localised in SI sites, and the spectrum with $g_\parallel = 2.10 + 2.13$ and $g_\perp = 2.065$ to Ni^{1+} in SII sites. Optical data were used to give a theoretical interpretation of the g-tensor values obtained from the EPR spectra. A wide absorption band at 450 nm was ascribed to Ni^{2+} ions in SII sites, and a band at 650 nm ($^2E_g \rightarrow {}^2T_g$ transition) was ascribed to Ni^{1+} ions in SII sites. The spin–orbital interaction constant found by comparing EPR and optical results was 500 cm^{-1}, in good agreement with the value for the free Ni^{1+} ion ($\lambda = 600$ cm^{-1}).

Adsorption experiments with oxygen, carbon monoxide, hydrogen, and ammonia on reduced forms of nickel zeolite have shown that Ni^{1+} ions localised on SII sites interact most strongly with adsorbed molecules, but at high temperatures the Ni^{1+} ions on SI sites also take part in the reaction $Ni^{1+} + O_2 \rightarrow Ni^{2+} + O_2^-$ during oxygen adsorption.

Olson[59] was able to confirm these conclusions by X-ray diffraction methods in his study of natural faujasite containing nickel ions ($SiO_2/Al_2O_3 = 4.6$). He found the following distribution of Ni^{2+} ions in the elementary cell of the mineral:

Site	SI	SI′	SII′	SII	SI′ + water fragment	SII′ + water fragment
Amount	10.5	3.2	2.0	6.5	5.8	2.9

From these data it was concluded that the results of X-ray diffraction analyses of zeolites in their calcium form cannot be applied automatically to zeolites containing transition-metal ions. Thus, whereas the preferred sites for alkaline-earth cations in the zeolite structure are the SI sites[60,61], and the preferred sites for rare-earth cations are the SI′ sites[31], transition-metal cations can be localised in other sites of the zeolite lattice even at low extents of exchange.

Detailed optical studies of type-A zeolite containing bivalent nickel ions have been reported by Polák and Černý[62] and Klier and Ralek[63]. The former have made computer calculations, using ligand-field theory, of the electronic spectra of ions with the $(3d)^{2,8}$ electronic configuration in a crystal field with D_{3h} symmetry. The latter workers used these theoretical calculations to analyse the diffuse reflectance spectra of NiNaA zeolites degassed at different temperatures.

They showed that in a fully hydrated zeolite the bivalent nickel ions are present as the $[Ni(H_2O)_6]^{2+}$ hexaquo complex, as shown by the almost exact correspondence of their spectra with those of aqueous solutions of nickel salts.

In partly dehydrated zeolites the Ni^{2+} ions retain approximately one molecule of water in their first coordination sphere, and they become firmly bonded to the zeolite lattice—probably in SII sites—thereby acquiring distorted tetrahedral surroundings. However, the observed optical spectra did not show the characteristic absorption maxima of tetrahedral nickel at 600–700 nm (see Ref. 51, p. 301). Further dehydration causes complete removal of the water, and the Ni^{2+} cations become localised in the plane of the six-membered oxygen window of the zeolite lattice, as shown by the good agreement between the observed and the theoretically calculated optical spectrum.

Studies were made also of the adsorption of nitric oxide, cyclopropane, ethylene, propene, and acetylene on dehydrated zeolite, and it was concluded that the process is monocentric and (with the exception of acetylene) reversible. It is assumed that the nickel cation completes its coordination sphere in the form of a trigonally distorted tetrahedron.

It has been shown by X-ray diffraction analysis[64] and by magnetostatic and ferromagnetic resonance methods[65] that Ni^{2+} ions are reduced to metallic nickel by treatment of the zeolite in a reducing atmosphere, forming microcrystals approximately 100 Å in size on the surface of zeolite single crystals.

Copper. The electronic configuration of the ground state of the free copper atom is $[A](3d)^9(4s)^2$. Many papers have been written on EPR studies of zeolites containing bivalent copper cations. Cu^{2+} ions, having the $(3d)^9$ electronic configuration (nuclear spin 3/2), give very sharp EPR spectra in magnetically dilute systems: the parameters of these spectra depend sensitively on the symmetry of the immediate surroundings of the ion. The isotropic and anisotropic hyperfine interaction constants, g-tensor components, and temperature dependence of the spectrum can often be used to determine not only the coordination of the Cu^{2+} ion, but also the percentage

covalency of the bond in the complex, and also the type of motion of the complex as a whole. Hence, zeolites containing Cu^{2+} ions are specially interesting to research workers.

We shall first of all consider some optical and magnetic properties of the Cu^{2+} ion in ligand fields with C_{3v}, C_{4v}, and D_{3h} symmetry in the light of the above calculations.

As Fig. 4*a* shows, the ground state of the Cu^{2+} ion in ligand fields with O_h symmetry is doubly degenerate, and therefore the three possible d–d transitions in the optical spectra merge into one. When the octahedron is stretched along the tetrad axis we expect (see Fig. 4*a*, $\eta < 2$, $\xi = 1$) the observed absorption band to split into two, one band remaining in its original position ($B_1 \rightarrow B_2$) and two other bands appearing at shorter wavelengths ($B_1 \rightarrow E$). In a compressed octahedron, as shown in Fig. 4*a*, the splitting of the absorption band is accompanied by a shift of all three maxima towards the short-wave end of the spectrum.

We shall now turn to the changes in the EPR spectra arising from these distortions. Octahedral complexes of Cu^{2+} ions, when subjected to a weak tetragonal distortion corresponding to stretching of the octahedron, are known to give EPR spectra whose parameters are described by the expressions

$$g_{\parallel} = 2 + \frac{8\lambda}{\Delta_{B_1B_2}}; \quad g_{\perp} = 2 + \frac{2\lambda}{\Delta_{B_1E}} \quad (\text{where: } \lambda > 0,\ \Delta_{ij} > 0).$$

Obviously, in a weakly stretched octahedron $\Delta_{B_1B_2} \simeq \Delta_{B_1E}$, and therefore $\Delta g_{\parallel}/\Delta g_{\perp} \simeq 4$. As Fig. 4*a* shows, the transition from a weakly stretched octahedron to a square pyramid or to a square plane does not affect $\Delta_{B_1B_2}$, but since Δ_{B_1E} increases, the ratio $\Delta g_{\parallel}/\Delta g_{\perp}$ must also increase.

Transition from an octahedron stretched along the tetrad axis to a compressed octahedron leads to the following expressions for the components of the g-factor: $g_{\parallel} = 2$; $g_{\perp} = 2 + 6\lambda/\Delta_{A_1E}$, and therefore the EPR spectrum should become inverted, since the perpendicular component of the spectrum now finds itself at a smaller field than the parallel component.

It is evident from Fig. 4*b* and 4*c* that the ground state of the Cu^{2+} ion is not orbitally degenerate in a compressed trigonal bipyramid or in a tetrahedron compressed along the trigonal axis (the expressions for the g-factors are given in Table 4).

We should stress that in this case, as in the case of a field with the symmetry of a compressed octahedron, the perpendicular component of the EPR spectrum experiences weaker fields ($g_{\perp} > 2$) than the parallel component ($g_{\parallel} = 2$). This is because the electronic ground level in both cases is described by a wave function with an angular component Y_2^0.

In fields with the symmetry of a stretched pyramid or of a tetrahedron stretched along the trigonal axis the ground level of the Cu^{2+} ion becomes doubly orbitally degenerate (see Figs. 4*b* and 4*c*). The angular parts of the wave functions corresponding to this doublet can be written in the following general form (see Table 4):

$$\psi_1 = \alpha Y_2^2 - \beta Y_2^{-1},$$

$$\psi_2 = \alpha Y_2^{-2} + \beta Y_2^1, \text{where: } 1 \leqslant \alpha < \sqrt{\frac{2}{3}},\ \alpha^2 + \beta^2 = 1.$$

The spin-Hamiltonian which describes the behaviour of the system allowing for spin–orbital interaction and interaction with a magnetic field can be written

$$\mathcal{H} = \lambda \mathbf{LS} + \beta(\mathbf{L} + 2\mathbf{S})\mathbf{H}, \quad S = {}^1/_2.$$

Since these interactions are much smaller than the interactions between the electrons and the ligand field, they can be calculated by perturbation theory. By applying this theory, and noting that λ is negative for the Cu^{2+} ion, it is readily shown that the orbital doublet is split into two doublets by the spin–orbital interaction, and that their behaviour in a magnetic field H is described by a spin-Hamiltonian of the form

$$\mathcal{H}_{sp} = g_{\parallel}\beta H_z S_z + g_{\perp}\beta(H_x S_x + H_y S_y)$$

where, according to first-order perturbation theory, $g_{\perp} = 0$ and $g_{\parallel} = 6\alpha^2\epsilon(6, 4)$ for the lower doublet and $g_{\perp} = 0$ and $g_{\parallel} = 4 - 6\alpha^2\epsilon(0, -2)$ for the upper doublet.

Obviously, $g_{\perp}$ will be different from zero in the higher orders of perturbation theory, but it will not be large, and since the strongest perpendicular component of the EPR spectrum occurs at very high fields for low values of $g_{\perp}$, the EPR spectra of copper ions may be impossible to observe.

We shall now review the results obtained by EPR and optical spectroscopy for zeolites containing Cu^{2+} ions.

Faber and Rogers [66] were the first to report EPR spectra from Cu^{2+} ions in zeolites. They made a theoretical analysis of the hyperfine interaction constants and the g-tensor components of the EPR spectra of fully hydrated and ammonia-saturated zeolites containing Cu^{2+} ions, and they obtained data on the degree of covalency of the bond in the complexes. However, no attempt was made to identify the structure of the zeolite, evidently because the problem had not yet been formulated at the time.

Nicula and coworkers [67] studied the hydrated, partially dehydrated, and fully dehydrated forms of CuNaY zeolite. From an analysis of the spin-Hamiltonian constants, and of the temperature dependence of the EPR spectra, they showed that the copper ions in the hydrated zeolite "float" in the large holes as the hexaquo complexes.

Unlike Polák and Cerný [62], Nicula and coworkers were able to observe hyperfine splitting in partly and fully dehydrated zeolites in perpendicular as well as in parallel orientations. Using experimental spin-Hamiltonian parameters, and theoretical expressions for a tetragonal ligand field with allowance for covalent bonding [68,69], they tried to explain the observed gradual change in the spin-Hamiltonian parameters in terms of changes in the degree of covalency of σ and π bonds in the complex upon replacing water ligands by lattice oxygen atoms. This explanation is well substantiated for tetragonally distorted, octahedral Cu^{2+} complexes, but (as will be shown later) the spin-Hamiltonian parameters do not vary smoothly in practice.

These workers point out that all the observed changes in EPR spectra are reversible only in type-Y zeolites, and hence they conclude that copper-containing zeolites of type X are decomposed by vacuum heat treatment.

In this paper, also, no attempt is made to "associate" the dehydrated copper cations with any specific site in the zeolite lattice.

Richardson [70–72] has published a series of three papers devoted to an EPR study of the localisation of copper ions in type-Y zeolites containing cations of various non-paramagnetic metals. He observed EPR spectra with parameters similar to those reported by Nicula and coworkers [67], and attempted to relate them to changes in coordination of the Cu^{2+} ion during dehydration of the zeolite. However, Richardson bases all his arguments on expressions for the spin-Hamiltonian parameters of the Cu^{2+} ion in a field with C_{4v} symmetry, and tries to assign

all the observed EPR spectra for hydrated and for dehydrated samples to copper ions localised in *SII* sites, where (as stated above) the ligand field has D_{3h} symmetry (dehydrated ion) or C_{3v} symmetry (ion in an *SII* site with 1 molecule of water of hydration). Clearly, an ion on an *SII* site can have trigonally distorted octahedral surroundings only by the adsorption of three water molecules, but Richardson ignores this possibility.

Krüerke and Jung[73] also published an EPR study of copper-containing X and Y zeolites. However, their results for type-X zeolites containing copper cations should be viewed with extreme caution, since considerable doubt exists on the stability of this zeolite lattice[67].

They studied the intensity of EPR signals from samples with a high copper content (~ 20 Cu^{2+} ions per elementary cell of the zeolite) as a function of the temperature of vacuum heat treatment, and also after adsorption of water and ammonia molecules, and they showed that the intensity of the EPR signal from a fully hydrated sample does not correspond to the analytically determined concentration of copper ions. The plot of intensity of the EPR signal against dehydration temperature had a distinct minimum at 150° (~ 50% of the initial intensity). Further increase in dehydration temperature caused the signal to increase, reaching 80% of the initial intensity at 350°, but at still higher temperatures the signal once again fell off. The dehydration process was found to be reversible.

On the incorrect assumption (see above) that these large changes in the integral intensity of the EPR signal cannot be due to changes in the configuration of the ligand field close to the site of the copper cation, Krüerke and Jung explain the decreased intensity of the EPR signals during dehydration by postulating the formation of cation pairs ($S = 0.1$) in *SI'* sites of the small holes in the sodalite cell, joined by hydrogen bridges.

The increased intensity of the EPR signal on further raising the dehydration temperature was ascribed to the removal of residual water molecules, resulting in migration of the copper cations to *SI* sites and dissociation of the cation pairs.

The subsequent decrease in the intensity of the EPR signal, at dehydration temperatures above 350°, is ascribed to irreversible changes in the zeolite structure.

The most interesting of Krüerke and Jung's results were obtained with samples containing less than 8 Cu^{2+} cations per elementary cell. By analysing the shape of the absorption line they were able to establish that the parameters of the EPR spectra change in discrete jumps rather than continuously during partial dehydration of the zeolite, and they showed that two types of copper ions are present, giving EPR spectra with the following parameters:

$$\text{I}-g_{\parallel}=2.35,\ g_{\perp}=2.06,\ A=120\ \text{Oe};$$
$$\text{II}-g_{\parallel}=2.31,\ g_{\perp}=2.06,\ A=175\ \text{Oe}.$$

The difference between the two sets of parameters is ascribed to the existence of two possible localisation sites for Cu^{2+} ions in the zeolite, with different arrangements of nearest neighbours.

Another interesting result is the gradual decrease in total intensity of the EPR signal with increase of dehydration temperature. Krüerke and Jung admit that the ideas which they had developed for zeolites with high copper concentrations cannot be applied directly to low-concentration samples, since ion-pair formation is not likely to be significant at low concentrations.

In this context it is relevant to note that Tikhomirova and Nikolaeva[74] also proposed a non-uniform distribution of cations in the zeolite and the presence of sites with a high concentration of cations from an analysis of the individual components of the EPR spectra and their temperature dependence. However, their results relate to type-A zeolites, containing low concentrations of Cu^{2+} and Mn^{2+}.

Almost at the same time as Krüerke and Jung, Slot and Verbeck published an EPR study of zeolites (type Y) containing approximately 15 Mg^{2+}, Zn^{2+}, or La^{3+} ions and 0.3 Cu^{2+} ions per elementary cell[75]. They examined only partly or fully dehydrated samples, and they also observed two types of copper cation, with EPR spectral parameters identical to those obtained elsewhere[72,73]. From measurements of relative spectral intensities for different heat treatments they concluded that dehydration is accompanied by the gradual migration of Cu^{2+} ions into the bulk of the zeolite. They propose two explanations for the constancy of the parameters of individual EPR spectra: 1) copper ions penetrate into the interior when they are replaced (by ion exchange) by hydrated ions, and they retain their coordination when the water is removed; 2) copper ions are partly or fully dehydrated at temperatures as low as 110°, and their state is unchanged when the dehydration temperature is further increased. In both cases the migrating species are thought to be copper complexes.

The former explanation does not stand up to critical examination, since heat treatment at 400° for 72 h in an oxygen atmosphere (as in Slot and Verbeck's experiments) is known to cause practically complete dehydration of the zeolite (see, for example, Ref. 70). The second explanation seems more convincing, but it can be shown by thermal analysis (see below) that the bulk of the water is removed only at temperatures of the order of 200–300°, and therefore it is hard to accept that the coordination sphere of the copper ions is broken down at a temperature as low as 110°, and that all subsequent changes in the EPR spectrum are to be ascribed only to migration of the ions.

Slot and Verbeck ascribe the difference between the parameters of their two EPR spectra to the existence of two types of localisation sites for the ions (*SI* and *SII*). They also point out that cation migration is strongly influenced by the main cation of the zeolite.

Summarising the published results, we may conclude that for copper zeolites (unlike manganese zeolites) there is acceptable agreement between the data from different laboratories. However, contradictions are apparent in the interpretation of the results. Most workers ascribe to Cu^{2+} ions in *SI'*, *SII'*, or *SII* sites (C_{3v} tetr or C_{3v} pyram symmetry) experimental EPR spectra which clearly correspond to copper ions in ligand fields with C_{4v} symmetry. In this context, we may discuss some results obtained by the writers (in collaboration with Shvets and Pecherskaya) by EPR and optical reflection spectroscopy[76,77].

The initial samples were prepared by cation exchange of Y-zeolite in the sodium form in a solution of copper acetate, and contained 2–4 Cu^{2+} ions per elementary cell.

With hydrated samples, the results were almost identical to those previously discussed. The conclusion that in fully hydrated zeolites the copper ions are accommodated in the large holes as hexaquo complexes was confirmed by optical measurements.

In partly dehydrated (100–300°) zeolites EPR signals of two types (I and II) have also been detected. Their parameters are practically identical to those reported by other workers (signal I: $g_{\parallel} = 2.38$, $g_{\perp} = 2.08$, $A = 126$ Oe; signal II: $g_{\parallel} = 2.32$, $g_{\perp} = 2.05$, $A = 162$, $B = 22$ Oe). The optical spectra of these samples showed enhanced

optical absorption in the region 400–800 nm. On raising the dehydration temperature the relative intensity of signal II (which is absent in the EPR spectra of initial or hydrated samples, where only signals of type I can be observed) increases, and the total intensity of the EPR spectrum decreases (by a factor of 10–20 for samples fully dehydrated at 500°).

These effects were interpreted as follows[72]. The type-I EPR spectrum and the optical spectrum of a fully hydrated zeolite, consisting of one broad maximum at 800 nm, are assigned to the Cu^{2+} ion surrounded by 6 water molecules. The EPR signal of the second type is assigned to Cu^{2+} ions in a square pyramidal or a plane square coordination. This is shown by the fact that, whereas the general structure of the EPR spectrum is retained, both the ratio $\Delta g_{\parallel}/\Delta g_{\perp}$ and the optical absorption at wavelengths shorter than those for the $[Cu(H_2O)_6]^{2+}$ complex are increased. Cu^{2+} ions in these coordinations are fairly strongly bound to the zeolite lattice (apparently in SIII sites), since, in contrast to hydrated samples, their EPR spectra are the same at room temperature and at liquid nitrogen temperature.

The strong reduction in the integral intensity of the EPR signals for vacuum heat-treatment temperatures of 400 to 500° can be explained in two ways: a change in the valency state of the Cu^{2+} ions (e.g. reduction to Cu^{1+}), or a very strong broadening of the EPR lines resulting from a change in coordination. The latter explanation is the more plausible, because the initial EPR spectra can be regenerated by water adsorption at room temperature but not by heating the dehydrated samples in an oxygen atmosphere. The Cu^{2+} ions in a dehydrated zeolite are assumed to occupy sites in the planar six-membered windows of the sodalite cells of the zeolite. As stated above, the ions in these sites experience an electrical ligand field with the symmetry of a planar triangle. Under these conditions it may not be possible to observe EPR signals, because $g_{\perp}$ differs very little from zero. Relaxation may also cause broadening of the EPR line, but measurements at 4.2°K failed to reveal a new signal in the EPR spectrum.

Two papers appeared while this review was in manuscript[78,79]. Gállezot and coworkers[78] showed, by an X-ray analysis of dehydrated Cu(57%)NaY zeolite, that most of the copper ions are located in SI′ sites, where they can interact with adsorbed ammonia and pyridine molecules. The second paper[79] reports an EPR study of Cu(7%)NaY zeolite. The intensity of the spectrum is found to be constant during dehydration, and the fall of intensity observed in the writers' work is ascribed to reduction of the copper ions (as discussed above) or cation-pair formation. The formation of pairs seems improbable, particularly in samples with a low copper content, but a special study of this problem seems desirable, together with a study of the effect of oxygen on the dehydration of copper-containing zeolites.

Copper ions localised in SII sites were found to be accessible to adsorption (at room temperature) of various polar molecules (methanol, ethanol, propanol, and isopropanol)[73]. The ions appear, from EPR measurements, to remain strongly bound to the zeolite lattice near the six-membered oxygen rings (SII sites), but their coordination increases to octahedral. Decomposition of the alcohol complexes of the Cu^{2+} ions in zeolite was found to set in at temperatures of the order of 200°, accompanied by dissociation of the alcohol molecules into hydrogen and acetaldehyde (in the case of ethanol). Catalytic dehydrogenation of alcohol under normal catalytic conditions (accompanied by dehydration[21]) begins at temperatures of this order. Thus, we may conclude that Cu^{2+} ions localised in SII zeolite sites act as active centres for the catalytic decomposition of alcohol into hydrogen and acetaldehyde.

The lack of catalytic activity towards the dehydrogenation of ethanol in calcium and sodium zeolites shows that the electronic structure of the zeolite cation plays an important role in determining the specificity of the catalyst.

In this context, the work of Richardson[70] has yielded some very interesting results. It describes a comparative study, by the EPR method, of the formation of cation-radicals on different forms of zeolites (including copper) on which electron-donor molecules such as anthracene, perylene, pyrene, and naphthalene had been adsorbed. Richardson points out that zeolites containing transition-metal cations, and also cadmium cations, are much more active than other zeolites towards the electron-transfer reactions leading to the formation of cation-radicals, because of the high electron affinity and strong polarising power of these cations.

These results are entirely consistent with those of Neimark and coworkers[80], who showed (from the luminescence spectra of naphthalene adsorbed on different forms of cationated zeolites) that alkali and alkaline-earth metals lead to the formation of charge-transfer complexes between naphthalene and the zeolite lattice, followed by catalytic oxidation of the naphthalene in air to α-naphthaquinone, whereas transition-metal cations produce luminescence quenching, which the authors ascribe to direct adsorption of the naphthalene on the cation (atmospheric oxidation being thus precluded).

Zinc. The electronic configuration of the ground state of the free zinc atom is $[A](3d)^{10}(4s)^2$. Bivalent zinc ions are not paramagnetic, and are inactive in the u.v. and visible regions of the spectrum. Hence, zeolites containing Zn^{2+} ions have not been examined by either of the methods discussed in this review.

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It is clear, from this review of the recent literature, that interesting information on the behaviour of ions of the first transition row in synthetic zeolites has been obtained by EPR and optical spectroscopy. Among the specific problems examined are the coordination and valency state of the cations after exchange and after various treatments, the sites on which ions are localised in zeolites, and the mechanism of adsorption of various molecules on these ions. In many cases, catalytically active centres have been unambiguously identified. The results on the coordination state of cations in dehydrated zeolites, and on the changes in coordination resulting from the adsorption of various compounds, are particularly interesting.

For most metals it has been reliably established that the ions enter the zeolite, during cation exchange, in the form of hexaquo complexes, which "float" fairly freely in the large holes of the sodalite cells.

Upon partial removal of the adsorbed water from the zeolite, the transition-metal ions become firmly bound to the zeolite skeleton, retaining their octahedral coordination. This reaction involves the partial replacement of the water in the coordination sphere of the ion by oxygen atoms of the zeolite lattice. Further removal of water from the coordination sphere of the ion begins (depending on the ion) at temperatures in the region of 150–250°, and goes to completion at 350–450°. The coordination of the metal

ions decreases to a square pyramid, or even to a trigonal configuration, after complete dehydration.

Unlike the alkali-metal cations, the bivalent ions of the first transition series can be stabilised in *SII* and *SII'* sites even at low extents of exchange: this effect may be due to the ability of the latter ions to form groupings of the type MOH^+. These trigonally coordinated ions (e.g. copper, cobalt, and nickel) can act as specific adsorption centres for polar molecules of water, ammonia, and alcohols. Tervalent metal ions (e.g. chromium) penetrate deep into the sodalite cell upon dehydration, and become stabilised on *SI'* sites, thus acquiring a more effective screening of their excess of positive charge by virtue of the negative charges on the zeolite lattice. Hence, these ions are relatively inaccessible to large molecules such as alcohols, aldehydes, etc.

We may also conclude from this review that contemporary workers hold conflicting views on the laws which determine the distribution of cations in zeolites. The scarcity of reliable experimental data is undoubtedly responsible for this state of affairs.

The results discussed in this review also show that synthetic zeolites provide a very interesting system for the study of the anomalous coordination states of transition-metal cations introduced into the zeolite by cation exchange. These ions (particularly when doubly charged) act as adsorption centres for a number of molecules; the possibility that the molecules thus coordinated are chemically activated and that the resulting catalytic properties of transition-metal ions can be exploited is a very interesting topic, which lies beyond the scope of the present review.

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Structure and Properties of Oxide Halides of Phosphorus and Certain Transition Elements

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Published information is presented on the structure and the properties of phosphoryl compounds and certain others containing oxo-groups. Modern views on the structure of the phosphoryl group are related to the presence of a σ-bond and also to d_π-p_π interaction between the orbitals of the phosphorus and oxygen atoms; this type of interaction is observed also at other bonds involving phosphorus (P-Hal). Compounds containing oxo-groups exhibit donor properties, forming complexes with acceptor molecules. The general properties of donor-acceptor complex compounds are discussed. A list of 196 references is included.

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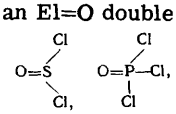
I. INTRODUCTION

Various halides containing an ElO group are of great practical value. They are widely used as non-aqueous solvents[1] and also for the separation of chlorides of different elements[2-5]. Interest is being taken at the present time in the application to laser technology of mixed-solvent solutions based on phosphoryl and other compounds containing ElO groups[6-11]. The structure of such compounds and their complexes involves several problems of theoretical inorganic chemistry, and therefore is of undoubted interest.

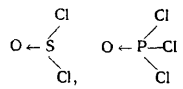
The present paper discusses certain aspects of the structure, chemical activity, and complex-forming power of halides containing an ElO group, attention being paid mainly to the phosphoryl group.

II. NATURE OF BONDING OF ATOMS IN OXIDE HALIDES OF GROUP III ELEMENTS

According to Werner the molecules NOCl, $POCl_3$, $SOCl_2$, $SeOCl_2$, etc. contain an El=O double bond:



According to the Lewis octet theory the bond between the central atom and the oxygen atom was regarded as of donor–acceptor type involving a pair of electrons on the central atom:

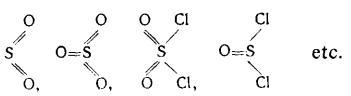


Experimental investigations of the molecular properties supported both views. The measured parachors for several compounds were lower than those calculated on the basis of Werner's formulae†, and compounds containing an El–O [type of] bond (S–O, P–O, P–S) exhibited less tendency to reactions involving addition than might have been expected for compounds containing a double bond. On the other hand, the El–O interatomic distances, the bond energies, and the dipole moments indicated the presence of a double bond[13–17].

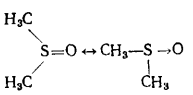
Siebert[13] characterised the ElO(S) bonds by their multiplicity, which he calculated in several oxides and oxide halides of non-metals by means of the rules that he had derived[18]. For sulphur compounds, for example, he obtained the values

SO_2	SO_3	SO_2Cl_2	$SOCl_2$	SO_2F_2	SOF_2
1.96	2.04	2.03	1.87	2.19	2.04

for the multiplicity of the SO bond. This is seen to be close to 2 in all the compounds, from which he concludes that a double bond S=O is present:



In the case of methyl derivatives, e.g. dimethyl sulphoxide, the multiplicity of the SO bond falls to 1.7, which Siebert attributes to an approach towards a donor–acceptor bond:

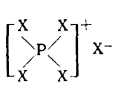


At one time Pauling regarded the resonance of two structures as the reason for the increase in the ElO bond energy‡. For phosphorus compounds the multiplicity of the PO bond is close to 2, and diminishes on passing from fluorides to bromides[20,21]; introduction of a methyl group diminishes the multiplicity considerably:

POF_3	2.34
$POCl_3$	2.09
$POBr_3$	2.02
$PO(CH_3)_3$	1.7

Discussion of the type of bond in ElO(S) groups in terms of its multiplicity is formal in character, and cannot give a complete idea of their structure.

According to modern views the nature of the (Hal)ElO bonds in Hal_3PO molecules is due to hybridisation of the atomic orbitals of the central atom, but the participation of *d*-orbitals of the central atom in bond formation is a matter of controversy[22,23]. Pauling, although the first to suggest the participation of *d*-orbitals in the formation of covalent bonds by elements in the third period, assumed for phosphorus compounds PX_5 the type of structure



in which the *d*-orbitals of phosphorus are not involved in bond formation. In the proposed formula combination of the five X atoms with the phosphorus atom can be effected by 3*s*- and 3*p*-orbitals together with electrostatic attraction between phosphorus and a unit negative charge distributed among the five X atoms. Atoms of elements in the second period—carbon, nitrogen—usually exhibit quadrivalency when they form covalent two-electron bonds. The participation of *d*-orbitals in the bond with elements in the third period may increase the coordination number of the central atom. On the other hand, the difference between the coordination numbers of elements in the second and third periods has been ascribed mainly to steric factors[24], not to the energy difference between the *d*-orbitals of the elements. The structure and the energies of the 3*d*-orbitals of isolated atoms of elements in the third period are such that their participation in bond formation is improbable[25–27].

Table 1. Energy of transition from ground state, eV.

Transition	Al	Si	P	S	Cl
One-electron					
$(s) \rightarrow (d)$	8.47	12.21	17.54	20.72	26.17
$(p) \rightarrow (d)$	3.90	5.51	7.23	7.89	11.07
Two-electron					
$(s)^2 \rightarrow (d)^2$	20.63	28.88	37.93		58.52
$(sp) \rightarrow (d)^2$	14.49	20.34	27.75	32.25	41.25
$(p)^2 \rightarrow (d)^2$		13.99	18.00		26.92

Table 1[28] shows that the $s \rightarrow d$ transition energy is rather lower in elements of the third period than in those of the second period, but is sufficiently high for the *d*-orbitals to take part in bond formation (in transition elements the energy of an $s \rightarrow d$ transition is ~ 8 eV). The radius of the 3*d*-orbitals of the phosphorus atom is 2.43 Å, considerably exceeding the radii of the 3*s*- and 3*p*-orbitals (0.47 and 0.55 Å respectively). The calculated overlap integrals of the *p*-orbitals of the ligands and the *d*-orbitals of an isolated phosphorus (sulphur) atom, e.g. the p_Z–d_{Z^2} overlap integrals, are negative, the *d*-orbitals being "smeared out" too much to form a σ-bond[28]. However the presence of ten or twelve electrons surrounding the central atom in the $POCl_3$, $SOCl_2$, etc. molecules, and the stable five- and six-coordinated compounds obtained with phosphorus, indicate the possible participation of *d*-orbitals of the central atom in the bonds. Additional interaction involving the *d*-orbitals of the central atom might explain also the high ElO, ElHal bond energies, the high vibration frequencies, and the short bond lengths between the central atom and oxygen in compounds of elements in the third period in comparison with those of elements in the second period. Quantum-mechanical calculations[29–34] have shown the possibility that *d*-orbitals of phosphorus and sulphur atoms may take part in forming σ- and π-bonds. The *d*-orbitals of the central atom undergo a considerable change of energy in the ligand field, which facilitates their participation in hybridisation.

The main factors influencing the size and energy of the *d*-orbital—(1) the spin contribution of unshared electrons, (2) the number of *d*-electrons, and (3) the formal charge on the atom—have been distinguished[22,35] according to the mode of excitation. The last factor has the greatest effect, and is explained in terms of formal concepts: electronegative substituents, by drawing electrons away from the central atom, increase its charge, which in turn leads to contraction of the *d*-orbitals.

† Sidgwick[12] showed that the parachor should decrease even with increase in the number of electrons around the atom from 8 to 10 or 12.

‡ The increase in bond energy has been discussed[19] in terms of hybridisation.

The contribution of d-orbitals to bond formation may vary. Cruickshank[36] suggested that they played an equivalent part together with s- and p-orbitals. The possibilities of sp^3d-hybridisation of the phosphorus atom have been discussed[27,37,38], and the energies of other excited states sp^2d^2, p^3d^2 have also been determined. Various energy levels have been calculated by the molecular orbital method for isolated P^0, P^+, and P^- atoms, although it is not possible to extrapolate data for individual atoms to molecules[39]. The sp^3d-hybridisation of a phosphorus atom represents the formation of five equivalent bonds.

The spatial arrangement of the hybrid orbitals may lead to various structures[40], among which a bipyramidial structure is energetically the most favourable. Phosphorus is then bound to oxygen by a σ-bond and a superimposed covalent π-bond resulting from overlapping of one of the five sp^3d-hybrid orbitals of the phosphorus atom and a p-orbital of the oxygen atom.

Molecular orbital calculations for Y_3PO molecules, taking into account the effect of substituents on the phosphorus–oxygen bond and the accompanying change in hybridisation of the phosphorus orbitals, led Wagner[41,42] to regard the σ-bond as of donor–acceptor type P → O. Two π-bonds, formed by $2p_x$- and $2p_y$-orbitals of oxygen and $3d_{xz}$- and $3d_{yz}$-orbitals of phosphorus, are superimposed on the σ-bond. This type of overlap of orbitals can be illustrated by Fig. 1[43,44], which shows the possibility of interaction between two d-orbitals of four-coordinated phosphorus and two p-orbitals of oxygen. If the molecule containing four-coordinated phosphorus is so oriented that the P=O bond lies along the x-axis, $d_\pi - p_\pi$ bonds can be formed by the binding of the phosphoryl oxygen to the phosphorus atom by a σ-bond produced by the overlapping of an sp^3-hybrid orbital of phosphorus with a p_x-orbital of oxygen and two π-bonds formed by $3d_{xy}$- and $3d_{xz}$-orbitals of phosphorus and p_y- and p_z-orbitals of the phosphoryl oxygen.

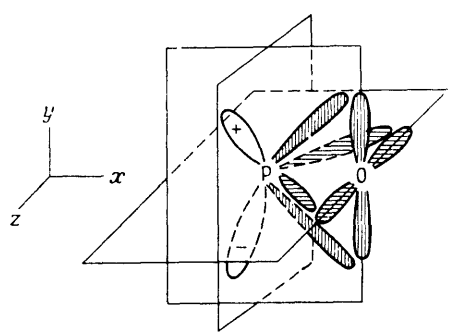


Figure 1. Scheme of $d_\pi - p_\pi$ interaction along the P–O bond.

Considering various types of substituents in the Y_3PO molecule, Wagner showed that the PO bond varies from single in trimethylphosphine oxide to almost triple in phosphoryl fluoride. The positive charge on the phosphorus atom passes through a minimum when the electronegativity of the substituent is 2.7 on Pauling's scale. In the two extreme cases—the most electronegative fluorine and the least electronegative methyl substituent—the charge distribution is

$$\underset{F_3}{-1.131} \equiv \underset{P}{+1.332} \equiv \underset{O}{-0.201} \quad \underset{(CH_3)_3}{+0.102} \equiv \underset{P}{+1.03} - \underset{O}{1.132}$$

This charge distribution shows that the dipole moment changes its direction on passing from phosphoryl fluoride to trimethylphosphine oxide. Fig. 2 illustrates the variation in the dipole moment with the electronegativity of the substituent. When the electronegativity of Y is 3.6, the dipole moment approaches zero§. Wagner's predicted variation in the dipole moment of the phosphorus–oxygen bond with the substituent has been confirmed experimentally[46,47]. It was found that the dipole moment, while depending almost solely on the electronic state of the phosphorus–oxygen (σ,π)-bond, does not vary monotonically on passing from some substituents to others, but passes through a minimum at certain substituent electronegativities. Analogous conclusions were reached from a consideration of the (σ,π)-bond of the sulphur atom in various derivatives[48].

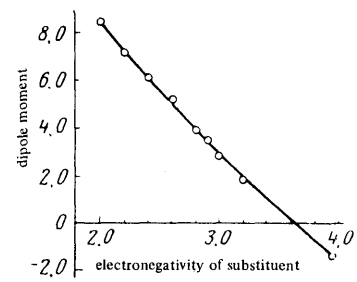


Figure 2. Variation in dipole moment of Y_3PO molecule with electronegativity of substituent Y.

In phosphoryl halides $POHal_3$ the d-orbitals of phosphorus may also interact with orbitals of the halogen atoms[49]: e.g. two $d_\pi - p_\pi$ bonds may be formed by the $d_{x^2-y^2}$ and d_{z^2} orbitals of phosphorus and the p-orbitals of the ligands[50,51]. Table 2 lists dissociation energies and bond multiplicities for several $POHal_3$ compounds[21,52]. The difference in the degree of interaction of the central atom with oxygen and with the halogen is evident. The degree of interaction diminishes in the sequence of substituents F → Br. It is apparent that $d_\pi - p_\pi$ interaction of the substituents has little effect on the P=O bond, since the presence of C_{3v} symmetry in the POX_3 system enables the orbitals of the X atoms to interact with d_π-orbitals of the phosphorus atom orthogonal to the orbitals used in the phosphorus–oxygen bond[44].

The way in which d-orbitals of the central atom are involved in the bonds has not yet been unequivocally settled. The phosphorus–oxygen and sulphur–oxygen bond lengths have been calculated[55] by the molecular orbital method for series of compounds with and without the involvement of

§ A triple phosphorus–oxygen bond has been found for the hypothetical molecule H_3PO calculated by the molecular orbital method, and the d-orbitals of the phosphorus atom are assumed to be involved in the bond[45].

d-orbitals. The results suggest that d-orbitals play a modest part in shortening these bonds, but the problem requires further consideration. The nitrogen–oxygen bond in nitrosyl trifluoride is shorter (1.15 Å) than the calculated value, as with compounds containing a P=O or an S=O bond, although the participation of d-orbitals is still less probable in this case. A possible explanation is the effect of the electronegative fluorine atom on the charge on the nitrogen.

Table 2. Energy of dissociation and multiplicity of bonds in the compounds $POHal_3$.

Hal	E, kcal mole^{-1} P–O	Multiplicity P–O	E, kcal mole^{-1} P–Hal	Multiplicity P–Hal
F	178*	2.47	90	1.35
Cl	161	2.24	61	0.91
Br	151	2.16	55	0.81

* Other numerical values have been given [53,54], but the general trend remains.

The presence of $p_\pi - d_\pi$ interactions is not indicated unambiguously by the experimental electronic, nuclear magnetic resonance, and nuclear quadrupole resonance spectra of series of compounds [56–59].

Table 3.

Compound	Force const.	Multiplicity	Compound	Force const.	Multiplicity
OPF_3	11.89	2.44	SPF_3	5.21	1.89
$OPCl_3$	10.24	2.15	$SPCl_3$	4.89	1.80
$OPBr_3$	9.74	—	$SPBr_3$	4.69	—
$OP(CH_3)_3$	9.14	1.88	$SP(CH_3)_3$	3.33	1.33

An examination has been made of the influence of the $3d_Z$-orbital component on several properties of sulphur- and phosphorus-containing molecules, including their ionisation potentials, electronic transition energies, dipole moments, and overlap integrals calculated by a semi-empirical method [60]. Introduction of this component only slightly improves the agreement between calculated and experimental values. Further investigation is required on these lines [22,23,27,39,55].

When the oxygen atom in $\rangle P{=}O$ is replaced by a sulphur atom, the multiplicity of the phosphorus–sulphur bond, the force constants, and the corresponding bond energies are smaller than in the original compound. Table 3 lists force constants and bond multiplicities for several compounds [61]. The phosphorus–chlorine bond length increases on passing from phosphoryl to thiophosphoryl chloride [62–64].

The influence of substituents on the P=O bond is probably mainly an inductive effect [65,66]. As mentioned earlier, $d_\pi - p_\pi$ interaction of the phosphorus atom with a substituent has little effect on the P=O bond. Bell et al. [67] showed that the vibration frequencies of the latter bond in the infrared and the Raman spectra vary linearly with the electronegativity of the other substituents attached to phosphorus.

Some authors regard the vibration frequencies as functions of the Taft σ^*-constants [68,69] characterising the inductive and mesomeric effect of the substituents, and also introduce into the equation constants to represent the electronic shielding of the phosphorus nucleus [70]. The force constants of the P=O bond vary linearly with the calculated π-bond energies [71]; the coefficients in the equation $K = a + bE$ depend on the nature of the substituents.

The integral intensity of the vibrational bands involving the P=O bond depends on the electronic properties of the whole POX_3 molecule, and is 80% determined [72,73] by the product

$$\left(\frac{\partial \mu_{P=O}}{\partial Q} + \frac{\partial \mu_{P-Cl}}{\partial Q}\right) Q$$

where Q is the normal coordinate of the bond and μ the dipole moment of the bond. The non-unique character of the vibrational bands of the PO bond in a series of substituted phosphoryl compounds has also been noted elsewhere [74]. No effect of the nitrogen and sulphur atoms on the vibrational frequencies and force constants of the P=O bonds was apparent in the series of compounds $(RS)_3PO$ and $(R_2N)_3PO$, and the difference found in the π-charge on nitrogen and sulphur atoms (+0.187 and −0.004) [75] was expressed in a corresponding change in the integral intensity of the P=O vibrational bands.

Table 4. Force constants of P–X bonds as function of type of hybridisation of atomic orbitals.

Force constant	pd	p	sp^3	sp^2
K_{P-H}		3.10[a]	3.30[b]	3.59[c]
K_{P-CH_3}		2.77[d]	3.05[e]	—
K_{P-F}	4.52[f]	5.19[g]	6.34[h]	6.38[f]
K_{P-Cl}	1.63[i]	2.36[j]	2.66[k]	2.78[i]
K_{P-Br}		1.84[l]	2.66[m]	
K_{P-OCH_3}		3.37[n]	4.87[o]	

Compounds
[a] PH_3, [b] $BH_3{\cdot}PH_3$, [c] H_2PF_3, [d] $P(CH_3)_3$, [e] $SP(CH_3)_3$, $OP(CH_3)_3$, [f] PF_5, [g] PF_3, [h] OPF_3, [i] PCl_5, [j] PCl_3, [k] $SPCl_3$, [l] PBr_3, [m] $SPBr_3$, [n] $P(OCH_3)_3$, [o] $OP(OCH_3)_3$.

Examination of the effect of various factors on the force constants of the phosphorus bonds in series of compounds is of interest [61]. Table 4 lists force constants as a function of the type of hybridisation of the orbitals of the central atom. Increase in the s-character of the bond is accompanied by an increase in the force constants. A similar effect is produced by increasing the electronegativity of the substituents and also the charge on the ions.

The above regularities are less clearly exhibited by thiophosphoryl compounds [61,76,77]. In view of the diminished ionic character of the phosphorus–sulphur bond in comparison with the phosphorus–oxygen bond, it may be supposed that the mass of the atoms in the substituents and the force constants of P–X bonds—not the electronegativity—will have the decisive effect on the P–S stretching frequencies. However, Zingaro [78], in calculating the frequencies of the P–S vibrations in thiophosphoryl compounds, attributed the decisive role to the electronegativity of the substituents. These two conclusions on the effect of substituents on the phosphorus–sulphur bond are not mutually inconsistent, as might appear at first glance.

It has been proposed[79] to separate thiophosphoryl compounds into different groups containing strongly electronegative and less electronegative substituents. The regular variation in the force constant of the P–S bond within the groups is explained by mechanical interaction with P–X stretching vibrations, in agreement with conclusions reached by other workers[76]. When, however, compounds having substituents differing strongly in electronegativity are compared, this difference must be regarded as the cause of the variation in the phosphorus–sulphur vibration, in agreement with Zingaro's conclusions. Thus, similarly to phosphoryl molecules, the position of the phosphorus–sulphur band in thiophosphoryl compounds is determined by the immediate environment of the phosphorus atom[80-83].

The nuclear magnetic resonance spectra of phosphoryl compounds do not enable a similar relation to be established between the chemical shifts and the electronegativities of substituents adjacent to phosphorus. Electronic shielding of the nucleus of the central atom by substituents adjacent to the phosphoryl P–O and thiophosphoryl P–S groups increases in the sequence

$$Se < S < C_{aliph} < C_{arom} \approx P < N \approx Cl < H < O < F$$

the more electronegative the substituent element, the greater the shielding at the phosphorus atom. An explanation is provided by interaction between the substituent and the P=O or P=S electron cloud: the more electronegative the substituent, the more strongly it "draws out" the electrons of the π-bond of this group and the greater becomes the shielding of the phosphorus.

In sum the structure of molecules of the type XYZElO, containing oxo-groups, depends on the presence in the El–O group of coordinate bonds superimposed on and opposite to the σ-bond. sp^3d-Hybridisation is improbable. The $d_\pi - p_\pi$ interaction of phosphorus and halogen atoms is possible in the Hal_3PO molecule.

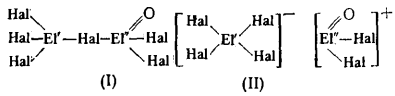
The geometrical configuration of the molecules corresponds to a distorted tetrahedron. For $POCl_3$ the P–Cl and P–O distances are 1.99 ± 0.02 and 1.45 ± 0.03 Å respectively, and the Cl–P–Cl angle is 103.6 ± 2°.[63]

III. DONOR–ACCEPTOR PROPERTIES OF OXIDE HALIDES IN CHEMICAL REACTIONS

Structural features of molecules containing oxo-groups govern their behaviour towards other compounds. The reactivity of such molecules, which is apparent in many reactions and has been discussed in detail, e.g. for organophosphorus compounds[40,44], is determined by the properties of the molecular and atomic non-bonding orbitals. Nucleophilic substitution at the phosphorus atom involves rupture of that one of the four phosphorus bonds that has the lowest electron density. Electrophilic reagents interact with the phosphoryl oxygen atom, which has the highest ME1 electrophilic superdelocalisability[84]. In the molecules XYZElO [or S] the O(S) atom and also the atoms X, Y, Z possess not only molecular orbitals but also non-bonding atomic orbitals with electron pairs, which may take part in the formation of bonds[85,86]. The possibility of their involvement in interaction with acceptor molecules depends on the factors discussed above, the interaction of hybrid molecular and atomic orbitals determining the donor properties of these molecules[87,88].

In view of the properties of the atomic orbitals of oxygen and chlorine (or other substituent) in molecules, we can in general imagine two mechanisms of interaction of molecules containing PO, SO, SeO, PS groups with various acceptors (e.g. chlorides of Groups III–V elements).

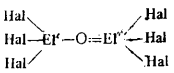
1. The donor–acceptor bond is formed by lone pairs of the halogen atom[89-96]:



(I) (II)

These structures differ in the share of the halogen Hal in the donor–acceptor bond. Case (II) involves formation of a tetrahedral ion of the type $ElHal_4^-$, which is stable with several metal chlorides.

2. The donor is the oxo-oxygen[97-109]¶:



Interaction occurs considerably more rarely according to scheme *1*, and is governed to a greater extent by the properties of the acceptor—the second component of the reaction—which is capable of forming a complex anion. The actual donor–acceptor interaction (scheme *2*) is the subject of discussion.

Substituents in XYZElO molecules, by exerting an inductive effect on the El–O bond, change its donor ability. For example, the donor power of the oxygen atom is weaker in oxide chlorides than in organic phosphoryl compounds, owing to the greater electronegativity of chlorine than of organic radicals and the stronger inductive effect of chlorine on the P=O bond. By "drawing out" the electrons from oxygen, chlorine lowers its capacity for participation in a donor–acceptor bond. The donor capacity of the compounds increases in the sequence

$$POF_3 < POCl_3 < POBr_3 < PO(CH_3)_3.$$

The electronegativity of the various organic substituents has the same effect[111].

The influence of the central atom on the properties of XYZElO molecules might be connected directly with the possibility and degree of participation of *d*-orbitals in the ElO bond: increased participation of those of the central atom should diminish the donor properties of the molecule. Phosphoryl chloride possesses donor properties; oxygen in the vanadyl(V) chloride molecule does not; while the molecules of transition elements—$TiOCl_2$, $MoOCl_2$, etc.—possess well defined acceptor properties[112,113].

On the other hand, the compound $(CH_3)_3NO$ is a poorer donor than is $(CH_3)_3PO$: the most convincing explanation here, as in the analogous case of bond shortening in the compound F_3NO, is based on the formal charge on the central atom[114].

Investigation of the complexing power of phosphoryl[89], seleninyl[115], acetyl[116-120], and thionyl[121] chlorides has made it possible to compare the donor properties of these molecules towards such acceptors as arsenic trichloride, tin tetrachloride, and titanium tetrachloride[97]. The donor properties of these molecules are found to decrease in the sequence

$$POCl_3 > SeOCl_2 > CH_3COCl > SOCl_2.$$

This donor sequence is consistent with the electronegativities of the central atoms in these molecules. It may

¶ Electrostatic interaction may be possible[110] as a consequence of the highly polar character of the phosphoryl P=O group.

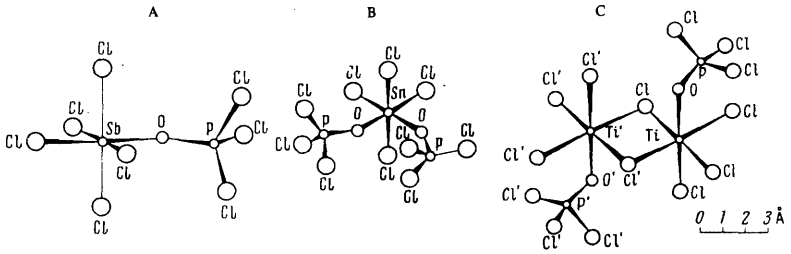


Figure 3. Structure of the compounds $SbCl_5.POCl_3$, $SnCl_4.2POCl_3$, and $(TiCl_4.POCl_3)_2$.

be supposed to a first approximation that the oxygen atom will have its maximum charge when the electronegativity of the central atom is least. The electronegativities of phosphorus, sulphur, selenium, and carbon are respectively 2.1, 2.4, 2.5, and 2.5. Increase in electronegativity increases the El–O bond order, by diminishing the donor power of the oxygen.

In view of the above mentioned inductive effect of substituents on the central atom in XYZElO(S) molecules and the appearance of a positive charge on the atom, such molecules can be assumed to possess acceptor properties. Indeed several molecules—those possessing the weakest donor properties—develop acceptor properties[97]. In this connection it is interesting that compounds are formed in mixtures of seleninyl chloride with carbon tetrachloride and of acetyl and thionyl chlorides with silicon tetrachloride, where these workers consider that the oxide chlorides are acting as acceptors, and the tetrachlorides in the uncharacteristic role of donors†. The investigation of binary mixtures with pyridine, which develops clearly defined donor properties, has established the presence of compounds when the second component of the mixture is seleninyl, acetyl, or thionyl chloride, etc.

The above considerations on the donor power of various oxo-compounds are based on experimental investigation of the complex compounds formed in mixtures and are fully valid only on the assumption of bond formation in them through oxygen.

A diminution in donor power is observed on passing from phosphoryl to thiophosphoryl chloride: thus mixtures of phosphoryl chloride with zirconium tetrachloride and niobium pentachloride are characterised by the formation of complex compounds[124–128]; no compounds are formed in the corresponding mixtures with thiophosphoryl chloride[129–131], the donor properties being determined in this case by the atomic orbitals of the sulphur atom.

IV. REACTIONS OF PHOSPHORYL CHLORIDE WITH GROUPS II–V CHLORIDES

A characteristic feature of molecules containing an oxo-group is the ability to react with valency-unsaturated chlorides of Groups III–V elements, their derivatives, and also halides of bivalent metals[132–134]. Examination of the equilibrium diagrams for systems formed by phosphoryl chloride with the chlorides $ElCl_3$ ($ElCl_4$, $ElCl_5$) by thermal analysis has established the presence of complex compounds, usually having the 1 : 1 composition, more rarely 1 : 2 and 2 : 1.[135–151] It is interesting that analogous compounds are obtained in the systems formed by two compounds containing oxo-groups—by phosphoryl chloride with molybdyl, tungstyl[112], or titanyl[113] chloride.

The resulting complexes are easily hydrolysed and are decomposed by alcohol. The melting point does not usually exceed 200°C. They are stable compounds, which can be isolated in the pure state; they dissolve in carbon tetrachloride and in nitrobenzene, while being less soluble in benzene. Dissolution in nitrobenzene is accompanied only by slight dissociation, and their stability in solution increases in the sequence

$$SbCl_5\cdot POCl_3 < NbCl_5\cdot POCl_3 < TaCl_5\cdot POCl_3 < AlCl_3\cdot POCl_3.$$

Coordination with oxygen has been found in several compounds of elements in Groups IV and V of the Periodic System[107,152–162], but the type of coordination is a matter of controversy for some double compounds with chlorides of Group III elements—boron, aluminium, gallium—and iron[94–96,104].

The main conclusions concerning the structure of these compounds were reached from a study of their infrared spectra. A shift in electron density from the El=O bond to M (scheme *2* in Section III) may be imagined to lead to an increase in the electronegativity of the phosphorus atom, influencing the displacement of electron density along the El–Cl bond: this is accompanied in the infrared spectrum by a fall in the vibrational frequency of the El=O bond and a rise in the El–Cl frequency. The newly formed M–O bond does not usually appear in the spectrum, evidently because of its low electron density[102]. On the other hand, formation of an El–Cl bond should lead to a slight shift in the El=O vibrational absorption band, but to a decrease in the El–Cl vibration frequency, as was established from investigation of complexes of nitrosyl halides[163–165]. The difficulties arising in recording the spectra of these hydrolysable substances prevent us from drawing unambiguous conclusions from the results.

X-Ray results obtained for the compounds $SbCl_5.POCl_3$,[156] $SnCl_4.2POCl_3$,[157] and $TiCl_4.POCl_3$ [158] indicate unequivocally the presence of coordination with oxygen. Fig. 3 shows the arrangement of the atoms in these compounds. The interatomic distances of the M–O donor–acceptor bond are (in Å)—TiO 2.10, SbO 2.18, $SnO_{(1)}$ 2.25, and $SnO_{(2)}$ 2.30 (for the 1 : 2 complex)—formation of an M ← O bond having hardly any effect on the P–O length, which is 1.46 Å for the compound with titanium tetrachloride, 1.46 Å for $SbCl_5.POCl_3$, and 1.41 and 1.49 Å for the tin complex (P–O bond length 1.45 Å for the $POCl_3$ molecule), and slightly increasing the ClPCl angle (by 3–4°)‡.

† The donor properties of these molecules have been noted by other workers[122,123].

‡ The mean phosphorus–oxygen distance in $POCl_3$ in the mixed complex $Mg(PO_2Cl_2)(POCl_3)$ is 1.42 Å, the molecules being slightly deformed[166].

The nuclear magnetic resonance spectra of the complex $TiCl_4.POCl_3$ (^{31}P) indicate an increase in the chemical shift δ from 2.2×10^{-6} for phosphoryl chloride to 16.6×10^{-6}, which is evidence of a decrease in the degree of shielding of the phosphorus nucleus in the complex and a diminution in the degree of π-overlap along the P=O bond[107].

Study of the chlorine-35 nuclear quadrupole resonance spectra of the complex compounds formed by antimony, iron, and titanium chlorides[167] enabled the type of chemical bond to be ascertained by comparing the state of the PCl_3 groups in the free phosphoryl chloride molecule and in the complex. The shift in the spectral bands was estimated by means of the formula

$$\Delta\rho = -\Delta I - \Delta\pi - \Delta(\alpha\sigma)$$

where I is the degree of ionic character of the bond, π is the degree of π-character, and α and σ are the degrees of s- and d-hybridisation of the bond. The state of the PCl_3 group is almost the same in the phosphoryl chloride molecule and in the complex, so that the frequency shifts obtained can be ascribed to a change ΔI in the ionic character of the bond. The frequency shifts found experimentally in the spectra of the complexes indicated that ΔI, representing the displacement of the electronic charge from chlorine to phosphorus on formation of the complex, varies in the sequence

$$SbCl_5 > FeCl_3 > SnCl_4 > TiCl_4.$$

The donor–acceptor bond M←O is stable: the compounds exist in the melt and in the vapour state. The calculated heats of dissolution of the complexes (ΔH, kcal mole^{-1})—$ZrCl_4.POCl_3$ 24.3,[131] $TiCl_4.POCl_3$ 23.3,[168] $FeCl_3.POCl_3$ 18.2,[169] $BCl_3.POCl_3$ 17.9,[151] $AlCl_3.POCl_3$ 28.4,[170] and $GaCl_3.POCl_3$ 22.6[171,172]—provide an energetic characteristic of the donor–acceptor bond.

The formation of a donor–acceptor bond can be characterised directly by a calorimetric study of reactions between donors and acceptors[111,171]. Heats of dissolution of acceptor chlorides in phosphoryl chloride have been measured according to the scheme

$$MCl_n + POCl_3 = Cl_nMOPCl_{3\,soln} \quad \Delta H_1\ n = 3\text{—}5$$
$$Cl_nMOPCl_{3\,solid} + POCl_3 = Cl_nMOPCl_{3\,soln} \quad \Delta H_2\ n = 3\text{—}5$$

The quantity $\Delta H_3 = \Delta H_1 - \Delta H_2$ is taken to be a direct measure of the donor-acceptor interaction:

$$MCl_{n\,solid\ soln} + POCl_{3\ soln} = Cl_nMOPCl_{3\,solid} \Delta H_3\ n = 3\text{—}5$$

Table 5 lists these thermal effects for a series of chlorides, among which those of Group III elements have the smallest values of ΔH_3. The nature of the coordination in them is a matter of controversy, and the general trend is due to an increase in the electronegativity of the acceptor metal atom. However, calorimetric results are only relative in character[111], since several secondary factors, e.g. changes in the structure of acceptor and donor, etc., are superimposed on the donor–acceptor interaction. Transfer of these compounds to the liquid phase involves their ionisation.

The Raman spectra of the complexes—$SnCl_4.2POCl_3$, $TiCl_4.2POCl_3$, and $SbCl_3.POCl_3$—in solution[102] indicate strong intermolecular interaction between phosphoryl chloride and the metal halide. It is usually difficult to isolate the solid adducts from solutions because of their tendency to supercooling[173] or because of the slowness of reaction between the components[89]. The composition of the solutions is complicated, and complex ions are present[174–179].

The ionisation of the complex compounds in solutions usually involves ionisation of the M–Hal bond with preservation of the MO...P donor–acceptor bond. The general scheme of ionisation is[180]

$$2\,DACl_n \rightleftarrows [D_2ACl_{n-1}]^+ + [ACl_{n+1}]^-$$

With variation in the donors the general tendency is for the degree of ionisation of the compounds in solution to increase with the donor strength[181–183].

Table 5. Heats of dissolution of acceptor chloride (ΔH_1) and of solvate (ΔH_2) in phosphoryl chloride and heats of donor–acceptor interaction [ΔH_3].

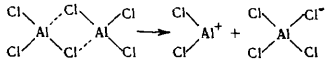
Acceptor chloride	$-\Delta H_1$	Solvate	$-\Delta H_2$	$-\Delta H_3$
$SbCl_5$	17.9	$Cl_5SbOPCl_3$	0.8	17.1
$TiCl_4$	20.7	$Cl_4Ti(OPCl_3)_2$	−1.7	22.4
		$Cl_4TiOPCl_3$	−2.7	
$SnCl_4$	20.2	$Cl_4Sn(OPCl_3)_2$	−2.1	22.3
$FeCl_3$	15.0	$Cl_3FeOPCl_3$	1.7	13.3
BCl_3	9.4	Cl_3BOPCl_3	1.5	7.9
$AlCl_3$	16.6	$Cl_3AlOPCl_3$	—	—
$GaCl_3$	11.0	$Cl_3GaOPCl_3$	0.8	10.2

Solutions of mixtures of aluminium, iron, titanium, etc. chlorides contain both cationic and anionic forms. Analysis of conductometric titration and electrical conductivity data for the solutions indicates that interaction in solution can be represented by the equation[173]

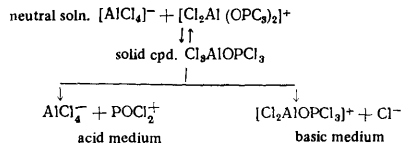
$$\text{Polymer} \rightleftarrows \text{Anion} + POCl_2^+ \rightleftarrows FeCl_4^- + POCl_2^+$$

which involves coordination with oxygen. The existence of iron in both cationic and anionic forms has been confirmed by the electrolysis of solutions of complexes of phosphoryl and thiophosphoryl chlorides with iron(III) chloride[184].

The structure of solutions of mixtures of aluminium and phosphoryl chlorides was examined in the light of possible simultaneous coordination with oxygen and chlorine[173,185]. Formation of such a complex can be pictured from a consideration of the breakdown of the dimer Al_2Cl_6:



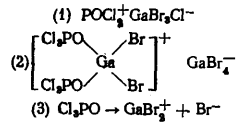
and the cation $AlCl_2^+$ combines with a donor molecule. The structure of a solution of aluminium and phosphoryl chlorides is then represented as



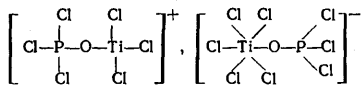
The dual character of oxygen and chlorine coordination in such solutions is supported by other work[186–188]: both a solvated O-coordinated complex and the ion $AlCl_4^-$ are present, the latter being formed in two ways:

$$1)\ AlCl_3 + POCl_3 \rightarrow AlCl_4^- + POCl_2^+$$
$$2)\ 4AlCl_3 + 6\,POCl_3 \rightarrow 3\,AlCl_4^- + [Al(POCl_3)_6]^{3+}$$

The investigation of mixed compounds in solutions of $GaBr_3.POCl_3$ suggests three possible ionisation paths with formation of the products[189]



Structure (3) is regarded[189] as the most probable; the P–O→M bond is preserved on dissociation, as in the above cases. This bond is stable also when the complex $TiCl_4.POCl_3$ dissociates in solution, and the ions



are assumed to be present[179]. A study of solutions of various donor–acceptor pairs ($GeCl_4$–acceptor) in phosphoryl chloride has established the presence of associated complexes containing the anion $[GeCl_6]^{2-}$.[190]

Binary mixtures from which individual complex compounds do not separate are of great interest. Such binary mixtures exhibit considerable departures from ideality. A positive deviation from Raoult's laws is characteristic of solutions of the mixtures $GeCl_4$–$POCl_3$, $SiCl_4$–$POCl_3$,[191,192] and $SeOCl_2$–$AsCl_3$,[193] the degree of departure from the laws of ideal solutions being proportional to the donor power of the donor (and the strength of the acceptor). Thus the $VOCl_3$–$TiCl_4$ system[194,195] can be regarded as ideal, which corresponds to the decrease in donor power in the sequence—$POCl_3 > SeOCl_2 > VOCl_3$.

We have already noted a decrease in the donor power of the P–S bond on passing from phosphoryl to thiophosphoryl chloride, but intermolecular interaction occurs between $PSCl_3$ and $SiCl_4$ in solution, producing a departure from ideal behaviour, though smaller than in the $POCl_3$–$SiCl_4$ system[196].

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The Reactions of Hydrazones

Yu.P.Kitaev and B.I.Buzykin

The chemical properties of organic compounds containing an open-chain hydrazono-group are surveyed systematically. A list of 412 references is included.

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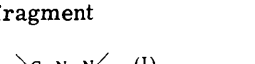
I. INTRODUCTION

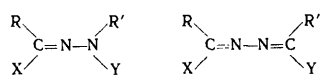
In the chemical literature hydrazones are not usually discussed as a separate class of organic compounds: most often they are regarded as derivatives of carbonyl compounds or of acids. The present review includes in the category of hydrazones all compounds whose molecules contain the triatomic fragment



(I),

not forming part of a heterocycle. However, the amino-nitrogen atom and/or the carbon atom may be included in a non-aromatic ring [1].

The close similarity of chemical and physical properties and the presence of a common functional group enable hydrazones (II) and azines (III) to be considered a single class of compounds:



(II) (III)

where R and R′ = H, Alk, Ar, Az, Ht†; Y = H, Alk, Ar, Ht, Az; X = H, Alk, Ar, Az, Ht, Hal, OR″, SR, CN, SO_2R, NO_2, NH.NR″R‴, NH.NHR″, N:NR″, COOR″, CO.NR″R‴. Several types of hydrazones have already been surveyed [2-51], and the electrochemical reduction of this class of compounds has been reviewed [52].

We have classified the numerous reactions undergone by hydrazones on the formal principle of the type of reactant.

II. REACTIONS OF HYDRAZONES WITH ELECTROPHILIC REAGENTS

Protonation

The distinguishing feature of the hydrazono-group is the presence of two nitrogen atoms—imino and amino—the valency electrons of which differ in their hybridisation (see formula II). The transition of a nitrogen atom from the sp^3 to the sp^2 state lowers its basicity. Amines possess more pronouncedly basic properties than do imines [2]. Conversion of an arylhydrazine into an arylhydrazone involves a substantial diminution in basicity [2,53-56]. Semicarbazones are less basic than semicarbazide by several orders of magnitude [56,57]. The basic character of azines (di-imines) is especially weak [2,44,49]: for example, acetone azine is 0.1% as basic as hydrazine [58]. Since the lone pair of electrons of the amino-nitrogen is delocalised in unsubstituted hydrazones as a result of conjugation with the π-system of the imino-bond [1], these compounds are also less basic than hydrazine: acetophenone hydrazone has $pK_a = 4.94$, whereas the value for hydrazine is 8.07. [59]

Increase in the electron-accepting character of R in (II) lowers the basic strength of hydrazones. This rule has been observed both with unsubstituted hydrazones [59] and with the phenyl-, [56] *p*-nitrophenyl-, [53,54] 2,4-dinitrophenyl-, [54,55] and nitroguanyl-hydrazones [60] of a large number of substituted benzaldehydes and aromatic ketones. A linear relation has been established between the Hammett constants of the substituents in the benzene ring of the carbonyl component and the pK_a value of the 2,4-dinitrophenylhydrazones [55]. The number of electron-accepting groups and their position in the benzaldehyde molecule affect the basicity of the phenylhydrazones [56].

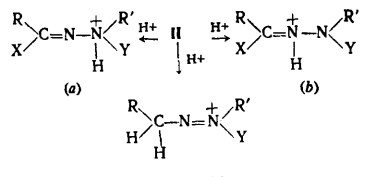
The substituent attached to the amino-nitrogen (R′ or Y in II) also has an effect. The basic character diminishes, for example, in the sequence unsubstituted hydrazones > > phenylhydrazones > *p*-nitrophenylhydrazones > 2,4-dinitrophenylhydrazones [1,2,10,45,48,53-56,59].

The introduction of electron-donor substituents into the hydrazone group will, of course, enhance the basicity, especially if the substituent is attached to the amine nitrogen. Dimethylhydrazones are stronger bases than unsubstituted hydrazones or phenylhydrazones [2]. Acetone *p*-nitrophenylhydrazone is a stronger base than the corresponding acetophenone derivative by a factor of 5. [54] The basic character of hydrazones is influenced not only by the nature of the substituents but also by the configuration of the molecule. Thus Vogel and Matter reported [61] that the *anti*-isomer of the *p*-tolylhydrazone of *p*-n-butylphenylglyoxylic acid has $pK = 6.6$, whereas the corresponding exponent for the *syn*-isomer is 5.1.

The hybridisation of the electrons of the amino-nitrogen atom varies with increase in the bulk of the substituents, depending on their nature [1], and sometimes approaches the

†Az = RCO = acyl; [Ht = heterocyclic group].

sp^2 state. As a consequence of this and the competitive influence of the substituents R, X and R', Y, hydrazones may undergo protonation either at the amine (*a*) or at the imine (*b*) nitrogen atom:



The more complicated case (*c*) is theoretically also possible, although it appears less probable.

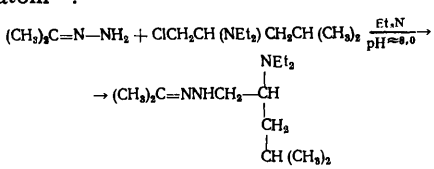
Semicarbazones are protonated at the carbamoyl group [57]. Dimethylhydrazones form quaternary salts on alkylation [62-64]; their protonation also takes place at the amino-nitrogen atom. The possibility of protonation at the imino-nitrogen is suggested by the insignificant change in basicity on passing from monoalkylhydrazones of aliphatic ketones to their *N*-acyl derivatives [65]. It is assumed that in 1,5-diarylformazans the amino-nitrogen of the hydrazone group is protonated.

Alkylation

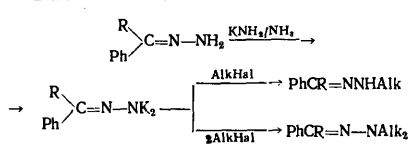
Unsubstituted hydrazones (II: R = Y = H) are converted by alkyl halides into azines of the same carbonyl compound [9,10,49]:

$$2\,PhCH{=}N{-}NH_2 + BrCH_2CH_3 \rightarrow PhCH{=}N{-}N{=}CHPh + CH_2{=}CH_2 + N_2H_4HBr$$

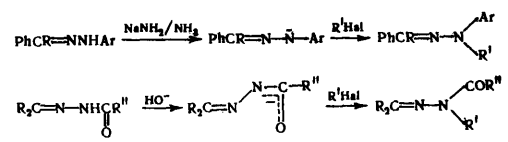
This reaction is accelerated in the presence of alcoholic alkali [66]. If, however, triethylamine in a buffer solution is used as the base, alkylation takes place at the amino-nitrogen atom [65]:



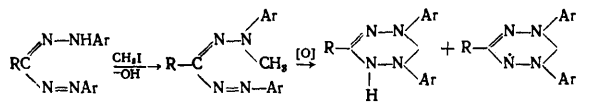
If an unsubstituted hydrazone is converted into a dianion by the action of potassamide in liquid ammonia, mono- or di-alkylhydrazones can be obtained depending on the quantity of alkyl halide taken [67]:



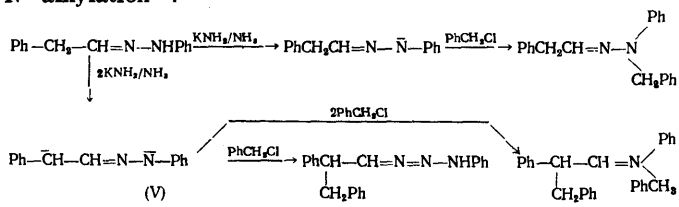
The less basic aryl- and acyl-hydrazones are usually alkylated after preliminary conversion into anions [2,9,10,45,49,68-70]. Conducting the reaction in liquid ammonia [69] generally gives high yields of alkylhydrazones:



The alkylation of formazans, like that of arylhydrazones, involves the intermediate formation of anions [47,71], although in some cases the reaction is complicated by the formation of 1,2,5,6-tetrahydro-1,2,4,5-tetrazine derivatives and then of verdazyl(IV). [72] The formation of (IV) may become the main reaction, because of the great tendency of $N_{(1)}$-methylformazans to undergo autoxidation:

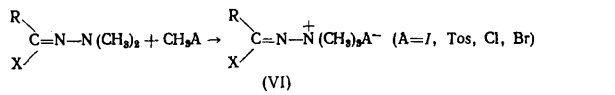


Arylhydrazones of carbonyl compounds having an α-methine group, on treatment with excess of potassamide, form the dianion (V), which is more liable to *C*- than to *N*-alkylation [70]:

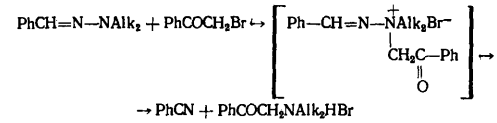


According to Grandberg et al. [73] arylhydrazones of aliphatic and alicyclic carbonyl compounds are alkylated by benzyl chloride and by dimethyl sulphate in boiling alcohol, after which they are converted into *N*-alkylindoles.

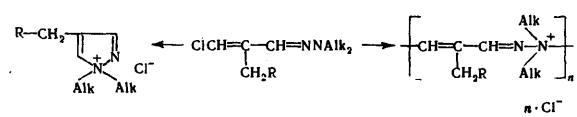
Dimethylhydrazones are easily converted into quaternary salts (VI) by the action of alkylhalides [62-64] and alkyl [arene]sulphonates [74]:



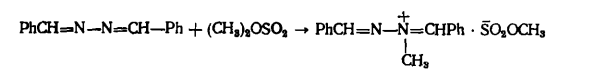
When α-bromoacetophenone is used, quaternary salts cannot be isolated from the dialkylhydrazones of aldehydes, evidently owing to their instability. In this case the products are a nitrile and an amino-ketone, resulting from rearrangement of an intermediate salt [75]:



Dialkylhydrazones of β-chlorovinyl-aldehydes are able to form polymeric quaternary salts [76]. Self-quaternisation with conversion into a 1,1-dialkylpyrazolium salt is also possible:



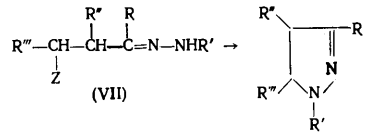
Benzaldehyde azine on treatment with dimethyl sulphate or ethyl iodide is converted into a saltlike product, whose structure is assumed [9,10,49] to correspond to a quaternary salt:



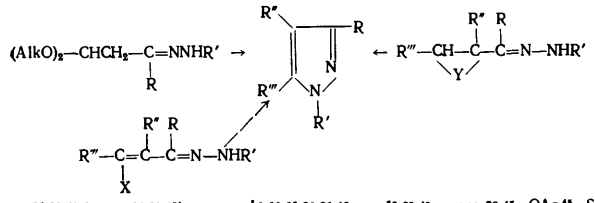
Ethyl iodide reacts similarly [9]. Diethyl sulphate and higher dialkyl sulphates do not form such salts. Aliphatic and alicyclic azines containing an α-methine group are converted by alkylating agents into a mixture of unsubstituted pyrazoline and an *N*-alkylpyrazoline [21,44,49,77].

Reactions involving the intramolecular alkylation of hydrazones with the formation of simple and fused heterocyclic systems are well known and have been widely studied [2,4,10,11,13,14,21,23,45,48,78,79]. The reaction mechanisms are largely obscure [21,23]: in parallel with an S_N

mechanism[21,23,78] the possibility is discussed of initial elimination of HZ from (VII) with formation of a hydrazone of an unsaturated oxo-compound followed by intramolecular addition of the HN fragment of the hydrazono-group at the resulting C=C bond[21,23,79]. The reactions involved in intramolecular alkylation can be represented by the schemes



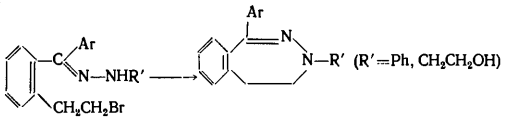
(Z=Cl[10,21,23,45], OH[10,21,45], OAlk[21], SH[23], SAr[45], NAlk$_2$[9,10,21,23,45,78,79], SeAr[23], $^+$NAlk$_3$[21])



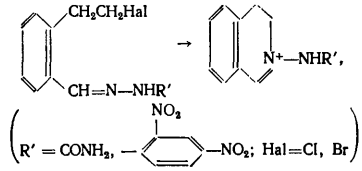
(Y=O[21,23,45,80] NH[21,23,45]) (X=OH‡[9,10,11,23,26,45], Cl[13,23,45], OAlk[23,45], OAr[45], SH[81], SAlk[82], SCN[28], Tos[23], NH$_2$[23,45], NHR[45], NAlk$_2$[23,45], NHNHR[45], —NHNH—C(=NH)—NH$_2$[83])

Here R″ and R‴ [10,84,85] and/or R and R′ [86] represent Alk, Ar, Ht, Az, a heterocyclic or a carbocylic fragment[87], a steroid residue[80], and possibly also nitroso[88] or arylazo[89,90].

Not only hydrazones of oxo-compounds having a reactive substituent in the β-position but also those in which the substituent is attached to a more remote carbon atom are capable of intramolecular alkylation. In particular, hydrazones of δ-halogeno-ketones are cyclised to diazepine derivatives by self-alkylation at the amino-nitrogen atom[91]:



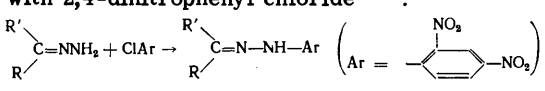
With increase in the electron-accepting properties of the substituent R′ attached to the amino-nitrogen atom the reaction centre may migrate, and self-alkylation involve the imino-nitrogen[35,45,92,93]:



The basic character of the imino-nitrogen diminishes more slowly than that of the amino-nitrogen under the influence of the acceptor substituent.

Arylation

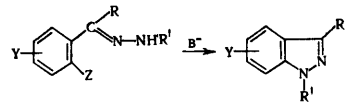
2,4-Dinitrophenylhydrazones of sterically hindered ketones are obtained by condensing unsubstituted hydrazones with 2,4-dinitrophenyl chloride[45,94]:



‡The monoenolic form of 1,3-dioxo-compounds.

This reaction was even recommended for the quantitative determination of unsaturated hydrazones[94]. Similar reactions can be used for the preparation of 2,4- and 2,6-dinitro- and the 3-R-2,4,6-trinitro-phenylhydrazones of benzophenone and fluorenone (R = H, Cl, CH_3).[95] Acetone azine reacts with picryl chloride in ethanol to form acetone 2,4,6-trinitrophenylhydrazone[45].

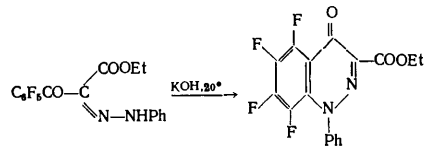
Monosubstituted and unsubstituted hydrazones of *ortho*-substituted benzaldehydes, acetophenones, and related compounds are converted by alkaline reagents into indazole derivatives (intramolecular arylation):[10,24,45,48,96-98]



(Z = Cl,[10,45] Br,[24,45] NO_2,[24,45,97] OH,[98] OAlk;[45,96] R = H, Alk, COOH, $CH_2C_6H_5$,[24,45] $COOC_2H_5$,[45] $COCH_3$,[97] R′ = H, Alk, Ph, *p*-$CH_3C_6H_4$, $Cl_XC_6H_{5-X}$,[24,45] 2,4-$C_6H_3(NO_2)_2$[45]).

Not only do hydrazones of 2,6-dinitrobenzaldehyde undergo this reaction, as assumed earlier[24], but also those of 2,4-di- and 2,4,6-tri-nitrobenzaldehydes[45] and pyridinealdehydes[98]. When Z = Hal, increasing the number of nitro-groups in the same ring increases the yield of indazole[24]. If the aryl ring contains a 2-chloro-substituent and a 6-nitro-group, the latter is the more readily replaced[45].

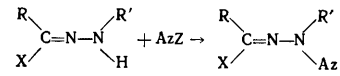
An example of intramolecular arylation with formation of a substituted cinnoline



has been reported[99].

Acylation

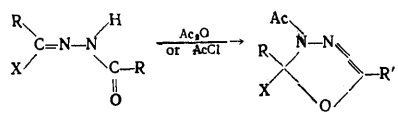
If Y = H in the hydrazone (II), acylation occurs in the usual way, and *N*-acylhydrazones (Y = Az) are formed[2,7,10,38,45,47,48,65,100-113]:



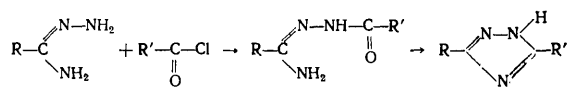
(R′ = H, Alk, Ar, Ht; Z=Cl,OEt, OAz).

Unsaturated hydrazones are converted smoothly into acylhydrazones[10,100]. Under the conditions of the Schotten-Baumann reaction many alkylhydrazones yield acetyl-, benzoyl-, and arenesulphonyl-alkylhydrazones[2,65]. Arylhydrazones are fairly easily acylated[45,48,101], but the resulting arylacylhydrazones tend to hydrolyse, and therefore the arylacylhydrazines and the oxo-compounds often separate instead of the acylated hydrazones[45]. A successful preparation requires an anhydrous solvent[45,102], and excess of the acylating agent or a catalyst (pyridine[102], zinc chloride[45,101]). 1,5-Diarylformazans are acylated with difficulty, and the yields of 1-acyl-1,5-diarylformazans are often low[47,103]. The acylation of phenylosazones is more successful[38]. Reaction between acylhydrazones

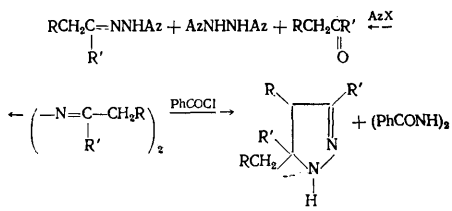
and acetic anhydride results most frequently in the formation of 1,3,4-oxadiazolines [104-107], although anomalies are observed [106]:



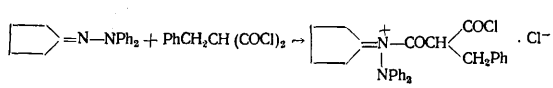
When arylhydrazones of quinones are acylated, the hydrazone form is fixed [108]. Amidrazones are acylated at the hydrazono-group [109,110], but reaction generally proceeds further with the formation of 1,2,4-triazole derivatives [45, 109-111]:



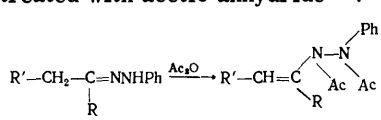
Azines, on treatment with acylating agents, are converted into acylhydrazones [49] or into mono- and di-acylhydrazines [49,112], and the methylene groups present undergo cyclisation into pyrazolines [44,113]:



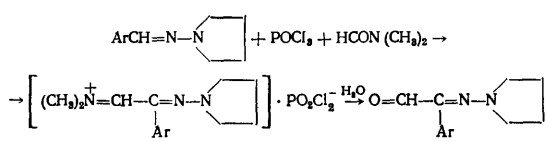
When the basicity of the amino-nitrogen atom is weakened considerably, the hydrazone may be acylated at the imino-nitrogen with the formation of a quaternary salt [114]:



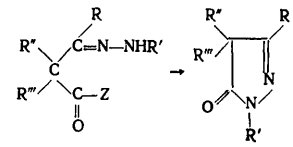
A product in which both nitrogen atoms of the hydrazone had been acylated was isolated when phenylhydrazones of aliphatic ketones, capable of conversion into alkenylhydrazines, were treated with acetic anhydride [115]:



Even disubstituted hydrazones of aldehydes do not form *C*-acyl derivatives under the usual conditions of acylation, and only in the Vilsmeier reaction are dialkylhydrazones of aromatic aldehydes converted into those of an arylglyoxal [116]:



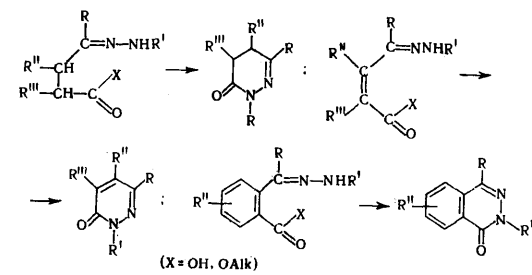
As in the case of alkylation, detailed studies have been made of intramolecular acylation with the formation of heterocyclic systems [2,9,10,23,45,83,99,114]. Hydrazones [23,45], alkylhydrazones [2,9,23,45], arylhydrazones [23,45,99], acylhydrazones [23,45], semicarbazones [23,45], thiosemicarbazones [23,45], selenocarbazones [117], and guanylhydrazones [83] of derivatives of β-keto-acids are cyclised to substituted pyrazolones:



(R′=H, Alk, Ar, Ht, —C(=O)—NH$_2$; Z=OH, OAlk, OAr, NH$_2$, NHR, NRR′, NHNHR, NHNH$_2$)

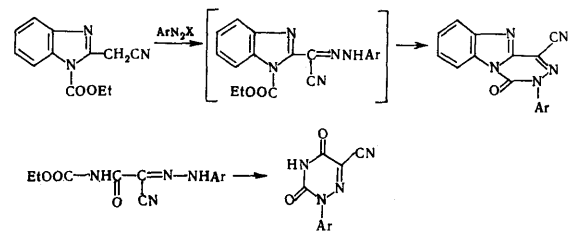
(S,Se)

Here R, R″, and R‴ may vary widely. Hydrazones of γ-keto-acids and their derivatives are cyclised to tetrahydro-3-oxopyridazines [9,10,25,26,45,46,118], and hydrazones of αβ-unsaturated γ-keto-acids to dihydro-3-oxopyridazines and tetrahydro-oxocinnolines [9,10,25,26,45,119-121]; however, hydrazones of *o*-formyl(or keto)benzoic acids are converted into dihydro-1-oxophthalazine derivatives [27,45,122]:

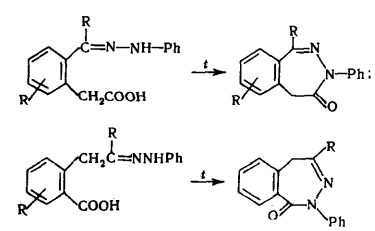


(X = OH, OAlk)

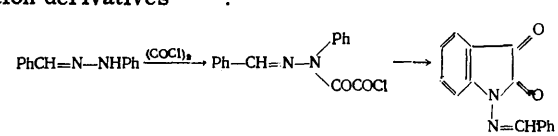
The hydrazone and carboxyl groups may be separated not only by a hydrocarbon chain but also by a fragment of a heterocycle [123] or by a carbamoyl group [124], when derivatives of tetrahydro-3,5-dioxo-1,2,4-triazine or its fused-ring analogues are formed:



Hydrazones of δ-keto-acids yield [91] substituted dihydro-3-oxoazepines:

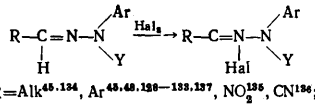


The acylation of phenylhydrazones with oxalyl chloride gives initially phenylacylhydrazones, and then *N*-aminoisation derivatives [45,125]:



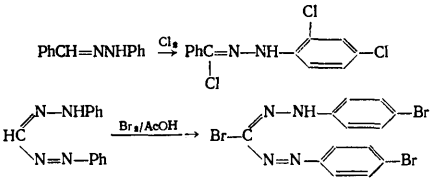
Halogenation

Halogens oxidise unsaturated hydrazones to azines [2,10,44,49] although substitutive halogenation is sometimes observed [126]. The action of halogens on arylhydrazones has been studied in greatest detail [45,48,127-137]. The hydrogen atom attached to the carbon of the hydrazone group (the methine hydrogen) in arylhydrazones of aldehydes can be replaced by a halogen atom [2,45,48,127-137]:

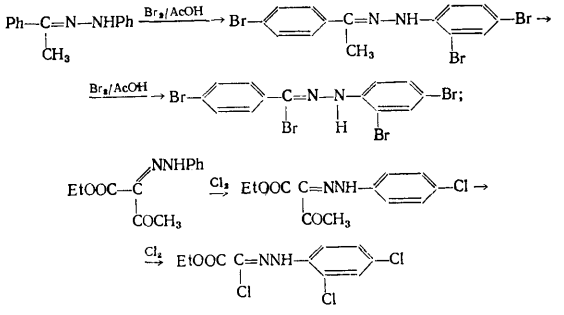


(R=Alk[45,134], Ar[45,48,128-133,137], NO_2[135], CN[136];
Y=H, CH_3; Ar=Ph, $(Hal)_nC_6H_{5-n}$, $(NO_2)_mC_6H_{5-m}$[45,48,129,130,133,134,137], Ht[128,131,133]).

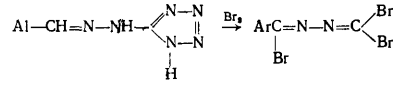
In phenylhydrazones substitution of the methine proton is accompanied by halogenation of the benzene ring attached to the amino-nitrogen atom [45,48,129], and halogens react similarly with 3*H*-formazans [43,138]:



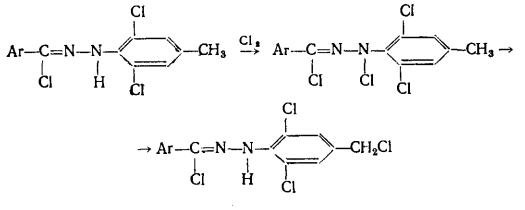
In arylhydrazones of ketones the ring is halogenated initially, after which the methyl or acetyl group may be replaced by halogen [45,48,129]:



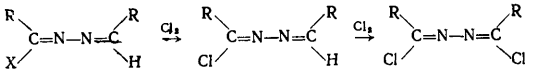
In the bromination of tetrazolylhydrazones replacement of the methine proton is accompanied by breakdown of the tetrazole ring [128]:



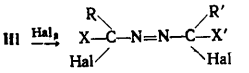
A kinetic study of the bromination of 2,4-dinitrophenylhydrazones of aliphatic aldehydes has shown that steric factors are more important than electronic factors in this series. The reason is that the *syn*-form, which does not react, must be converted into the reactive *anti*-form [134]. Arylhydrazones can undergo not only *C*- but also *N*-halogenation. The resulting derivatives are unstable, like all *N*-halogeno-compounds, and rearrange into more stable products (the Chattaway–Adamson rearrangement): [45,48,127,129]



Azines of aldehydes undergo substitution halogenation on treatment with halogens, with the stepwise replacement first of one and then the second hydrogen atom of the azine group [2,10,44,45,49,139]:

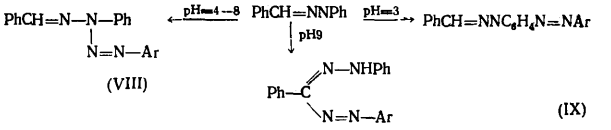


Under severe conditions of halogenation azines of the anthraquinone series undergo nitrile cleavage [139]. Azines of ketones do not undergo substitution, but add the halogen molecule at the 1,4-positions [2,10,11,44,48,140,141]:

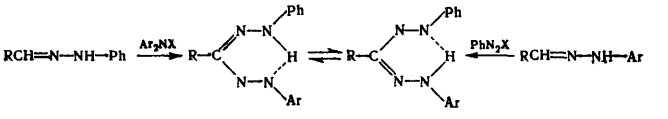


Reactions with Arenediazonium Salts

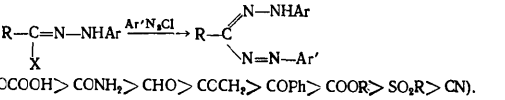
Phenylhydrazones of aldehydes react with arenediazonium salts to yield various products depending on the conditions [45,47,103,142]:



Production of the brightly coloured formazans (IX) has been the most thoroughly studied [2,11,31,38-40,47,48,71,103,137,143,144]. Arylhydrazones [47,103,117,143-146] and heterocyclic hydrazones [47,103,147-150] of aromatic [47,103,142,143,148,150], heterocyclic [47,103,143]; and aliphatic [144,147,149] aldehydes can be coupled, as well as arylhydrazones and arylosazones of sugars [38-40,47]. In general the isomeric forms of unsymmetrical formazans cannot be isolated, since they exist in equilibrium [47,103,143,145] and the two possible routes for the preparation yield the same product [145]:

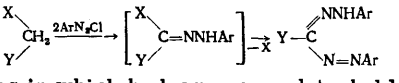


Among arylhydrazones of ketones only those in which the hydrazone carbon atom is combined with an easily eliminated group are able to undergo this reaction [47,103,144]:

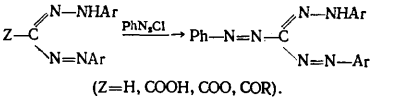


(X=COOH> H> CCCOOH> $CONH_2$> CHO> $CCCH_3$> COPh> COOR> SO_2R> CN).

Formazans are often produced by the action of diazonium salts on compounds containing an active methylene group (in the presence of a labile activating group) or a methyl group, since the rate of the second coupling (with the hydrazone formed as intermediate) far exceeds that of the first coupling [47,144]. In compounds containing an active methylene group one of the activating groups (listed above) is split off [47,144,151-155]:

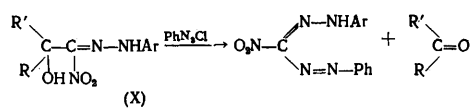


Formazans in which hydrogen or a detachable group is combined with the carbon atom react with diazonium salts analogously to arylhydrazones of aldehydes [47,108]:



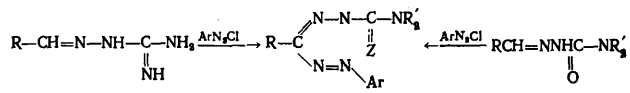
(Z=H, COOH, COO, COR).

Arylhydrazones of general formula (X) also yield formazans by eliminating a molecule of a carbonyl compound [144]:



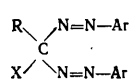
(X)

It has been reported [83,103] that analogues of formazans, the so called guanazyls, have been prepared from guanylhydrazones; among semicarbazones only $N_{(4)}N_{(4)}$-disubstituted derivatives yield such products, whereas acyl- and thioacyl-hydrazones do not react with arenediazonium salts [156].



(a) Z=NH, R'=H, (b) Z=O, R'=Ar.

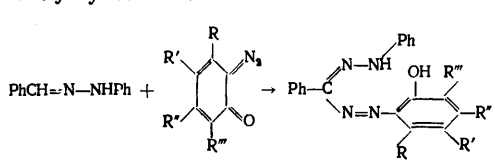
Since disubstituted hydrazones of aldehydes and $N_{(5)}$-alkylated formazans do not undergo the reaction, it was supposed that the formation of formazans involved tetrazens (VIII) as intermediates [47,103,142,148,157]. It has been shown recently, however, that the intermediate compounds are bisarylazo-derivatives (XI)



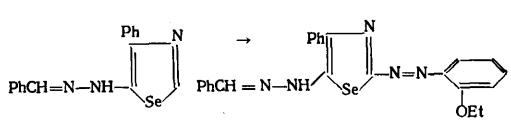
(XI)

(X=H, COOH, COOR, etc.)

In alkaline medium they isomerise rapidly into formazans (IX). [48,72,158,159] The possibility of direct substitution of the hydrogen atom in arylhydrazones of aldehydes by an arylazo-group has also been discussed [116,142]. The probability of this mechanism is supported, in our opinion, by the coupling [160] of arenediazonium salts with 1-aryl-2-pyrazolines, which are cyclic analogues of hydrazones. Diazoquinone derivatives react similarly to arenediazonium salts with arylhydrazones [161,162]:

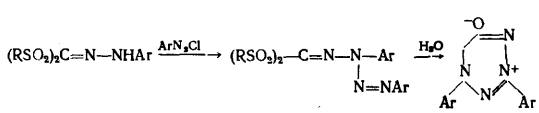


However, not all hydrazones can be converted into formazans. Thus compound (XII) is obtained from 5-benzylidenehydrazino-4-phenylselenazole and diazotised *o*-phenetidine [117]:

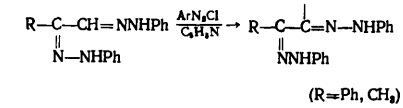


(XII)

Although arylhydrazones of bisalkylsulphonylformaldehydes split off the sulphonyl group, 1,3-diaryltetrazol-5-ones, which exist in the betaine form, are produced instead of the expected formazans [31,163,164]:



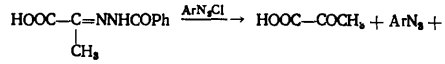
Phenylosazones of monosubstituted glyoxals are converted into phenylosazones of α-diketones [45,47,165,166], *C*-arylation occurring instead of azo-coupling:



(R=Ph, CH_3)

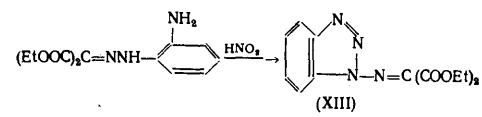
Nevertheless, formazans (azaformazans) are formed smoothly from arylosazones of sugars [38,39,47].

Acylhydrazones yield aryl azides, amides of the corresponding acids, and carbonyl compounds [167]:



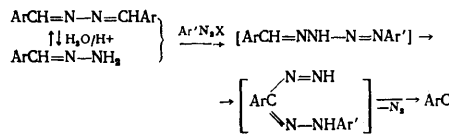
This reaction is assumed [167] to involve the intermediate formation of tetrazens, and support for this view will be found in Refs. 45 and 168.

The ability of *o*-aminophenylhydrazones to undergo intramolecular azo-coupling at the amino-nitrogen atom has been used recently by Campbell and Rees [169] to prepare derivatives of benzo-1,2,3-triazol-1-amine (XIII):



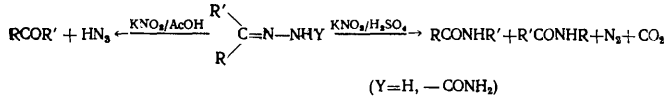
(XIII)

Azines and unsubstituted hydrazones (into which the former are initially hydrolysed under the reaction conditions) of aromatic aldehydes react with arenediazonium salts in acetic-acid solution to give arylhydrazones of the aldehydes [170]:



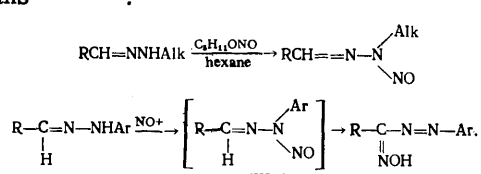
Nitrosation

In acetic-acid solution the nitrite ion decomposes hydrazones and semicarbazones with formation of an oxo-compound and an azide ion [2,171], but in concentrated sulphuric acid the Schmidt rearrangement occurs to the corresponding acid amide [2,172,173]:



(Y=H, $-CONH_2$)

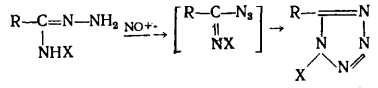
Monoalkylhydrazones of aldehydes are nitrosated by nitrous acid and its esters to relatively stable *N*-nitroso-derivatives [2], whereas the monoarylhydrazones are rapidly converted by nitrosating agents into arylazo-aldoximes (nitrosazones), which are oxime analogues of formazans [2,45,48,174]:



The formation of arylazo-aldoximes (XV) involves intermediate formation of the compound (XIV). [2,45,48,174-176].

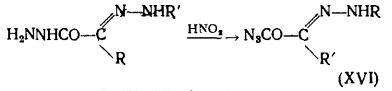
Bulky *ortho*-substituents in aromatic arylhydrazones prevent both nitrosation and the formation of arylazo-aldoximes [174].

Amidrazones, hydrazidines, and α-hydroxyamino-hydrazones, on treatment with nitrosating agents, are cyclised into tetrazoles via a stage of azido-derivatives [10,31,110,177-179]:



(X=H, NHR', OR", R'=H, Ph, 2,4-$C_6H_3(NO_2)_2$, R"=H, Alk, Ar).

When the hydrazone molecule contains an amine or a hydrazide group (not attached to the hydrazone group), attack by the nitrite ion takes place firstly at the former groups, not at the hydrazone fragment [45,170,180,181]:

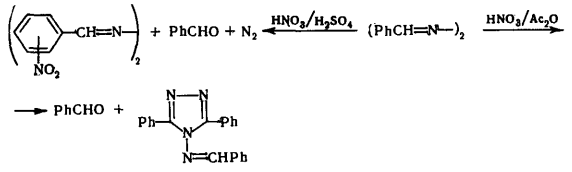


(XVI)

(R=H, Alk, Ar; R'=H, Ar).

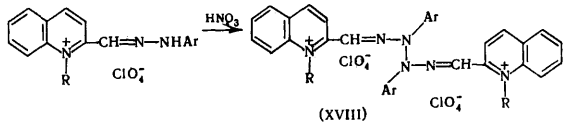
Nitration

On treatment with nitric acid in sulphuric acid, benzaldehyde azine undergoes oxidative cleavage and is partly nitrated, with formation of the azines of *p*- and *o*-nitrobenzaldehydes; when the reaction is conducted in acetic anhydride, only benzaldehyde and 4-benzylideneamino-3,5-diphenyl-1,2,4-triazole (XVII) are formed [182]:



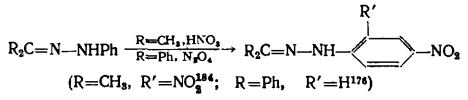
(XVII)

Aldehyde arylhydrazones are evidently more liable to be oxidised than to be nitrated by nitric acid. Thus arylhydrazones of 1-substituted 2-formylquinolinium perchlorates are easily oxidised to dimeric products (XVIII):[183]



(XVIII)

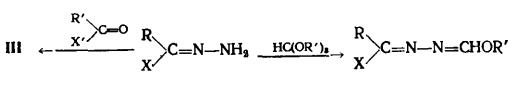
Under mild conditions phenylhydrazones of ketones are nitrated in the aniline ring by nitric acid [184] or by oxides of nitrogen [176]:



(R=CH_3, R'=NO_2 [184]; R=Ph, R'=H [176])

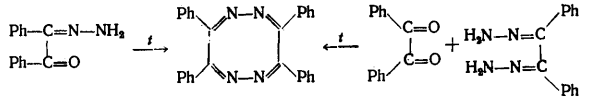
Reactions with Carbonyl Compounds

Carbonyl compounds react at the amino-nitrogen in unsubstituted hydrazones, and convert them into azines, a reaction very frequently used for the preparation of unsymmetrical azines [2,9,10,44,49,109,185,186]:

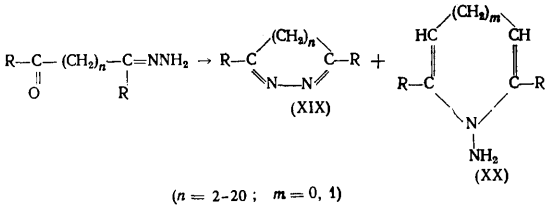


Dihydrazones of cyclohexane-1,3-dione [187] and the 1-hydrazone 2-methylphenylhydrazones of α-dicarbonyl compounds [188] react similarly. Unsubstituted amidrazones are converted into amino-azines [110]. The carbonyl compounds can be replaced by their acetals [10,44,49]. Ortho-esters give α-alkoxy-azines with hydrazones [45,189].

Monohydrazones of α-diketones when heated form an eight-membered heterocycle [190], which can be obtained also from the α-diketone together with its dihydrazone [191]:



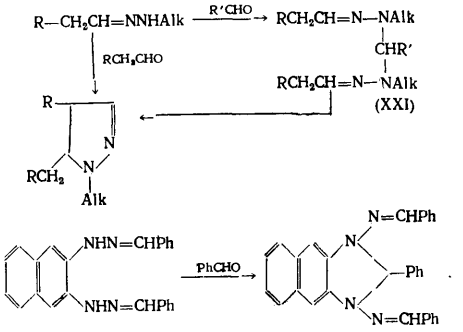
However, this reaction is not general [192]. Monohydrazones of β-dicarbonyl compounds are converted into pyrazoles (see subsection on alkylation). Monohydrazones of γ–ω-dicarbonyl compounds are able to yield either polyazines or heterocyclic compounds of the type (XIX), [2,10,25,49,193] as well as compounds of type (XX) (derivatives of *N*-aminopyrrole and *N*-aminodihydropyridine respectively) [10]:



(XIX) (XX)

(n = 2-20; m = 0, 1)

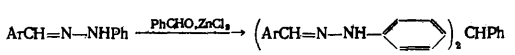
The higher electron density on the amino-nitrogen atom in monoalkylhydrazones facilitates electrophilic attack by oxo-compounds at this atom, and the reaction products are geminal dihydrazones (XXI); [2,9,10,194,195] in the aromatic series a similar reaction has been reported for a vicinal naphthylenedihydrazone of benzaldehyde [45,196]:



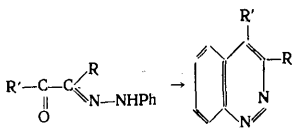
Compounds of type (XXI) are highly reactive: anhydrides of carboxylic acids acylate them to acylhydrazones [100], alkylhydrazines convert them into the corresponding hydrazones [194], and in the presence of excess of the aldehyde they are transformed into pyrazolines [194] (when Alk = H in (XXI), aldehydes yield azines [100]). It is supposed [194] that compounds (XXI) are formed as intermediates in the conversion of alkylhydrazines [194,197] or alkylhydrazones and aldehydes [194,197,198] into pyrazolines. Ioffe et al. have shown [198] that a pyrazoline is formed very easily from an aldehyde and its alkylhydrazone, but in the cross condensation of aldehydes with monoalkylhydrazones of other aldehydes and ketones the process is complicated by transhydrazonation, which occurs widely among hydrazones [199-212].

Arylhydrazones are more liable to transhydrazonation on reaction with carbonyl compounds, although phenylhydrazones form products of the triphenylmethane type,

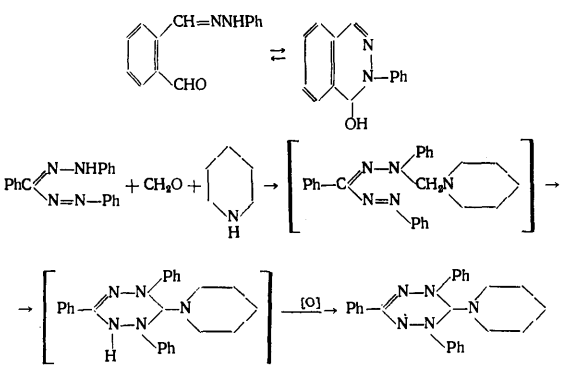
involving condensation at the *para*-position; the reaction is catalysed by zinc chloride and by acids[45]:



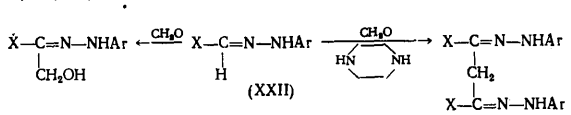
The phenyl ring is involved also in the intramolecular cyclocondensation of monophenylhydrazones of α-dicarbonyl compounds, which leads to the formation of cinnoline derivatives[26]:



The amino-group of arylhydrazones is also capable of condensation with carbonyl compounds. Phthaldehyde monophenylhydrazone exists in equilibrium with 1,2-dihydro-1-hydroxy-2-phenylphthalazine[27]; and 1,3,5-triphenylformazan reacts with formaldehyde and piperidine to give 1,3,5-triphenyl-5-piperidinomethylformazan, which under the reaction conditions cyclises into a 1,2,3,4-tetrahydrotetrazine derivative, and this oxidises spontaneously to verdazyl[213]:

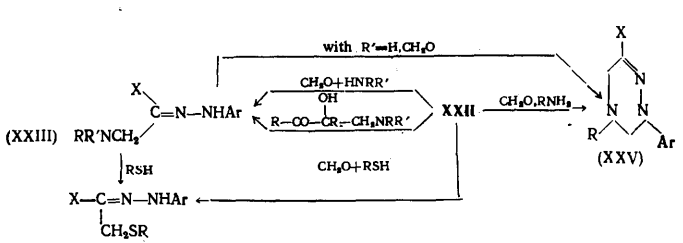


Oxo-compound arylhydrazones of type (XXII) (X = Az, NO_2, N:NAr, Ht, sometimes Ar) behave as if they contain a mobile hydrogen atom, and form arylhydrazones of α-hydroxy-ketones or bisarylhydrazones of 1,3-diketones[2, 10, 26, 45, 157, 214, 215]:



If the phenyl group in (XXII) contains an *ortho*-carbonyl group, intramolecular cyclocondensation may occur, leading ultimately to cinnoline derivatives[26].

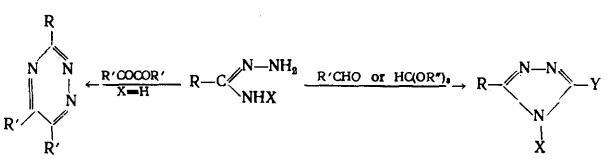
As compounds (XXII) (including 3*H*-formazans[157]) contain a mobile hydrogen atom, they undergo the Mannich reaction[45, 215-219], being converted into (XXIII), and with formaldehyde in the presence of thiols they yield (XXIV):[219]



A case of detachment of an acetyl group has been reported in the preparation of Mannich bases of the type (XXIII) from 2,3,4-trioxopentane 3-phenylhydrazone, formaldehyde, and piperidine[220]. The dialkylamino-group in (XXIII) is quite mobile, and can be substituted by the action of secondary amines, compounds containing a reactive hydrogen atom[218], and thiols[219] (including benzenethiols[220]), which helps to explain certain anomalies observed when these reactions are carried out[215]. The activity of (XXII) in the Mannich reaction is extremely high: they displace the dialkylaminomethyl group from Mannich acyloin bases[217].

When R′ = H in (XXIII), the *syn*-forms are able to condense with a further aldehyde molecule to 2,4,6-trisubstituted 2,3,4,5-tetrahydro-1,2,4-triazines (XXV).[221] Hahn showed[222-225] that the same products are formed by the reaction of hydrazones of type (XXII) with formaldehyde and primary amines. The formation of 1,2,4-triazine derivatives (XXV) from hydrazones of type (XXII) is a variety of the Mannich reaction, is quite general in character[222-226], and can be termed the Mannich–Hahn reaction.

Amidrazones and hydrazidines are also cyclised to 1,2,4-triazine derivatives on reaction with α-dioxo-compounds[110, 227-230], and into 1,2,4-triazole derivatives on treatment with aldehydes, acetals, or orthoesters[28, 45, 110, 231-233]:

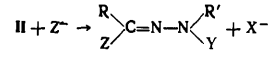


(X=H, Alk, Ar, NHR; Y=R′ or OR″).

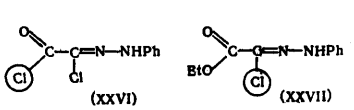
III. REACTIONS OF HYDRAZONES WITH NUCLEOPHILIC REAGENTS

1. Substitutions at the Carbon Atom of the Hydrazone Group

Substitution occurs readily at the carbon atom attached to the hydrazono-group if the substituent X in the general formula (II) for a hydrazone is chlorine, hydroxyl, nitrile, an *NN*-dialkylaminoarylazo-group, etc.[2, 31, 32, 45-47, 123, 130, 134, 138, 143, 179, 187, 189, 234-251] (see Table):



A chlorine atom attached to the hydrazone carbon atom is less reactive than one attached to a carbonyl carbon but more reactive than an ethoxy-group; and the circled chlorine atoms in (XXVI) and (XXVII)

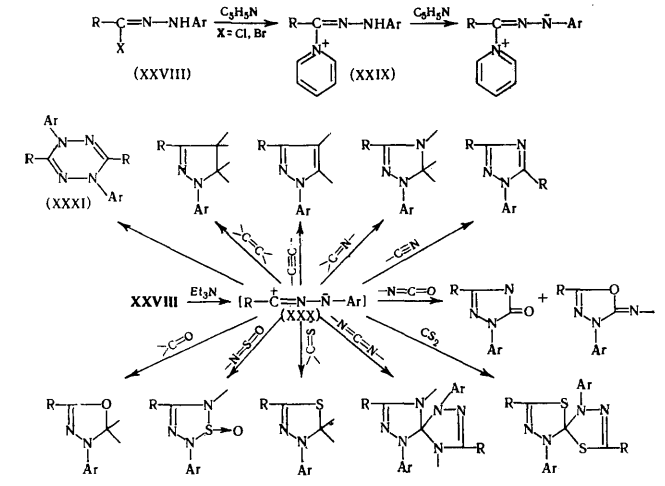


are replaced by the action of the azide ion[237, 239, 243].

There are also cases in which the products of nucleophilic substitution of hydrazones then undergo cyclisation[23, 31, 45, 131, 243-248]. Azines also undergo S_N reactions readily if X = Hal, CN, NO_2, etc. in (III),[22, 29, 31, 128, 138, 167, 189, 249-251] but cyclisation is then observed considerably more frequently[22, 29, 31, 32, 45, 133, 250, 251].

2. Reactions of Halogenated Hydrazones with Tertiary Amines

Halogeno-hydrazones (XXVIII) are able to react with tertiary amines by the usual mechanism of nucleophilic substitution to give a quaternary salt (XXIX),[45] but more frequently XH is eliminated with the formation of the extremely reactive "nitrilimine" (XXX), one of the most thoroughly studied 1,3-dipolar reagents[2,31-35,45,252,253]:



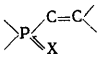
X	Z	Ref.	X	Z	Ref.
— Cl	— OH[a]	45,234	Br	— OH[a]	130, 133, 134 240, 241
	— OAc	45			
	— OAlk	45,234		— OAlk	45, 234
	— SH[a]	144		— NHAr	128, 134
	— SR	47			
	— NH_2	2, 45, 47, 138		— NH_2	45
	— NHAlk	45, 138		— $NHNH_2$	134, 179, 236
				— NHNHAr	47, 137
	— NHAr	2		— N_3	134, 236
	— $NAlk_2$	45, 138, 237 258	— NH_2	— NHAlk	189, 241
	— $NHNH_2$	31, 32, 45, 237		— $NAlk_2$	241
	— $NHNHR^b$	47, 143		— $NHNAlk_2$	240
	— N_3	31, 167, 239			
	— CN	45	— NHAlk	— OH[a]	189
	— I	47	— OAlk	— N_3	45
— $NHNAlk_2$	— NHAlk	241		— NH_2	194
	— OH[a]	45		— NHAlk	189, 242
	— SH	47			
	— CN	46		— NHAr	242
	— NHPh	2		— $NAlk_2$	189
— CN	— NHR	250		— $NHNHAr^b$	45
— OH[c]	— $NHNHR^b$	143		— NAlkAr	189
			— N = N — Ar	— OH	230

[a] Under the reaction conditions rearranges into a hydrazide (thiohydrazide).
[b] Very easily oxidised to formazan[47,143].
[c] The hydrazide of the acid is used.

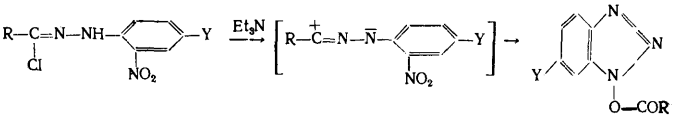
A nitrilimine cannot be isolated in individual form, since it either dimerises to a dihydrotetrazine (XXXI)[31-35,45,252-255] or, in the presence of an unsaturated compound in the reaction medium, undergoes 1,3-dipolar cycloaddition with the formation of various five-membered heterocyclic systems. The mechanism of the latter type of reaction has been discussed many times in the literature[253,256,257], and a multicentre cyclic transition state is the most probable. 3-Halogenated formazans can also serve as source of nitrilimines[31-35,45,252,253]. Various types of ethylenic compounds (including cyclic and heterocyclic), alkenylamines, alkynes, nitriles, azomethines, isocyanates, aldehydes, thioaldehydes, carbon disulphide, and carbodi-imines have been used as dipolar reagents[31-35, 45,252-263]. The enhancement of the electron-accepting properties of the substituents R and Ar in (XXX) diminishes its reactivity towards addition at the double bond and increases the probability of dimerisation[268].

A nitrilimine adds more easily at a C=C than at a C≡N[264] or a C≡C[259] bond, but reacts less actively with a >C=N fragment[260]. In pent-1-en-4-yn-3-ones the nitrilimine reacts with the multiple bond having fewer substituents[261]. Cycloaddition is a stereospecific reaction: the most highly substituted carbon atom of the ethylenic or acetylenic group becomes position 5 of the pyrazoline or pyrazole ring[262].

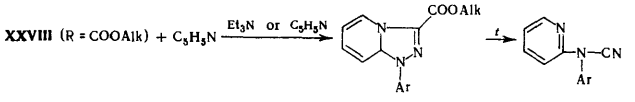
The cyclic products formed by the reaction of (XXX) with aldehyde oximes and azines rapidly undergo further reaction, splitting off a molecule of water in the first case and cleaving at the N–N bond in the second, to give substituted triazoles as final products[268]. Vinyl derivatives of quinquevalent phosphorus, containing the group



undergo the usual type of 1,3-dipolar cycloaddition with nitrilimine[264], whereas $\alpha\beta$-unsaturated phosphonites and phosphines react by a mechanism of 3 + 3 addition[265]. Acylhydrazones, as well as semicarbazones and α-halogeno-aldehydes, are converted by tertiary amines into oxadiazole derivatives[2,266]. If the aryl ring in (XXVIII) contains an *o*-nitro-group, the resulting nitrilimine rearranges rapidly into a 1-acyloxybenzotriazole[267,268]:



Pyridine, quinoline, and isoquinoline can also act as dipolarophilic agents in reactions with hydrazones of type (XXVIII) in which R = COOAlk, but at high temperatures the products rearrange into heterocyclic *N*-arylcyanamides[269,270]:

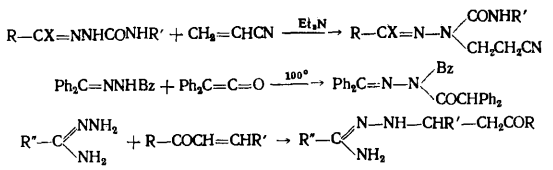


IV. ADDITION REACTIONS

1. Addition of Hydrazones at Multiple Bonds

Unsubstituted and monosubstituted hydrazones of aldehydes and ketones, as well as disubstituted hydrazones of aldehydes, contain a mobile hydrogen atom, and therefore are able to undergo the Michaelis reaction[2-7,9-12,21,23,24,25, 271-281]. Addition can take place at azo[45,282-284], ethylenic[2-7,9-12,21,23,45,271,272,285,287], acetylenic[9,10,23,24,45,286], azomethine[45,100,103,180,181,209,273-277], nitrile[2-7,9-12,23,45, 278-281], and carbonyl[27] groups, the amino-proton being more mobile than the hydrogen atom attached to carbon.

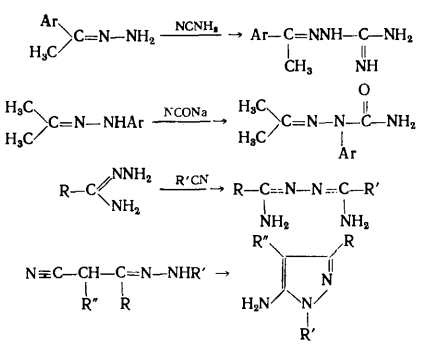
The reaction between semicarbazones and acrylonitrile is catalysed by tertiary amines[271]; benzophenone benzoylhydrazone reacts with diphenylketen in hot (100°C) xylene[287]; whereas amidrazones (amino-hydrazones) add to the ethylenic bond in vinyl ketones already at room temperature[272]:



The cyclisation of hydrazones of $\alpha\beta$-unsaturated carbonyl compounds, which occurs by a mechanism of intramolecular nucleophilic addition[23], is the most widely developed method for obtaining pyrazolines. The ease of ring closure depends on the nature of the substituents in carbonyl and hydrazine residues, and it occurs either when the hydrazones are formed or when they are heated in solution, often in the presence of acids[21,23]. The capacity for cyclisation diminishes with increase in the electron-accepting character of R′. Addition of the N–H group of hydrazones to an acetylenic bond has been observed mainly in cases of intramolecular cyclisation with the formation of pyrazoles[2-7,9-12,23,45]. Unsubstituted hydrazones[273], alkyl-, aryl-, and acyl-hydrazones[45,273,274], 1,5-diarylformazans[47,103], and substituted amidrazones[275,276] are easily added at the C=N bond of alkyl, aryl, and acyl isocyanates and isothiocyanates to give *N*-substituted semicarbazones and thiosemicarbazones respectively.

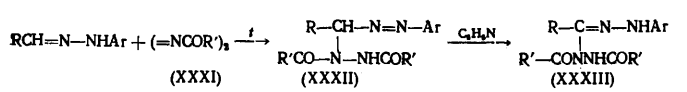
An example has also been reported of the preparation of a pyrazoline by the intramolecular nucleophilic addition of a hydrazone at the C=N bond of an azomethine[277], and an example of the addition of an unsubstituted hydrazone at a C=N bond of an azine[100].

The NH group of a hydrazone adds also to a C≡N bond, although with greater difficulty than at an ethylenic bond[271]. Acetophenone hydrazone and cyanamide in boiling alcohol yield the guanylhydrazone of this ketone[278], and $N_{(2)}$-arylsemicarbazones are obtained from sodium cyanate and arylhydrazones[45]:



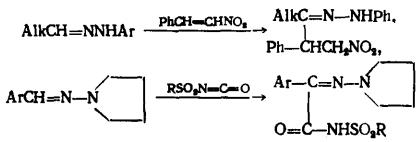
Amidrazones add to mono- and di-nitriles in the presence of triethylaluminium[279]. The intramolecular addition characteristic of hydrazones of α-cyano-carbonyl compounds provides a method for preparing aminopyrazoles[2-7,9-12,23,45,280,281].

The nature of the reaction products obtained from arylhydrazones and azo-acyls (XXXI) has been discussed many times. It is now considered that an azo-hydrazine (XXXII) is formed, which under the reaction conditions sometimes—and then only partly—rearranges into the hydrazidine (XXXIII); but (XXXII) easily passes into (XXXIII) on dissolution in pyridine[45,282-285]:

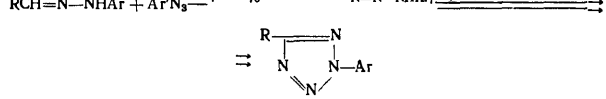


The ability of hydrazones to add to a C=O bond has been discussed above (Section II, subsection on reactions with carbonyl compounds).

Hydrazones are able to add to ethylenic[286], acetylenic[287], and azomethine[209] bonds by means of the =C–H fragment, but few examples of these reactions have been reported hitherto:



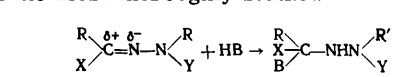
The reaction of aldehyde hydrazones with azides in the presence of sodium alkoxides leads to the formation of 2,5-diaryltetrazoles[31,45,288,289]. If the reaction is conducted under milder conditions, however, it is possible to isolate intermediate addition products—1,4,6-trisubstituted 1,2,3,5,6-penta-azahexa-2,4-dienes—which on further heating are cyclised to the tetrazoles[45,167,288]. Hence the first stage involves addition to the 1,3-dipolar reagent, and the second stage intramolecular azo-coupling:



Unsubstituted hydrazones, in the form of an anion, add to toluene-*p*-sulphonyl azide, but the products are unstable, and decompose into a diazo-compound, nitrogen, and toluene-*p*-sulphonamide[290,291].

2. Addition at the C=N Bond of the Hydrazone Group

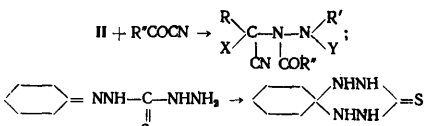
Reactions involving the addition of nucleophilic reagents have been the most thoroughly studied[1,2,9,10,32,44,45,48,49,292-314]:



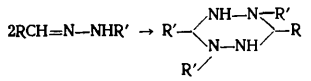
(B=—CN [2,10,32,44,45,48,49,292—294], —NHN=CRX [100], —NHNHR″ [295], —OR″ [1,296], —SR″ [297], —P(O)(R″)$_2$ [298—300], —HCR′NO$_2$ [301,302], —R″ (R″MgX, R″Li) [2,9,10,44,45,292,303—308]).

In azines both azomethine fragments are capable of addition[2,9,10,44,49].

Hydrocyanic acid adds relatively easily to unsaturated hydrazones[10,45], alkylhydrazones[292], arylhydrazones[2,45,48], semicarbazones[2,10,45,292], and azines[2,32,44,49,292] of aliphatic and alicyclic aldehydes and ketones, which are converted into α-cyano-substituted hydrazines. Acetone cyanohydrin can be used instead of hydrocyanic acid[293]. α-Ketonitriles behave similarly to hydrocyanic acid, adding at the azomethine bond of arylhydrazones of aliphatic aldehydes and ketones to form acylated α-cyano-substituted hydrazines[45,294]:

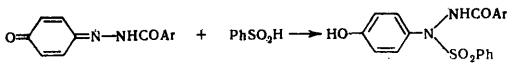


Hydrazines[295] and hydrazones[100] are able to add to the C=N bond of hydrazones. The transhydrazonation of hydrazones by hydrazines evidently also involves an intermediate stage of addition. The dimerisation of unsaturated hydrazones of aliphatic aldehydes[45,309] and of monoalkylhydrazones[32,310,311] and phenylhydrazones[312] of formaldehyde to 1,3,4,6-tetrasubstituted hexahydro-1,2,4,5-tetrazines is due to the addition of the NH group of one hydrazone molecule at the C=N bond of another molecule:



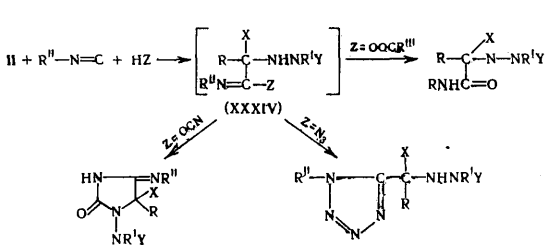
(R=H, Alk; R'=H, Alk, Ph)

The hydroxy-groups of cellulose react with the thiosemicarbazone of formaldehyde[296], and hydrogen sulphide with its azine[297]. Ring–chain tautomerism of 2'-hydroxyethylhydrazones also involves addition of a hydroxyl at the azomethine bond (Ioffe and Potekhin, Dorman—see Ref. 1 for literature). Dialkyl(and aryl)phosphines[298,299], dialkyl hydrogen phosphines[300], and nitroalkanes[301,302] add normally to hydrazones. Arenesulphinic acids and to mono(benzoylhydrazones) of *p*-benzoquinone at the 1,6-substituents[45]:

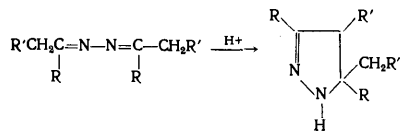


Mixed organomagnesium compounds react with unsaturated hydrazones, alkyl-, aryl-, and dialkyl-hydrazones, and azines of aldehydes to form hydrazines. This involves alkylation (or arylation) of the carbon atom in the hydrazone group[2,9,10,44,45,292,303–305]. The reaction is complicated by several secondary and consecutive processes, such as cleavage of the N–N bond, reduction, and rearrangements[2,45,304–308]. Organolithium compounds add somewhat more readily at the azomethine bond of hydrazones, and the yields of hydrazines are higher[304]. Strengthening the electron-accepting properties of the aryl group in dimethylhydrazones of substituted benzaldehydes favours the addition of an organolithium compound.

In the presence of acids isocyanides react with acetylhydrazones and azines to form an addition product (XXXIV),[2,31,313,314] which tends to rearrange or cyclise (Ugi's reaction):

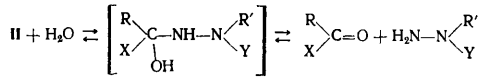


Less study has been made of reactions in which electrophilic addition takes place at the C=N bond in hydrazones. The aldol type of condensation in the presence of acid catalysts must be included among such reactions. Thus azines of carbonyl compounds containing an α-methine group cyclise to pyrazolines under the influence of acidic reagents[2,9,10,21,23,44,49,105,113,315,316]:



A kinetic study of the formation of 1-*cis*-3'-phenylpropenyl-5-phenylpyrazole in the pyrolysis of the azine of cinnamaldehyde has shown that this reaction is intramolecular[317], and so can indeed be included in the present type.

Hydrolysis. Being a weak nucleophilic reagent, the water molecule adds with difficulty at the C=N bond of hydrazones. The resulting *gem*-hydrazino-alcohols are unstable and decompose into the hydrazine and the carbonyl compound, or else lose the molecule of water and are converted back to the hydrazone, so that a dynamic equilibrium is established that under normal conditions is almost entirely displaced to the left:



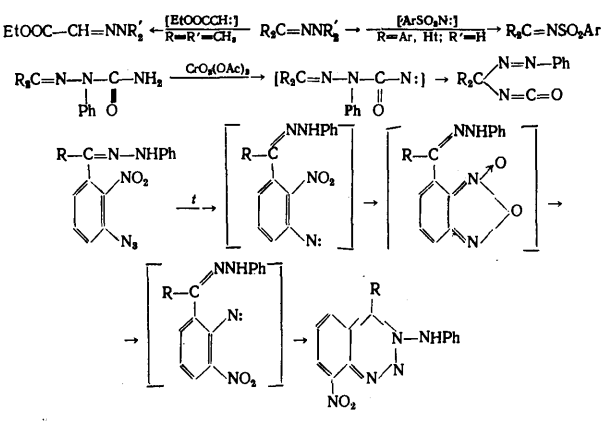
Alkaline[2,45,48] and especially acid catalysis[2,9,10,41,45,48,101,209,292] facilitates considerably the hydrolytic cleavage of hydrazones. The hydrolytic stability of these compounds is very greatly dependent on the nature of the substituents[2,45,48]: quaternary salts of hydrazones are most easily hydrolysed[9,10,49], followed by unsubstituted hydrazones[45] and alkyl- and acyl-hydrazones[2,9,10,49,292]. Arylhydrazones are more difficult to hydrolyse than are semicarbazones. Increasing the number of electron-accepting groups in the phenylhydrazone molecule improves its stability to acid hydrolysis[45,48]: for example, acetone 2,4-dinitrophenylhydrazone remains unchanged under conditions such that the phenylhydrazone is completely hydrolysed[45]. Arylhydrazones of α-keto-acids and α-dicarbonyl compounds possess improved stability. Arylosazones of sugars readily eliminate an arylhydrazine when boiled in acid medium[35,45]. Whereas the rates of hydrolysis of stereoisomeric oximes differ substantially, those of the stereoisomeric hydrazones of *p*-methoxybenzophenone differ insignificantly[318]. Almost all types of hydrazones and azines can be cleaved hydrolytically to the carbonyl compound, but if in (II) the substituent X = Hal, AlkO, ArO, NO_2, CN (see Section III, 2), ArN:N (formazans)[319], a hydrazide (a tautomeric form of a hydroxy-hydrazone: X = OH) is formed initially, and is then hydrolysed to the carboxylic acid and the hydrazine.

The hydrazone group is hydrolysed with greater difficulty than ester[10,38,45] and acylamino[10,45] groups. If these are present in a hydrazone molecule (X = COOR, OAr, NHAz, CONHR), they can be hydrolysed without the hydrazone fragment being affected.

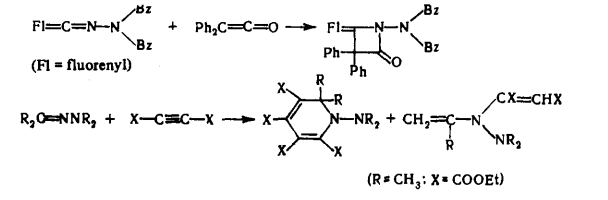
3. Cycloaddition

In contrast to alkenes and azomethines, which form three-membered rings with carbenes and nitrens[11,320], hydrazones are cleaved by these reagents. A carbene displaces the residue of the carbonyl compound[321,322],

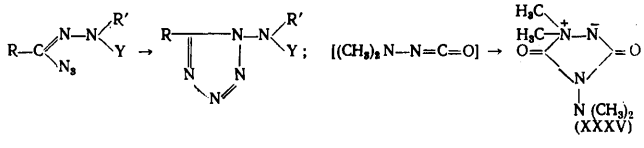
and a nitren the hydrazone fragment[323]; examples of 1,1-cycloaddition to hydrazones are not yet known. If a nitren is formed directly in the hydrazone molecule, the reaction is complicated by rearrangement[324,325]:



The possibility of 1,2-cycloaddition with hydrazones is shown by the reaction of aromatic diacylhydrazones with ketens[282]. Hydrazones do not react by 1,2-cycloaddition with acetylenic derivatives, perhaps owing to the instability of the ring: either linear 1 : 1 adducts are formed, or a second acetylenic molecule is involved to yield a cyclic 1 : 2 adduct[326]:

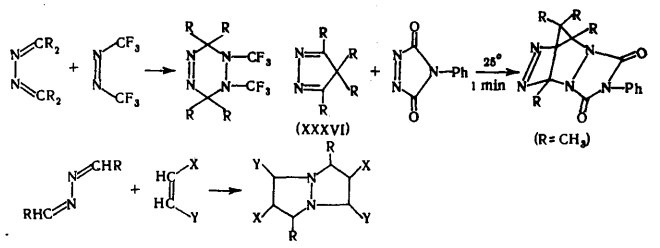


Reactions involving the 1,3-cycloaddition of hydrazones and azines to nitrilimine have been discussed above (Section III, 2). The formation of tetrazole derivatives from azido-hydrazones and azido-azines (very often at the instant of formation)[31,174] and the dimerisation of the dimethylhydrazone of carbon dioxide (dimethylamine isocyanate) into an ylid (XXXV)[327]



must be included in this type of reactions.

Examples of hydrazones functioning as dienophiles in the Diels–Alder reaction could not be found. A very attractive idea was to use azines as dienes, but the investigations showed[28,44,49,328] that only in very rare cases[329] could azines undergo 1,4-cycloaddition: usually they behave as "criss-cross" bis-1,3-dipolar reagents and form 1 : 2 adducts that are derivatives of tetrahydropyrazolo[1,2-*a*]pyrazole[28,44,328,330–333]. Aromatic and aliphatic aldazines and ketazines, and azines of perfluorinated carbonyl compounds react with alkylated alkene derivatives of acrylic, maleic, hydrocyanic, cyanic, and thiocyanic acids, and with alkyl, aryl, and acyl isocyanates, in conformity with this scheme of "criss-cross" addition[28,44,49,328,330–333]:

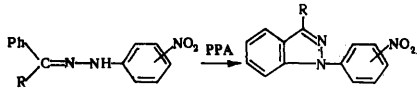


Such behaviour of azines towards dienophiles must evidently be explained by the non-coplanarity of azine molecules[1,334] and by steric hindrance to formation of the S-*cis*-form. The cyclic azine (XXXVI) very readily undergoes the Diels–Alder reaction[335].

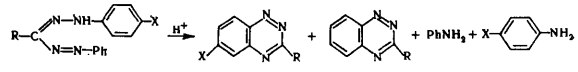
V. CATALYTIC CONVERSIONS

Action of Acids

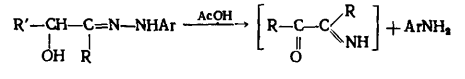
Several reactions of hydrazones in the presence of acids have already been discussed. The conversion of arylhydrazones of carbonyl compounds into indoles, known as the Fischer–Arbuzov reaction, also takes place under the influence of acids and acidic reagents[2,15–19,45,336]. Information on the catalysts used in this reaction will be found in Refs. 16–19. The formation of pyrroles from azines (the Piloty reaction) is a form of the Fischer–Arbuzov reaction[2,16–19,49]. The process involved in the formation of products of non-indole type under conditions for the synthesis of indoles has been termed an "anomalous Fischer–Arbuzov reaction".[16–19,337–341] Nitrophenylhydrazones of acetophenones, benzaldehyde, and aromatic ketones are cyclised into indazoles under the influence of polyphosphoric acid (PPA):[24,342–344]



Formazans are converted by strong acids into benzo-1,2,4-triazines and anilines[45,47,103,143,345]. Phenazine derivatives have been isolated as secondary products. Unsymmetrical formazans yield two benzo-1,2,4-triazines:

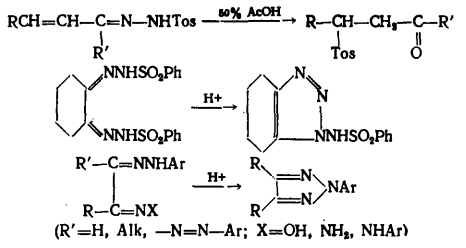


Heating arylhydrazones of α-hydroxy-carbonyl compounds in acetic acid results in fission of the nitrogen–nitrogen bond with formation of an unstable α-iminoketone, formed as intermediate in the preparation of osazones from α-hydroxy-carbonyl compounds and hydrazines[346,347]:

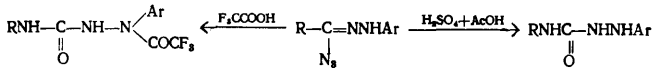


Toluene-*p*-sulphonylhydrazones of αβ-unsaturated ketones are converted in hot 50% acetic acid into good

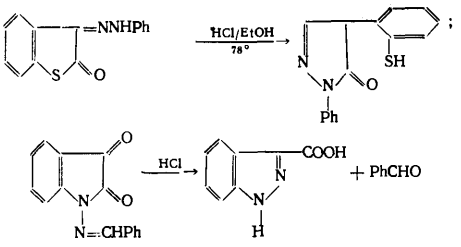
yields of β-tosylated ketones[348], whereas bisbenzenesulphonylhydrazones of α-diketones in acid medium form 1-substituted 1,2,3-triazoles[349]:



Formazan osazones[38,39], bisarylhydrazones, and hydrazone oximes of α-dicarbonyl compounds cyclise under these conditions to give 2-substituted 1,2,3-triazoles[20,28,88,350]. α-Azido-hydrazones in acid medium undergo rearrangement into 1,4-disubstituted semicarbazides (Curtius type of rearrangement)[236]:

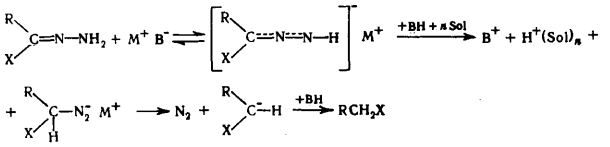


Several hydrazones of heterocyclic aldehydes and ketones, as well as hydrazones containing a heterocyclic radical, are able to rearrange under the influence of acids to form a new heterocyclic system, most often a pyrazole ring[25,45,351] (recyclisation):



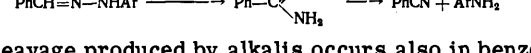
Action of Bases

Strong alkalis (potassium hydroxide and alkoxides) convert unsubstituted hydrazones and semicarbazones into saturated hydrocarbons (Wolff–Kishner reductions)[2,10,11,36,37,352–354]:

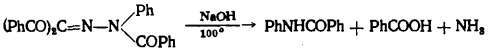


(B=OH⁻, RO⁻, $CH_3SOCH_2^-$; Sol = ROH, dimethyl sulphoxide)

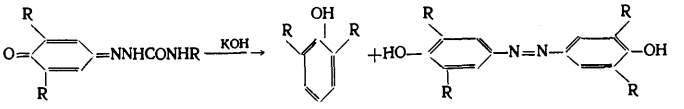
Azines undergo complicated changes in the presence of strong bases, evidently through an intermediate stage of nitrile cleavage. Thus under the influence of potassium *t*-butoxide in boiling xylene benzaldehyde azine gives a mixture of products, mainly 3,5-diphenyl- and 1-benzyl-3,5-diphenyl-1,2,4-triazoles together with benzoic acid[355]. Boiling arylhydrazones of aromatic aldehydes in the presence of potassamide or sodamide in xylene or benzene leads to the formation of amides[11,45,50,356–358] (the Robev rearrangement), which under the reaction conditions may decompose into an arylamine and a nitrile. This reaction involves an intermediate stage of homolytic cleavage of the nitrogen–nitrogen bond[357,358]:



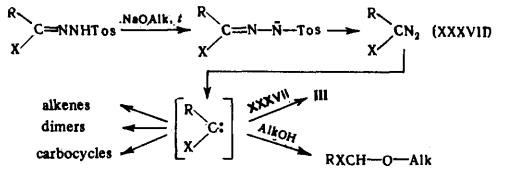
Such cleavage produced by alkalis occurs also in benzoylphenylhydrazones of quinones[359] or aromatic ketones[360]:



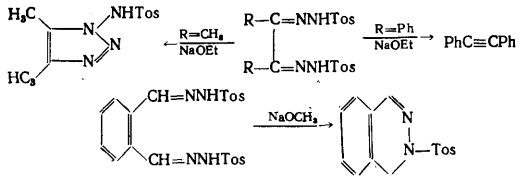
Semicarbazones of quinones decompose in hot alkali into phenols[361,362], and azophenols have been isolated as by-products[362]:



Diazo-compounds are formed by the hot alkaline cleavage of toluene-*p*-sulphonylhydrazones of aliphatic, mono-, di-, and tri-cyclic, aromatic, and steroid aldehydes and ketones[11,320,363]. They are not usually separated from the hydrazones, but are converted *in situ* into carbenes[10,11,321,363–372]. Decomposition of the dry sodium salts of toluene-*p*-sulphonylhydrazones gives similar results[365,370,371]:

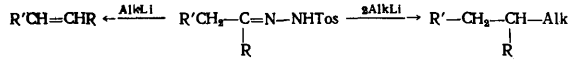


Toluene-*p*-sulphonylhydrazones of $\alpha\beta$-unsaturated ketones behave similarly on alkaline decomposition in protic solvents[372], whereas in an aprotic medium cyclopropenes are formed[373]. Depending on the nature of the groups in the carbonyl component, bistoluene-*p*-sulphonylhydrazones of α-dicarbonyl compounds form either alkynes or 1,2,3-triazole derivatives[363]:



The alkaline cleavage of the corresponding dihydrazone of phthaldehyde also yields a heterocycle, not a dicarbene[374].

The action of a lithium alkyl on toluene-*p*-sulphonylhydrazones of carbonyl compounds containing an α-methine group provides a convenient method for obtaining alkenes[375,376] and dienes[377] that are particularly inaccessible, e.g. in the terpene or steroid series. The abnormally high content of *cis*-alkenes in the products is evidently due to the fact that intermediate formation of a carbene is not involved[378]. Toluene-*p*-sulphonylhydrazones of $\alpha\beta$-unsaturated ketones are converted by butyllithium or sodium hydride into pyrazoles[372]. The use of excess of a lithium alkyl yields the alkylated hydrocarbon without the formation of alkenes[379]:



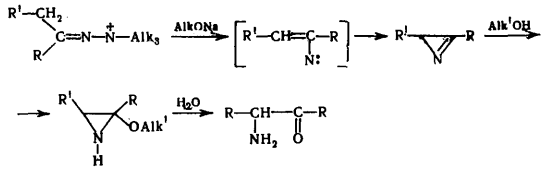
Under the influence of alkalis quaternary hydrazonium salts of aldehydes undergo amino–nitrile cleavage with rupture of the nitrogen–nitrogen bond [2,11,49,51,63,74–76,380–383]:

$$RCH{=}N{-}\overset{+}{N}Alk_3 \xrightarrow{OH^-} RCN + Alk_3N$$

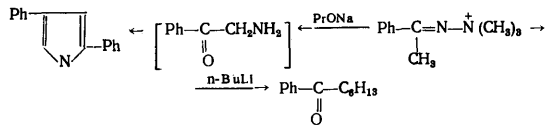
This is a general reaction for cyclic and acyclic hydrazonium salts [51] containing the fragment

$$-CH{=}N{-}\overset{+}{N}\lessgtr .$$

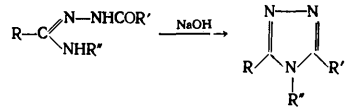
Quaternary salts of disubstituted hydrazones of ketones containing an α-methine group are cleaved by alkalis to α-amino-ketones [2,8,62,384–386]. The intermediate nitren isomerises into an azirine, which adds a molecule of an alcohol to form the alkoxyaziridine, and this is converted by water into the amino-ketone [62,384–386]:



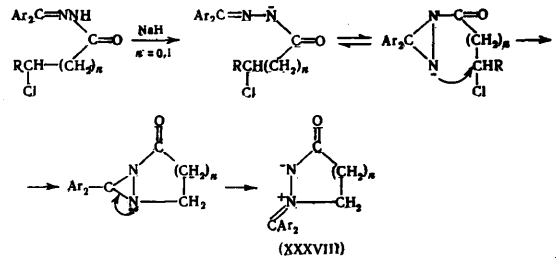
Acetophenone trimethylhydrazonium iodide is converted by an alkoxide into 2,4-diphenylpyrrole [386], and n-butyllithium yields 1-phenylheptanone [387]:



In the presence of alkalis or acids dihydrazones and oxime hydrazones of α-dicarbonyl compounds are cyclised to 1,2,3-triazole derivatives [28,45], whereas acylated amidrazones in alkaline medium are cyclised to 1,2,4-triazole derivatives [22,28,388]:



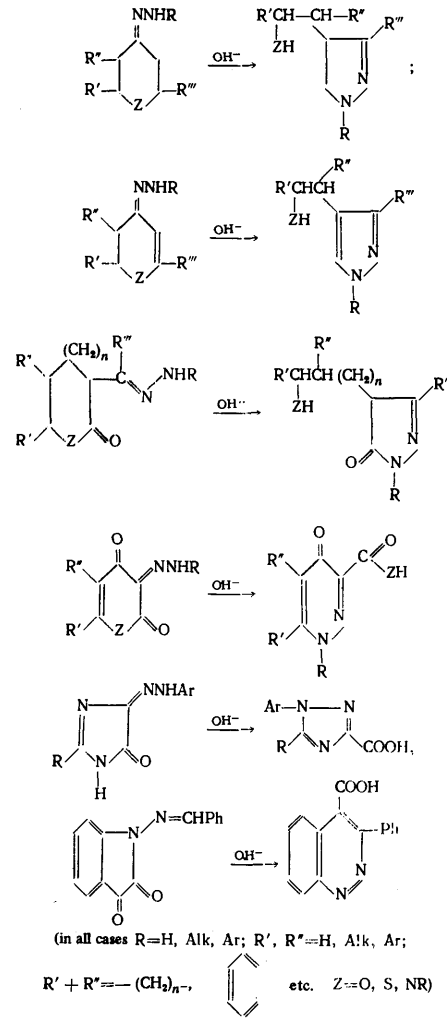
Acylhydrazones of aromatic ketones, obtained from hydrazides of α- and β-chloro-carboxylic acids by the action of bases such as sodium hydride, form cyclic ylides (XXXVIII), [389] most probably by the following series of reactions:



(XXXVIII)

Hydrazones of certain heterocyclic ketones undergo rearrangement with formation of a different heterocyclic system [9,10,23,25–27,45,49,390–396], more often in alkaline than in acid solutions. Monosubstituted and unsubstituted hydrazones of flavanones [45,390,391] chromones and thiochromones [45], 3-acylchromones [392], pyrones [23,45,49], α-acyl-γ-lactones [23,45] and thiolactones [45,393], and 3-acylindoles [49,394] when heated in alkaline medium rearrange to derivatives of pyrazole, pyrazoline, or pyrazolone.

Hydrazones of α-acyl- and α-oxo-δ-lactones [26,27,45,395] are converted into pyridazones (cinnolines), and 5-arylhydrazones of unsubstituted, 2-alkylated, and 2-arylated imidazoline-4,5-diones into 1-aryl-5-R-1,2,4-triazole-3-carboxylic acids [396]. Hydrazones that are derivatives of *N*-amines of nitrogenous heterocycles also tend to undergo such rearrangements [26,45,125]. A common feature of these reactions is rupture of the Z–C bond in the heterocycle with nucleophilic attack on the amino-nitrogen atom of the hydrazono-group and formation of a carbon–nitrogen bond in a new heterocycle:



(in all cases R=H, Alk, Ar; R′, R″=H, Alk, Ar; R′ + R″=—(CH$_2$)$_n$—, etc. Z=O, S, NR)

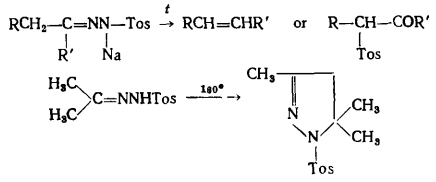
Pyrolysis

Heating to 200–300°C aryl-, diaryl-, and acyl-arylhydrazones of aldehydes, sometimes also of ketones [397], often in the presence of transition-metal chlorides, leads to heterolytic cleavage of the nitrogen–nitrogen bond with formation of a nitrile and an arylamine [2,10,45,50,101]:

$$RCH{=}NNHR'Y \xrightarrow{200-300^\circ} RCN + R'NHY$$

Alkylhydrazones of aldehydes are also capable of nitrile cleavage, but the reaction occurs with greater difficulty [50,197]. Trialkylhydrazonium salts of aldehydes of type (VI) are cleaved considerably more easily [50,51].

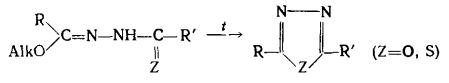
In the case of bisarylhydrazones of 1,4-diketones heating leads to the formation of *N*-arylpyrroles[17]. Pyrolysis of the sodium derivatives of toluene-*p*-sulphonylhydrazones is one method for generating carbenes[320,398,399], whose further transformation depends on the structure of the carbonyl component, mostly yielding alkenes[398], sometimes ketones containing a *p*-tolylsulphonyl group[399]:



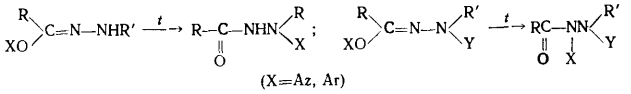
Pyrolysis of acetone toluene-*p*-sulphonylhydrazone is "anomalous" and leads to the formation of 3,5,5-trimethyl-1-*p*-tolylsulphonyl-Δ^2-pyrazoline[400]. Thus the products are analogous in structure to those obtained by the catalytic decomposition of acetone phenylhydrazone[339]. Derivatives of Δ^2-pyrazoline are formed also by pyrolysis of the perchlorate of acetophenone dimethylhydrazone[101].

When acylhydrazones, including semicarbazones and thiosemicarbazones, are boiled in solvents or are heated above their melting points, azines are formed[44]. The pyrolysis of aromatic azines at temperatures around 300°C passes through a stage in which diazo-compounds are formed[2,11] and then carbenes[338,401], yielding stilbene derivatives[2,10,44,49,402], but cyclopropane derivatives when alkenes are present[332]. Aliphatic azines decompose analogously, but the possibility of isomerisation into azo-compounds produces conditions under which various alkanes can be formed[44,49,403].

Amidrazones, acylamidrazones, and hydrazidines are cyclised at 150–200°C to 1,2,4-triazole derivatives[2,28,110,404], but dihydrazones and oxime hydrazones of α-diketones form 1,2,3-triazole derivatives[20,28,405]. Acyl- and thioacyl-hydrazones, including semi- and thiosemi-carbazones, of α-alkoxy-carbonyl compounds (acylhydrazones of esters) are cyclised at high temperature to oxadiazoles or thiadiazoles[10,316,406]:



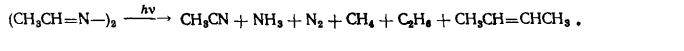
Arylhydrazones and disubstituted hydrazones of α-acyloxy- and sometimes α-aryloxy-carbonyl compounds (arylhydrazones of acid anhydrides or esters), however, undergo a Chapman rearrangement under these conditions[31,45,407]:



(X=Az, Ar)

Photolysis

When benzaldehyde phenylhydrazone is illuminated, the nitrogen–nitrogen bond is broken with the formation of benzonitrile, aniline, and benzaldehyde, the last produced from its imine[408]. Diazo-compounds[409] and then carbenes[369] are intermediates in the photolysis of toluene-*p*-sulphonylhydrazones, but the products obtained are different from those from the alkaline or thermal decomposition of this group of hydrazones[369,409,410]. Thus photolysis of the sodium salt of the toluene-*p*-sulphonylhydrazone of nortricyclanone yields 3-nortricyclyl *p*-tolyl sulphone, whereas its pyrolysis gives 4-ethynylcyclopentene[410]. The photolysis of aromatic azines involves rupture of both nitrogen–nitrogen and carbon–nitrogen bonds with the formation of aryl cyanides, *cis*- and *trans*-stilbenes, and aromatic imines, which are hydrolysed to aldehydes[2,44,411]. In aliphatic azines the cleavage of carbon–carbon bonds in the carbonyl component is also observed[44,49,412]:



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Stereochemistry of Free-radical Additions in the Bicyclo[2.2.1] heptene and Bicyclo[2.2.1]heptadiene Series

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The stereochemistry of free-radical additions to norbornene and norbornadiene systems is examined. The dependence of the direction of radical attack on the degree of substitution of the bicyclene, and on the position and steric and electronic effects of the substituents is discussed. A mechanism of radical rearrangement of the corresponding norbornene radicals is considered. 109 references.

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1. INTRODUCTION

Among the various bridged cyclic hydrocarbons the system containing a norbornene skeleton is one of the most interesting and also closest to important natural compounds of the terpene type. The rigid fixed geometry of bicyclo[2.2.1]heptane and its derivatives leads to distortion of the valence angles and hence to the establishment of a different type of strain. This in turn brings about an unusual interaction of the electronic and steric effects of the substituents and the reactivity of the latter is closely connected with their position in the molecule.

Owing to the extensive development and use of modern methods of separation and identification of compounds it has recently become possible to find more precisely the structure of intermediate products and also the stereochemical results of the behaviour of these systems under various conditions. Exceptions to the stereochemical rules previously thought to be firmly established are now being found. For example, there is now very extensive discussion of the nature of norbornyl cations, instances of non-stereospecific addition of polar reagents are being reported, and the question of the possible existence of non-classical 7-norbornyl radicals is being discussed.

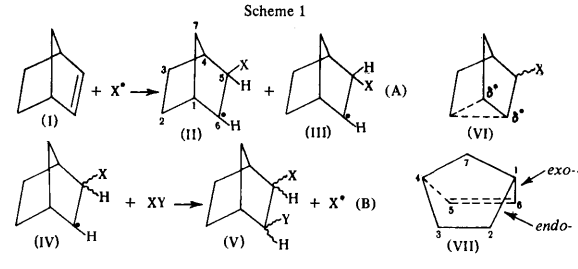
Davies and Cristol [1] have already reviewed the addition of free radicals to norbornene and norbornadiene systems but only dealt with the literature up to 1963. The relatively extensive investigation of such reactions and especially of their stereochemical aspect began again after 1963 and a critical appraisal of the new results is very desirable†. This is all the more important in that in this field new methods of investigation (especially NMR spectroscopy and gas–liquid chromatography, or GLC) have disclosed significant departures from the known stereochemical rules, and also to the observation of interesting free-radical rearrangements. In the present review we used the results of investigations in which the radical nature of the process has been rigorously proved and the stereochemistry of the products reliably established.

† When the present review had almost been completed, we learnt that a review by Davies [2] dealing with free-radical reactions in the bicycloheptane series had appeared in 1970 in a Chemical Society Special Publication. However, it examines the published information from a somewhat different aspect.

2. FREE RADICAL ADDITION TO NORBORNENES

Since it is known that most of the reagents concerned react with alkenes by a free-radical chain mechanism [3,4], the stereochemistry of the products of addition to norbornene (NB) (I) will be determined mainly by the stereochemistry of two stages: (A) the addition of the free radical X·, and (B) chain transfer (scheme 1).

Scheme 1



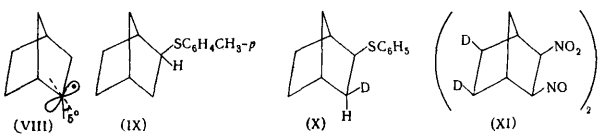
Even the first investigations in this field led to the conclusion of the participation in the reaction of classical free radicals of type (II) as opposed to a non-classical radical of type (VI), analogous to a non-classical carbocation [5]. The absence of addition products of the Wagner–Meerwein rearrangement type during the course of the free radical reactions also evidently agreed with this conclusion.

The *exo*-direction is evidently the most accessible for attack by a free radical in the NB molecule and therefore *exo*-radical attack was considered the rule until recently [6]. The greater accessibility of the *exo*-side of molecule (VII) is evidently due to its lesser steric blocking by the methylene bridge in comparison with the obstacles at the side of the dimethylene bridge in the *endo*-approach of the radical. A second factor favouring the formation of radical (II), and not (III), is the absence in transition state (II) of shielding of the $C_{(5)}$ and $C_{(4)}$ hydrogens, shown in an increase in the torsional strain effect [7].

A theoretical calculation of the structure of the 6-norbornyl radical appeared recently [8]. It was shown

that its most stable configuration has the deformed sp^2 planar structure (VIII) ($H_{(6)}$ emerges from the $C_{(1)}-C_{(6)}-C_{(5)}$ plane at an angle of ~5°), and the orbital with an unpaired electron has maximum extension in the *exo*-direction from $C_{(6)}$. This should also be apparent on assuming the *exo*-approach of the reagent to the norbornyl radical.

Hence both at the stage of initial attack and also at the stage of chain transfer with participation of the norbornyl radical *exo*-approach of the reagents, leading to *cis*-*exo*-addition, is postulated.

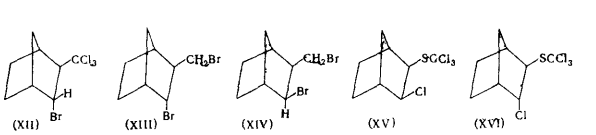


Actually, stereospecific *exo*-addition was observed in the reaction of NB with thiols [*p*-thiocresol[5], methanethiol, 2-methylpropane-2-thiol, thioacetic acid (TAA), and thiophenol[9]], acetone and acetaldehyde[10,11], formamide[12,13], in the free-radical chloroalkylation by chloroalkanes of the RCH_2Cl type[14]. In every instance exclusively *exo*-products of type (IX) were formed. The nature of the addition products did not allow any differences between the *cis*- and *trans*-addition to be distinguished. However, in an investigation specially made for this purpose, Davies and coworkers showed[9] that *S*-deuteriothiophenol adds to NB with the formation exclusively of the *cis*-*exo*-addition product (X). The reaction of N_2O_3 with *exo*-*exo*-2,3-dideuterionorbornene (XI) proceeds in an analogous manner[15].

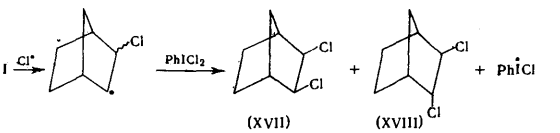
When an attacking radical has a sufficiently large steric volume, the initial addition from the less inconvenient *exo*-side in every instance (with participation of NB) without exception. However, chain transfer can be effected from various sides of the intermediate radical (II), depending on the nature of the reagent and substituent already present in the NB molecule. In this instance the stereoelectronic interaction between group X of Scheme 1, p. 516, and the molecule of the carrier can bring about *trans*-addition, despite the unfavourable effect of the torsion strain. Thus bromotrichloromethane[16-19], *p*-toluenesulphonyl chloride[20], and perfluoroiodopropane[21] give products of the *trans*-addition type (XII) with NB. CCl_4 adds similarly[16]. True, a recent repeat investigation[22] showed that for CCl_4 the ratio of *cis*-*exo*- and *trans*-addition products is 1 : 18.2.

In addition to the above reagents, which give predominantly *cis*-*exo*- or *trans*-products, there are also others for which the stereoelectronic interaction is intermediate. Then a mixture of *cis*-*exo*- and *trans*-addition products is obtained.

Thus a mixture of products of type (XIII) and (XIV) was obtained on the addition to NB of methylene dibromide, methyl bromoacetate[9], t-butyl hypochlorite[23], *N*-chlorourethane[24], N_2O_4,[25] ethyl chloroglyoxalate[26], and bromodicyanomethane[27].



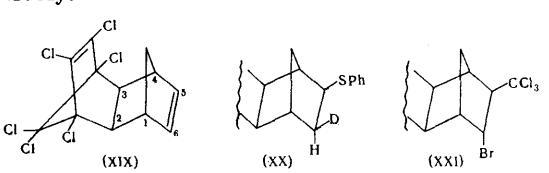
A similar intermediate example is evidently the addition to NB of trichloromethanesulphenyl chloride with the formation of a mixture of the products (XV) and (XVI) in 40 : 60 ratio[28].



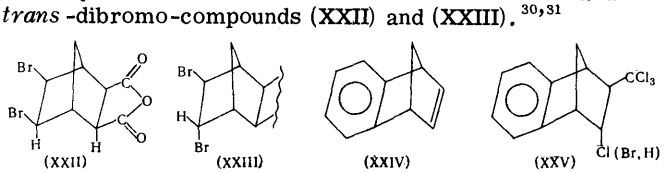
The radical chlorination of NB is yet another example. In the thermal or photochemical generation of chlorine radicals from phenyl iododichloride at 0–80°C, a mixture of the *cis*-*exo*- and *trans*-dichloro-compounds is formed; (XVIII) : (XVII) = 2.4.[29]

During photoinitiated halogenation‡ with chlorine[29], when a less bulky reagent participates in chain transfer, approximately equal amounts of the *cis*-*exo*- and *trans*-dichloro-compounds are formed.

Chain transfer from the endo-side of the intermediately formed radical can probably favour the electronic interactions of group X with the end of the carrier molecule. For example, with CCl_3Br and CCl_4 the repulsive forces that arise act together with the steric factors, leading exceptionally to *trans*-addition. How does the presence of substituents in the norbornene ring affect the stereochemistry of the addition? Evidently, 2,3-*exo*-substituents do not affect the direction of either the initial attack by the radical, or the chain transfer stage. Actually, the reactions of aldrin (XIX) and NB take place analogously: *S*-deuteriothiophenol[1] adds in the *cis*-*exo*-position but bromotrichloromethane, CCl_4,[17] *p*-toluenesulphonyl chloride[20], and perfluoroiodopropane[21] in the *trans*-position with the formation of products of type (XX) or (XXI) respectively:

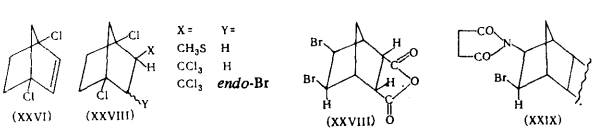


Bromination of the *exo*-anhydride of norbornenedicarboxylic acid leads to a mixture of the *cis*-*exo*- and *trans*-dibromo-compounds (XXII) and (XXIII).[30,31]



The addition of chloroform, CCl_4, or CCl_3Br, to benzonorbornadiene (XXIV),[32] just as for NB itself, leads to *trans*-products of the (XXV) type.

Evidently, 1,4-substituents also do not affect the stereochemistry of the process. The addition of methanethiol, bromotrichloromethane, and chloroform to 1,4-dichloronorborn-5-ene (XXVI) leads to products (XXVII) analogous to those obtained from NB itself[33]:

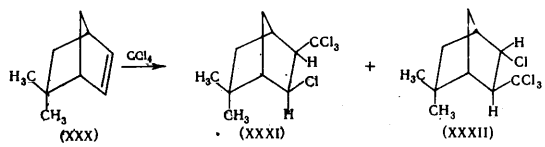


‡ In parallel with the homolytic processes in the above reaction ionic addition also occurs, but the investigators were able to extrapolate the "pure" radical halogenation from the experimental results for the products.

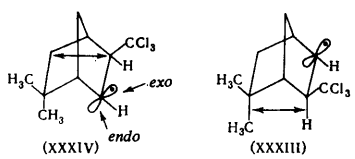
When the substituent occupies the 2- and/or 3-*endo*-positions or is at the double bond of the norbornenyl ring then when *exo*-selectivity is retained in the first stage this can significantly affect the stereochemical results of the reaction.

The exclusive formation of *cis*-*exo*-products occurs in the bromination [30,31] and reaction with *N*-bromosuccinimide [34] of the *endo*-anhydride of norbornenedicarboxylic acid, compounds (XXVIII) and (XXIX). Screening of the *endo*-side of the norbornene ring by the anhydride ring makes *cis*-*exo*-addition the only possibility.

In the reaction of CCl_4 with 2,2-dimethylnorborn-5-ene (XXX) a mixture of the *cis*- and *trans*-products (XXXI) and (XXXII) in the ratio 1.2 : 1 is formed [22]:



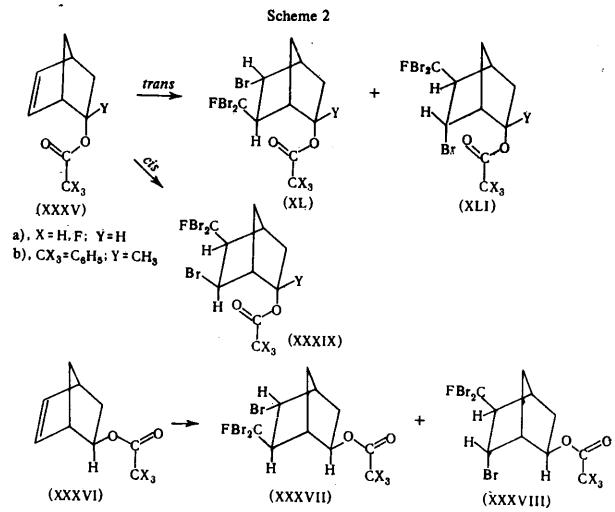
Since the quantities of *cis*- and *trans*-products are approximately equal, clearly the 2-methyl groups have an insignificant effect on the entering CCl_3 radical. As follows from the structure of the products obtained, the influence of the 2-*endo*-methyl group is especially pronounced at the chain transfer stage. Whereas for the radical (XXXIII) *trans*-addition takes place (as for unsubstituted NB), in the radical (XXXIV) the *endo*-methyl group exerts a greater steric barrier than the *exo*-CCl_3 group, which leads to the *cis*-product (XXXI):



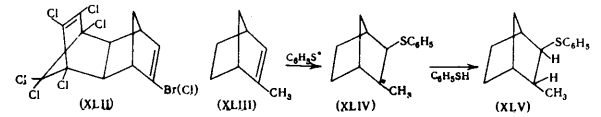
Osborn and coworkers assume [22] that the 2-*endo*-methyl group is situated closer to the line of formation of the new bond than the CCl_3 group and this is evidently also connected with the more rigid steric control of the 2-*endo*-substituent. It is noteworthy that the decrease in steric strain in *exo*-attack at the radical (XXXIV) evidently here plays a more important part than electronic interactions (the forces of repulsion of the two electron-withdrawing substituents in *exo*-attack, and conversely, the attraction of two different substituents in *endo*-attack at the chain transfer stage).

An analogous conclusion about the influence of 2,3-*endo*-substituents was drawn by Ludwick and Martin [35]. In studying the addition of tribromofluoromethane to norborn-5-ene-*endo*-2,3-dicarboxylic anhydride and to norborn-5-ene-2-*endo*- and 2-*exo*-acetate (or -benzoate) (XXXV) or (XXXVI), they found that the ratio of *exo*-*cis*- and -*trans*-addition products is determined by steric requirements produced by the 2-*endo*-substituent. Thus whereas the reaction with NB itself or with the 2-*exo*-acetate (XXXVI) leads to the formation of only the *trans*-products (XXXVII) and (XXXVIII), the 2-*endo*-substituted compounds (XXXV) always form a mixture of the *cis*-*exo*- and *trans*-addition products (XXXIX)–(XLV), and on going from the acetate (XXXVa) to the benzoate (XXXVb) the *trans*-product of type (XLI) almost disappears from the reaction mixture (see Scheme 2):

Scheme 2

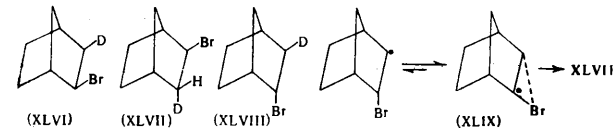


The addition of chloroform to 6-bromoaldrin (XLII) [17] or *p*-thiocresol to 6-chloroaldrin [36], and also of thiophenol to 6-methylnorbornene (XLIII) [9] proceeds by a *cis*-*exo*-process with the formation of products of the type (XLV):



This is evidently connected with the decrease in the torsion strain in the transition state during chain transfer from the *exo*-direction, and also the existence of a steric barrier for *cis*-distribution of two bulky substituents.

Hence in the norbornene series the rule of initial *exo*-radical attack would seem to be strictly obeyed. However, in 1964, in studying the deuteriobromination of NB, Kwart and Nyce [37] obtained a mixture of three bromo-compounds containing 60% of the product of *exo*-*cis*-addition (XLVI) together with 40% of a mixture of approximately equal amounts of the *trans*-bromo-compounds (XLVII) and (XLVIII)§:



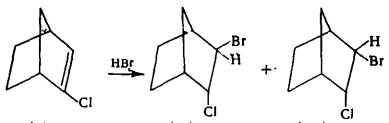
Here *exo*-attack is no longer exceptional, although it remains preferential (4 : 1). Kwart and Nyce assume the possibility of the formation of *trans*-bromo-compounds

§ Kwart and Nyce did not isolate the bromo-compounds (XLVII) and (XLVIII) and the assignment of the corresponding structures was made on the basis of a degradation analysis of the dehydrobromination products. In this it was assumed that in every instance *cis*-elimination takes place preferentially. Later investigations showed that in a series of norbornene halogeno-derivatives *trans*-elimination is six times more preferable than *endo*-*cis*-elimination [30]. Hence the true ratio of the bromides in the complementary investigation may be different.

through a bridged radical of type (XLIX). The greater stability of the latter also evidently brings about a decrease in the steric barrier for *endo*-attack.

The intermediate formation of bridged radicals owing to the possible extension of the valence cloud of the sulphur and halogen atoms was demonstrated earlier in additions to alkenes [39,40] and suggested to explain the comparatively ready 1,2-radical migration of halogen and alkanethio- or arylthio-groups [41]. The existence of such radicals was also confirmed by the EPR method [42].

The hydrobromination of 6-bromo- or 6-chloro-norbornene (L) also leads to a mixture of dihalogeno-compounds owing to both *exo*-attack (LI) and *endo*-attack (LII) by the bromine atom (ratio ≃ 7 : 3). [42-45]



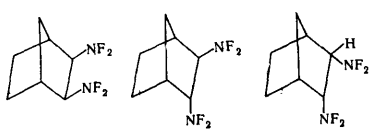
(L) (LI) (LII)

However, the assumption of the possibility of the existence of bridged radicals cannot explain the hypothetical formation of *cis*-*exo*-halogeno-compounds in all the above examples.

The observed instances of *endo*-attack can evidently also be explained without involving the concept of bridged radicals.

For this we must consider the other side of the question: the steric compactness of the attacking radical, which evidently markedly reduces the steric interactions of the entering substituent with the 2,3-*endo*-hydrogen atoms of the NB molecule.

Thus it was recently observed that a mixture of *cis*-*exo*-, *trans*-, and *cis*-*endo*-5,6-difluoroamines, (LIII)–(LV), is formed in the radical addition of tetrafluorohydrazine to NB. [46] In this instance the addition is no longer *exo*-stereospecific, although it still remains *cis*-*exo*-stereoselective.



(L II) (LIV) (LV)

Evidently this also applies to the radical halogenation of NB (see p. 522) in which the formation of *trans*-dihalogeno-compounds is probably partly linked with the initial *endo*-attack.

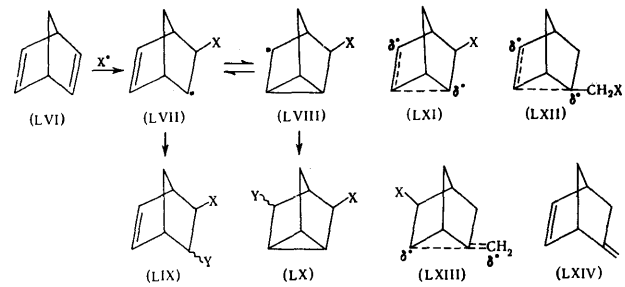
Even more significant changes in the stereochemical rules of radical attack are observed for norbornadienes with 7,7-substituents, especially well screened at the *exo*-side of the molecule. Examples of this series will be examined below.

3. FREE RADICAL ADDITION TO NORBORNADIENE (NBD)

The main feature of the reactions of NBD (LVI) is participation of the second double bond in the process, with the formation of substituted nortricyclene compounds of type (LX) owing to homoallyl interaction (see Scheme 3).

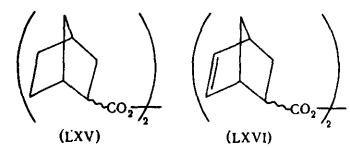
Just as in the NB series, the many investigators have not presented convincing arguments in support of the successive formation of classical intermediate radicals of type (LVII) and (LVIII) and against the existence of a non-classical radical to the type (LXI).

Scheme 3



It is now certain that neither the $C_{(1)}-C_{(2)}$ σ-bond in NB, nor the $C_{(2)}-C_{(3)}$ π-bond in NBD participates significantly in the delocalisation of the radical centre in these systems¶. The investigation of the competing addition of the trichloromethyl radical to a mixture of NB and NBD showed [48] that the effect of the second double bond is strictly additive: NBD is twice as reactive as NB. There is therefore no basis for assuming the existence of a transition state with lower energy, leading to a non-classical radical of type (LXI). The relative rates of addition of the methyl radical† to NB and NBD are 50 and 115 respectively [49]. The ratio of these quantities for NB and NBD probably also shows the absence of significant homoallyl strain. Similar results against the non-classical radicals of the (LXII) and (LXIII) type were obtained in studies [50,51] of the reactions of 5-methyl-norborn-2-ene (LXIV).

The activation parameters for the homolysis of *endo*- and *exo*-bonds of t-butylnorbornyl- and norbornenyl percarboxylates have been compared [52]. The results also rule out the probability of the formation of non-classical radicals at the rate-determining stage of the reaction. Similar results were also obtained in studying the thermal decomposition of diacyl peroxides of the (LXV) and (LXVI) type [53]. The participation of classical free radicals has also been confirmed in many other studies [5,6,36,37,51,54].



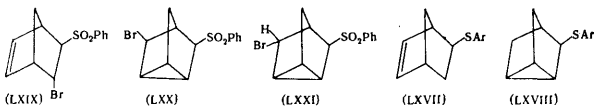
(LXV) (LXVI)

A convincing proof in support of the existence of discrete radicals (LVII) and (LVIII) is, for example, the change in the ratio of the reaction products (Scheme 3) with the concentration of the ligand and its reactivity. For example, *p*-toluenesulphonyl chloride [20], mercapto-acetic acid [55], perfluoroiodopropane [21], chloroform, butanal, heptanal, diethyl phosphite [48], and CCl_4 [56]—reagents with a relatively low transport constant—lead only to the corresponding nortricyclenes. On the other hand *p*-thiocresol and thiophenol [57] give a mixture of 5-*exo*-arylthionorborn-2-enes of type (LXVII) and the nortricyclene thioethers of type (LXVIII). An analogous

¶ True, the participation of the $C_{(2)}-C_{(3)}$ π-bond in the delocalisation of the radical centre at $C_{(7)}$ in the generation of C–7-radicals by the decarbonylation of the corresponding aldehydes is accepted [47], but this is not an addition reaction.

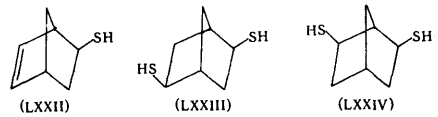
† In relation to the rate of withdrawal of hydrogen from iso-octane by the methyl radical.

mixture of products is formed in the reaction of NBD with CCl_3Br.[56] Phenylsulphonyl bromide forms the *trans*-addition compound (LXIX) and a mixture of the nortricyclene bromides (LXX) and (LXXI) in the ratio 4 : 3:[58]



(LXIX) (LXX) (LXXI) (LXVII) (LXVIII)

However, under the action of ultraviolet radiation H_2S gives only 5-mercaptonorborn-2-ene (LXXII) and the 2,5- and 3,5-dimercaptonorbornanes (LXXIII) and (LXXIV):[59]

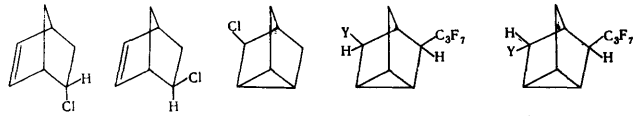


(LXXII) (LXXIII) (LXXIV)

In the reaction of phenylsulphonyl halides with NBD the relative amounts of nortricyclene products of type (LXX) and (LXXI) increase as the ligand activity in halogen transfer is reduced in the sequence: sulphonyl chloride > bromide > chloride[60].

The results of a series of recently published investigations can be explained satisfactorily by considering not only the existence of discrete radicals of structures (LVII) and (LVIII), but also the mobile equilibrium between them. For example, in the reduction of norbornenyl and nortricyclyl bromides and chlorides by tri-n-butyltin hydride the composition of the resulting mixture of NB and nortricyclene did not depend on the initial bromide (or chloride)[61]. In other words, the equilibrium between the norbornene and nortricyclene radicals was established more rapidly than their stabilisation. In the reduction of nortricyclyl bromide with triphenyltin hydride the relative amount of nortricyclene hydrocarbon was increased when the hydride concentration was raised, which agreed completely with the existence of an equilibrium pair of classical radicals. Similar results were also obtained in other methods of regenerating the radicals: by heating di-t-butylpercarboxylates of NB,[52] by decarboxylation of the corresponding aldehydes in chlorobenzene in the presence of peroxides[47], from the corresponding bromides in the presence of cobalt chloride and Grignard reagent in ether[61].

Other interesting examples of homoallyl–cyclopropylcarbinyl rearrangement have been published. For example, Cristol and Glason[62] found that in the reduction of *endo*- and *exo*-norbornenyl and nortricyclyl chlorides (LXXV)–(LXXVII) with sodium diphenyl at room temperature the composition of the reaction products (NB : nortricyclene = 1 : 3) did not depend on the initial chloride, that is, the equilibrium of the radicals was established more rapidly than the capture of an electron from the diphenyl radical-anion. However, at −58°C (LXXV) and (LXXVI) gave a mixture in which there was only 30% nortricyclene, but (LXXVII) a mixture in which there was up to 90% of the latter. Hence the reaction proceeds through classical radicals and the activation energy for their rearrangement is greater than for the capture of electrons from the radical-anion.



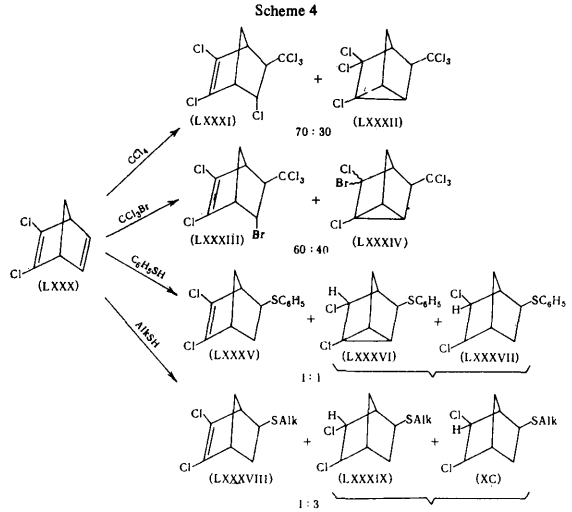
(LXXV) (LXXVI) (LXXVII) (LXXVIII) (LXXIX)

As regards the stereochemistry of addition to unsubstituted NBD, until recently it was always observed that initially there is *exo*-attack by the radical. Chain transfer for the nortricyclene radical (LVIII) evidently proceeds equally readily from both sides of the molecule, as a result of which in every instance mixtures of products of the type (LXXVIII) and (LXXIX) are formed[48,56,58].

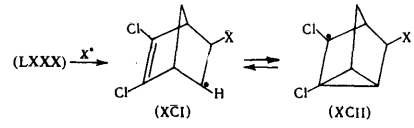
Just as in the NB series, substituents can significantly affect the stereochemical result of additions to NBD and the position of the nortricyclyl–norbornenyl equilibrium.

Thus it has been shown that free-radical addition to 2,3-dichloronorborna-2,5-diene (LXXX)[63] gives products represented in Scheme 4:

Scheme 4



In comparison with the corresponding reactions for unsubstituted NBD, the quantity of nortricyclene derivatives is less in the present instance. Actually, a norbornene derivative of type (LXXXV) is completely absent in the reactions of NBD with, for example, CCl_4, and with thiophenol only 19% of the norbornene addition product (LXXXV) is formed in comparison with 50% of the thioether (LXVII). This is shown by the decrease in reactivity of the 2,3-chloro-substituted double bond of the intermediate radical (XCI) towards intramolecular radical attack, leading to the formation of (XCII), which extends the lifetime of (XCI) in the non-isomerised state:

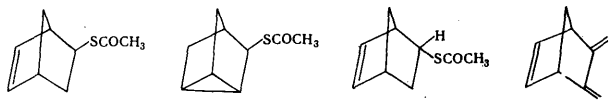


(XCI) (XCII)

The product ratios (LXXXI) : (LXXXII) and (LXXXIII) : (LXXXIV) are evidently regulated in this instance not only by the rate with which the molecule of the attacking agent transfers the chain (dissociation energy of the C–Br bond in $CBrCl_3$ 49.5 kcal mole^{-1}, compared with 67.9 kcal mole^{-1} for C–Cl in CCl_4), but also by steric factors at the chain transfer stage. Finally, we note the formation of *trans*-products with bulky ligands and the absence of appreciable steric differences for chain transfer by the radical (XCII) with *endo*- and *exo*-sides of the molecules.

In all the above examples in the NBD series, *exo*-radical attack is observed initially. However, exceptions have been observed very recently. It has been found that *endo*-addition products are formed in this instance not only with

large addends (for example, N_2F_2 [46]), but also in the addition of thiols [64]. Thus in the reaction with thioacetic acid in addition to 35% *exo*- (XCIII) and 37% nortricyclene (XCIV) thioacetates, 17% of the *endo*-thioacetate (XCV) was observed:



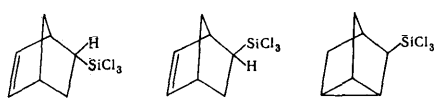
(XCIII) (XCIV) (XCV) (XCVI)

Interestingly, when thiophenol is used the proportion of the *endo*-isomer is reduced‡.

Another example is that of the *endo*-attack by the SPh radical on the intracyclic double bond of the triene (XCVI). [65]

Evidently, the absence of 2,3-*endo*-substituents in the NBD series allows even large ligands to overcome the relatively less availability of the *endo*-side of the diene molecule than is observed in the NB series.

The *endo*-isomer (XCVII) was also observed, together with *exo*- and nortricyclene derivatives (XCVIII) and (XCIX), in the reaction of NBD with trichlorosilane (in 7 : 28 : 53 ratio respectively), which was explained by the coordination of the system of double bonds of NBD with the *d*-orbitals of the silyl radicals participating in the reaction [66]:



(XCVII) (XCVIII) (XCIX)

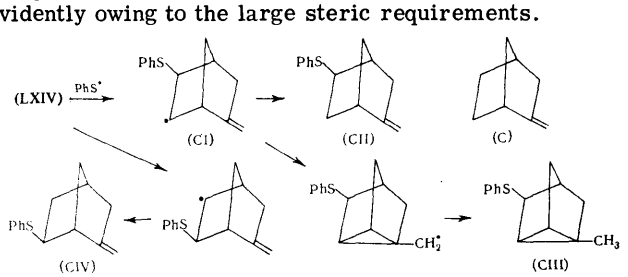
In the radical chlorination of benzonorbornadiene (XXIV) with nitrile chloride, *trans*-dichlorides, formed as a result of initial *endo*-attack by the chlorine atoms, were also isolated [67].

4. ADDITION TO NORBORNANE AND NORBORNENE SYSTEMS WITH HEPTACYCLIC (EXOCYCLIC) DOUBLE BONDS

The presence of a heptacyclic bond significantly affects the reactivity of the bicycloheptene system in homolytic reactions and the stereochemistry of the addition products.

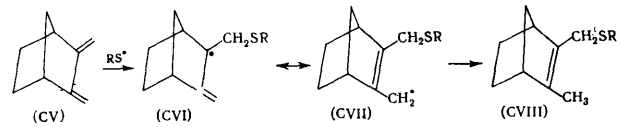
It must first be noted that the heptacyclic double bond is less reactive than an intracyclic one, which follows, for example, from the results on the competitive addition of thiols to NB and methylenenorbornane (C) [65,68] (ratio of reaction rates C/NB = 0.027 for thiophenol [65]).

From the reaction of 6-methylenenorbornene (LXIV) with thiophenol [69], three thioethers, (CII)–(CIV), were isolated, formed by the addition to the more reactive intracyclic double bond. The existence of three discrete radicals—precursors of the thioethers which are formed—was proved. However, the trichloromethyl radical is thought to be added at the heptacyclic double bond [50], evidently owing to the large steric requirements.



‡ In earlier studies the *endo*-thioether was never observed in this instance [57].

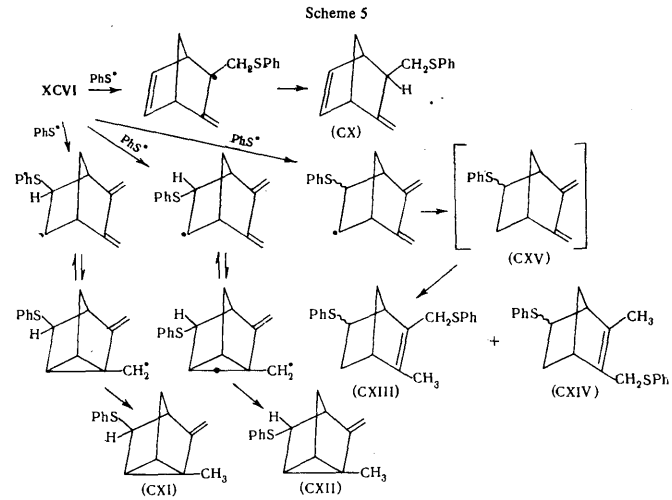
The reaction of *p*-thiocresol [70] and thiophenol [65] with 5,6-dimethylenenorbornane (CV) leads to a 1,4-addition product (CVIII). The formation of the latter is evidently favoured by the greater steric accessibility of the radical centre in (CVII) in comparison with that in (CVI):



(CV) (CVI) (CVII) (CVIII)

On reaction with thiophenol the triene (XCVI) gives a mixture of five thioethers (CX)–(CXIV), see Scheme 5.

Scheme 5



Here, judging from the ratio of the products, attack at the intracyclic double bond—thioethers (CXI)–(CXIV)—and at the 5,6-diene system—thioether (CX)—proceed to approximately the same extent. The diene (CXV) is more active and under the reaction conditions only the products of the addition to it of a second thiol molecule could be isolated. Interestingly, in this instance *endo*-attack by the thiyl radical on the *endo*-cyclic double bond occurred—ratio of thioethers (CXI) : (CXII) = 7 : 3.

In studying the reactions in the competing addition of thiophenol, methyl mercaptoacetate [65], and methyl and trichloromethyl radicals [48] to alkenes with various combinations of intra- and hepta-cyclic double bonds, results were obtained which mainly agreed with the order of reactivity of these systems. For example, the relative rates of addition for methyl mercaptoacetate are:

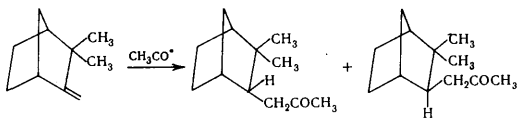
(I)	(LXIV)	(CV)	(XCVI)	(LVI)
1.00	1.44	3.55	1.72	1.83

The slight increase in the reactivity of (LXIV) in comparison with that of NB can be attributed to the somewhat greater strain of the molecule owing to the introduction of the heptacyclic double bond. The diene (CV) is the most active, that is, the intracyclic double bond in the triene (XCVI) decreases the activity of its diene system. According to Trecker and Henry [48] the reason for this is that the transition state for the sterically more favourable 1,4-addition leads to a strained NBD system. In the transition state itself, 1,2-addition evidently destroys the allyl stabilisation of the radical centre owing to conjugation with the π-electrons of the 2,3-double bond and consequently a general reduction in the reactivity of the

triene is observed. Furthermore, from these results it is clear that the intracyclic double bond and the diene system have comparable activities in homolytic reactions.

5. ADDITION TO 1,4,7-SUBSTITUTED NORBORNENES AND NORBORNADIENES

The above examples of *endo*-radical attack with participation mainly of comparatively small addends would appear to be only a few exceptions to the general rule of *exo*-addition. However, even the direction of approach of the addend in stage B (Scheme 1, p. 516) depends on the nature of the substituent present in the alkene molecule or introduced into it in the attack stage. In a recent paper [11] on the addition of various carbonyl compounds to camphene (CXVII) it was shown that even with acetaldehyde 7% of the product formed (CXIX) is due to chain transfer from the *endo*-side of the intermediate radical:



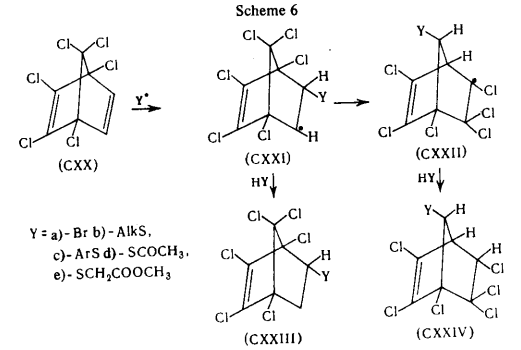
(CXVII) (CXVIII) (CXIX)

It can therefore be assumed that the accumulation of bulky substituents, especially in position 7, can significantly affect the stereochemical results of the reaction. Actually, in studying the addition of ethanethiol to 1,2,3,4-7,7-hexachloronorborna-2,5-diene (HCNBD) (CXX), we observed for the first time the formation of considerable amounts (up to 50%) of an *endo*-addition product (CXXIII).[71]

Subsequent study of the reactions of polysubstituted NBD, undertaken in parallel by Soviet and English chemists (Davies and coworkers, King's College, London), also led to extremely interesting results.

Thus, it was found that the hydrobromination [72-81] and thiylation of HCNBD by various thiols [72,82,83] (alkylthiols, arylthiols, thioacetic acid, methyl thioglycollate) proceed with a high degree of *endo*-stereoselectivity (Scheme 6):

Scheme 6

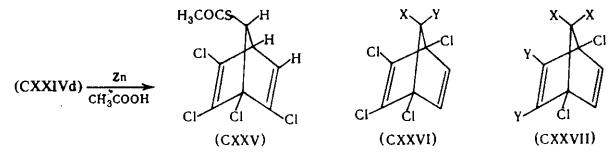


(CXX) (CXXI) (CXXII) (CXXIII) (CXXIV)

In addition to the *endo*-addition products (CXXIII), their isomers with substituents in the 7-*syn*-position (CXXIV) were observed, which showed that the reaction was accompanied by a free radical isomerisation which takes place under mild conditions and which is analogous formally to the well known Wagner–Meerwein cationic rearrangement (the mechanism of this rearrangement is discussed in more detail below). The 7-*syn*-structure of the isomers (CXXIV) was proved by the *endo*-position of the substituent in the corresponding intermediate radical (CXXI), and consequently by the *endo*-stereospecificality of the initial radical attack.

For some time the structure of products of type (CXXIV) was questioned§ in view of the fact that there is some difficulty in proving it rigorously. However, the *syn*-configuration of the substituent was established reliably on the basis of an analysis of the NMR spectrum of the dechlorination products from the 7-*syn*-thioacetate (CXXV) [73,75-78] and by a comparison of the NMR spectra of corresponding sulphides of the HCNBD and 1,2,3,4,7-*anti*-pentachloronorbornadiene (CXXVIb) series [84].

The complete reversal of the direction of radical attack observable in additions to HCNBD was explained [73,74,82,83] mainly by steric screening of the *exo*-side of the molecule of the diene by bulky electronegative 1,4,7-substituents:



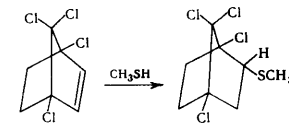
(CXXV) (CXXVI) (CXXVII)

a), X = Cl; Y = H
b), X = H; Y = Cl

a), X = Cl; Y = SMe
b), X = OCH3; Y = Cl

Actually, 1,4,7,7-tetrachloro-2,3-methylthionorborna-2,5-diene (CXXVIIa) and 1,2,3,4-tetrachloro-7,7-dimethoxynorborna-2,5-diene (CXXVIIb), which also contain bulky electronegative substituents at the bridge and alkylthiols mainly in the same manner as HCNBD.[85]

Even in the presence of 2,3-*endo*-hydrogen atoms, 1,4,7,7-tetrachloronorborn-3-ene (CXXVIII) adds ethanethiol *endo*-stereospecifically [86]:



(CXXVIII) (CXXIX)

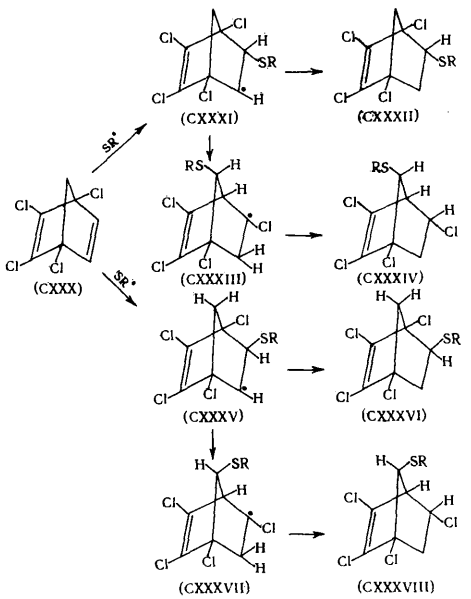
However, the substituent at the bridge is not the only steric barrier against *exo*-attack by a radical. The thiylation of 1,2,3,4-tetrachloronorborna-2,5-diene (TCNBD) (CXXX) with thioacetic acid [72-74] or ethanethiol [84] proceeds nonstereospecifically with the formation of a mixture of *endo*- and *exo*-epimers (CXXXII) and (CXXXVI) and the corresponding products of their rearrangement—7-*syn*- and 7-*anti*-epimers (CXXXIV) and (CXXXVIII) (Scheme 7). About 30% of the products are due to *endo*-radical attack.

Evidently, the absence of bridging chlorine atoms in TCNBD, as compared with HCNBD, greatly facilitates the *exo*-approach of the radical to the multiple bond. The latter also appears in the experimental conditions under which the reaction is effected: heating for 48 h at 60°C for HCNBD and by an exothermic reaction for TCNBD.[73]

Hence the direction of radical attack on the polychloro-substituted NB and NBD is controlled both by the bridge $C_{(7)}$ and also, although to a lesser degree, by the bridge-terminal $C_{(1)}$ and $C_{(4)}$ chlorine atoms. However, the introduction of 1,4-substituents in itself is probably not sufficient condition for the *endo*-approach of a radical, since it has been proved that 1,4-dichloronorbornene (XXVI) forms only *exo*-products with CH_3SH, CCl_3Br, and $CHCl_3$.[33] The absence of 2,3-*endo*-hydrogen atoms in the substituted NBD greatly facilitates *endo*-attack by the

§ Davies and coworkers [82,83] accepted the *cis*-configuration of the substituent on the basis of the absence of the corresponding *exo*-product; the *anti*-configuration has been proposed [72,74] on the basis of analogy with additions to tetrachloronorbornadiene.

Scheme 7



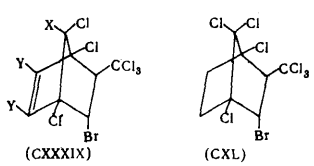
radical. In this the screening effect of the 2,3-*endo*-hydrogen atoms in NB is probably comparable in magnitude with the similar but oppositely directed effect of the 1,4-chlorine atoms in TCNBD: in the addition of thioacetic acid to NBD 17% of an *endo*-thioacetate of type (XCV) is isolated[64], but for TCNBD under comparable conditions the amount of *endo*-epimer (CXXXII) is doubled[73].

Evidently, of the two bridging substituents it is the 7-*anti*-chlorine atom that acts as a steric barrier against *exo*-attack. Thus, it has been proved[84] that in reaction with ethanethiol and thiophenol 1,2,3,4-*syn*-7-pentachloronorborna-2,5-diene (CXXVIa) behaves like TCNBD, and its 7-*anti*-isomer (CXXVIb) like HCNBD.

Even now it can be stated that the "*exo*-addition" rule cannot be considered all-embracing and the direction of attack by the free radical is a function of the degree of substitution of the diene and of the position and nature of the substituents.

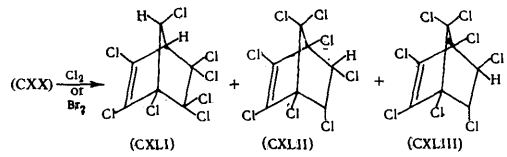
However, all the bicyclic alkenes investigated above contained substituents of similar inductive effect (OCH_3, Cl). It remained uncertain whether the effect of the bulky substituents on the direction of radical attack in polysubstituted NB and NBD is a purely steric effect or whether in this instance an electronic effect is also apparent.

From this point of view it is interesting that the addition of CCl_3Br to HCNBD, TCNBD, 7-*anti*-pentachloronorbornadiene (CXXVIb), 1,4,7,7-tetrachloronorbornene (CXXVIII), and 2,3-dimethylthio-1,4,7,7-tetrachloronorbornadiene (CXXVIIa) leads, just as for NB itself, solely to products of *trans*-addition with the *exo*-disposed trichloromethyl group of the type of (CXXXIX) and (CXL):[86]



where X = Cl or H, Y = Cl; or X = Cl, Y = SCH_3.

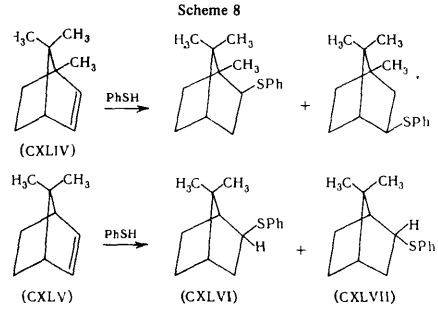
In studying the bromination and chlorination of HCNBD, although they were not able to inhibit the ionic processes, Davies and Parrot[87] also showed that *exo*-radical attack by halogen atoms takes place and a large proportion of the 7-*anti*-isomer (CXLI) is formed as a result of isomerisation of the product of radical *exo*-addition[87]:



Purely radical chlorination of HCNBD was effected by the same investigators by the action of sulphuryl chloride with the formation of the same three isomers but in another ratio. It is notable that whereas the *cis*-*endo*-product (CXLII) is almost absent in the reaction with Cl_2, it amounts to 11% of the isomeric mixture when SO_2Cl_2 is used, which is evidently associated with the greater size of the carrier-addend.

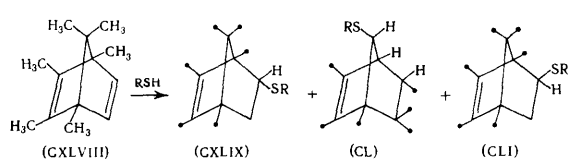
On the basis of the exceptional *exo*-attack by the bulky CCl_3 radical and the analogous behaviour of halogen atoms, Davies and coworkers[9,86] concluded that the direction of radical attack in the series of substituted NB and NBD is controlled mainly by electronic, and not steric, factors. In this, the relatively more electron-deficient $CCl_3^{\cdot}$ and $Br^{\cdot}$ radicals will experience some attraction at the side of the bridge chlorine atoms and the less electrophilic thioradicals $CH_3S^{\cdot}$ are repelled by the same substituents, which facilitates *endo*-radical attack. Davies and Rowley[109] think that this assumption agrees with the exclusive *exo*-addition of thiophenol to bornylene (CXLIV) and apobornylene (CXLV)[109] (Scheme 8).

Scheme 8



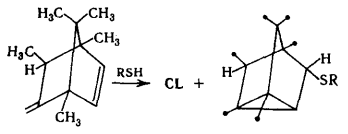
Brown and Kawakami's reinvestigation of the last reaction confirmed the high degree of *exo*-stereoselectivity, but it was found that in this instance up to 5% of the *endo*-thioether (CXLVII) is formed in comparison with 0.5% for NB itself.

On the other hand, it was shown recently[89,90] that the addition of 2-methylpropane-2-thiol to hexamethylnorbornadiene (HMNBD) (CXLVIII) proceeds with a high degree of *endo*-stereoselectivity with the formation of the 5-*endo*-, 7-*syn*-, and 5-*exo*-sulphides (CXLIX)–(CLI) in the ratio 51 : 45 : 4, respectively:



where R = t-C_4H_9.

Stereospecific *endo*-radical attack was also observed in the reaction of 2-methylpropane-2-thiol with methylenepentamethylnorbornene (CLII).[89,90] As a result, nortricyclene and 7-*syn*-sulphides (CL) and (CLIII) were obtained—both by addition of the thiol to the intracyclic double bond of the diene¶:



(CLII) (CLIII)

where R = t-C_4H_9.

Of the two dienes, (CXLVIII) and (CLII), the first was much more reactive in thiylation, but the intracyclic double bond of the diene (CLII) was much more reactive than the heptacyclic, just as was found earlier for unsubstituted alkenes[48,65] (see p. 521).

Taking into account the results of the thiylation of the polymethylated bicyclenes it must be assumed that the stereochemistry of the free radical addition to norbornene and diene systems is probably determined by a complex combination of electronic and steric factors. It seems that there is a definite lower limit for most of the steric and electronic factors under discussion produced by the substituents present either in the norbornyl system or in the molecule of attacking agent. Agents with not very demanding steric requirements (halogens, hydrogen halides, certain thiols, tetrafluorohydrazine, and nitryl chloride) can attack the molecule of unsubstituted NB and NBD from the *exo*- and the *endo*-directions, with preferred *exo*-attack. For 2-*endo*-substituted NB and NBD the ratio of the products depends on the stereoelectronic interrelations of the 2-*endo*-substituent and addend at both stages of the addition. For NB and NBD with 1,4,7-substituents, the 7-substituent, located above the plane of the double bond, and to a lesser extent the under-bridge substituents exhibit considerable steric control. However, the latter cannot appear for addends with low steric requirements (as evidently occurs in the reaction of thiophenol with bornylene and apobornylene).

An analogous proposal was recently made by Brown and Kawakami[88], who investigated the addition of various reagents under polar and radical conditions to NB and apobornene (CXLV) (including radical thiylation). They concluded that the breakdown of *exo*-stereospecificity in the reactions of apobornylene is the consequence of the appearance of steric control at the side of the 7-methyl substituents. However, the latter may not appear, depending on the mechanism of addition of the addend and the steric requirements of the latter.

In this connection it is also relevant to mention two recent papers[91,92], in which it was noted that the relative reactivity of the alkene under radical additions depends mainly on the induction effect of the alkyl substituent for the addition of small radicals, and is determined by the steric requirements in attack by large radicals.

In speaking about the electronic effects of the substituents evidently discussion must not be limited to consideration of only their electrostatic interaction with the attacking radical. This point of view, adopted by Davies and Rowley[86] to explain the exclusive *exo*-addition of CCl_3 radicals to polychloro-substituted NB and NBD ascribes relative nucleophilic properties to thiyl radicals, which clearly contradicts known results[93,94]. Evidently, in addition to the electrostatic interaction of the substituents their effect on the double bond of the bicyclene must be considered to a lesser extent. For example, it is known that whereas NB and NBD add various electrophilic reagents very readily[95,96], in the HCNBD molecule the 5,6-double bond has almost lost its nucleophilic nature and the corresponding reactions occur under much more severe conditions and with very small yields[73,83].

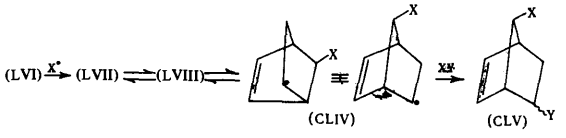
Bearing in mind the magnetic anisotropy of the double bond (for example, the shift of the signals of the 2,3-vinyl protons under the action of 7-*syn*-CH_3 groups[97]) it seems most probable that in these systems the direction of radical attack will be determined by the complex stereoelectronic effects of the substituents in addition to the steric factors.

Undoubtedly further accumulation of experimental results in this field will allow the influence of steric and electronic effects on the stereochemical results of the reactions to be distinguished more sharply.

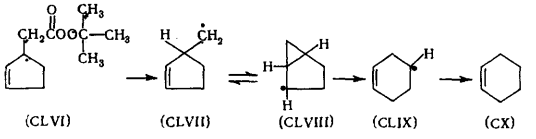
6. MECHANISM OF ISOMERISATION OF NORBORNENYL RADICALS

The results described in the preceding section show that addition to NBD is usually accompanied by the rearrangement of intermediate radicals with the formation of nortricyclene structures or compounds with 7-*syn*- or 7-*anti*-substituents. Usually the formation of both isomerised products is not observed in a single reaction. However, it was extremely strange, that the nortricyclyl (cyclopropylcarbinyl) radical (LVIII) found in equilibrium with the norbornyl radical (LVII)[61,62] does not exist in equilibrium with radical (CLIV), apparently because the breaking of the 2,6-bond is equally probable (Scheme 9),

Scheme 9



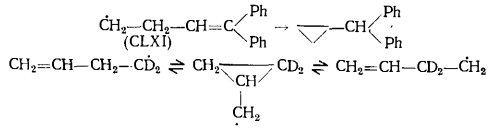
particularly as in several recent papers the formation of the cyclopropylcarbinyl radical is taken as the intermediate stage of the 1,2-migration of the vinyl groups. Such a mechanism was, for example, proposed for the thermal rearrangement of t-butyl cyclopent-2-enylperoxoacetate (CLVI):[96]



We note that during the rearrangement of ester (CLVI) rearrangement of the primary radical centre (CLVII) into the secondary (CLIX) takes place. Although Slaugh[98] also does not consider this sufficient driving force, nevertheless the reverse isomerisation (from the corresponding cyclohexenyl derivative) does not occur under these conditions.

¶ In this instance, in addition to free-radical isomerisation of the Wagner–Meerwein type already mentioned, 1,3-migration of hydrogen in the intermediate radical was observed, this will be considered in more detail below, p. 525.

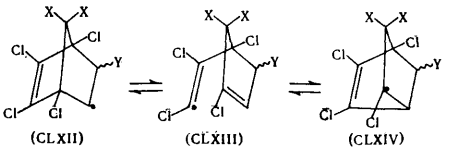
Confirmation of the proposed mechanism is given by the formation of cyclopropyldiphenylmethane in the generation of 4,4-diphenyl-3-butenyl radicals (CLXI) from the corresponding per-esters [98] or the formation of a mixture of but-1-ene-3,3-d_2 and but-1-ene-4,4-d_2, by the radical decarbonylation of 4-pentenal [99]:



Taking into account all the above information, it would be expected that the nortricyclyl radical (LVIII) can also play the part of an intermediate product in the process of 1,2-vinyl migration with the formation of 7-substituted NB (CLV).

Alden and Davies [100] also proposed just such a scheme for the mechanism of the above-mentioned radical rearrangement of the Wagner–Meerwein type, and then confirmed it reliably by a series of experimental facts, and it has now been adopted in the studies of other investigators. It was first assumed that the rearrangement proceeds according to a scheme [10,72,101] analogous to that proposed earlier for the high-temperature isomerisation of bornyl radicals [32]. However, in none of the instances investigated was a substituted allylcyclopentene corresponding to the radical (CLXIV) observed. The formation of an isomerised radical (CLXIV) both directly from (CLXII) and also through the stage of formation of (CLXIII) requires the (relatively unfavourable from the energy point of view) breaking of the $C_{(1)}-C_{(2)}$ vinyl bond (the dissociation energy of this bond is 10 kcal mole^{-1} above the dissociation energy of the C–C bond in alkanes) [102].

Scheme 10

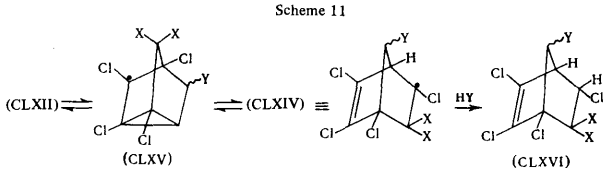


(CLXII) (CLXIII) (CLXIV)

Since until recently in reactions involving NBD itself only the formation of substituted nortricyclenes was observed, evidently an important factor for the occurrence of homolytic isomerisation according to Scheme 9 is the introduction into the molecule of the diene of substituents favourable to β-breaking with the shift of the equilibrium towards the side of formation of the radical (CLIV). This agrees completely with the known general position of free-radical chemistry [103,104].

The driving force for the observed rearrangement is evidently the greater stability of radical (CLXIV) in comparison with radical (CLXII), brought about by stabilisation of the radical centre by the neighbouring chlorine atom. The latter is consistent with the results of Nesmeyanov and coworkers on the isomerisation of acyclic halogen-containing radicals [41,105,106]. In a similar manner, the change from secondary to tertiary radical centre is probably the driving force for rearrangement in reactions involving HMNBD (Scheme 12, p. 526).

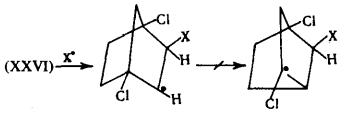
Scheme 11



(CLXV) (CLXVI)

Here in the reaction with HCNBD the *syn/endo* ratio of the sulphides (CXXIV)/(CXXIII) (Scheme 6, p. 522) was ~3 : 1, [73] and under similar conditions with HMNBD it becomes only ~1 : 1. [90] This is in good agreement with the known greater stabilising effect of the chlorine atom standing at the radical centre in comparison with the corresponding effect of the methyl group [41].

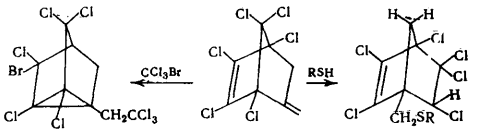
Characteristically, in the absence of a second double bond in the molecule of 1,4-dichloronorbornene (XXVI) even in the presence of a chlorine atom, which should be favourable to the stabilisation of a new radical centre, isomerisation products were not observed [33]:



In accordance with the proposed mechanism, the structure and ratio of the final products of addition to saturated NBD should be determined by the action of steric and electronic factors on the position of the equilibrium (CLXII) ⇌ (CLXV) ⇌ (CLXIV) and the rate of chain transfer of the radicals formed intermediately.

Actually, in the addition of thioacetic acid to TCNBD [73] the decrease of steric strain at the chain transfer stage from the *exo*-radical (CXXXV) to the *endo*-radical (CXXXI) (Scheme 7), evidently leads to an increase in the lifetime of the first. This, in turn, significantly alters the ratio of the products: *exo/anti* (CXXXVI)/(CXXXVIII) ≃ 1 : 1, whereas *endo/syn* (CXXXII)/(CXXXIV) ≃ 18 : 1. The screening of the 7-*anti*-chlorine atom of the *exo*-side of the HCNBD molecule in comparison with TCNBD also appears in the ratio of the thioacetates obtained: *endo/syn* (CXXIIId)/(CXXIVd) ≃ 0.7 : 1, but for *endo/syn* (CXXXII)/(CXXXIV) ≃ 18 : 1.

In studying the reaction of HCNBD with methanethiol and ethanethiol at various temperatures and addend concentrations and also under comparable conditions but with different thiols [73], it was shown that the ratio of the products, and consequently also the position of the equilibrium of the corresponding radicals (Scheme 11, X = Cl), depends significantly on the experimental conditions and rate constants of chain transfer to the addend participating in the reaction. The latter is also confirmed by the example of reactions with participation of hexachloromethylenenorbornene (CLXVII): only the corresponding nortricyclene (CLXVIII) was isolated in the reaction of this diene with CCl_3Br whereas addends with a lesser transfer constant (alkanethiols, thioacetic acid, methyl thioglycollate) give only products of rearrangements of the type (CLXIX): [97]

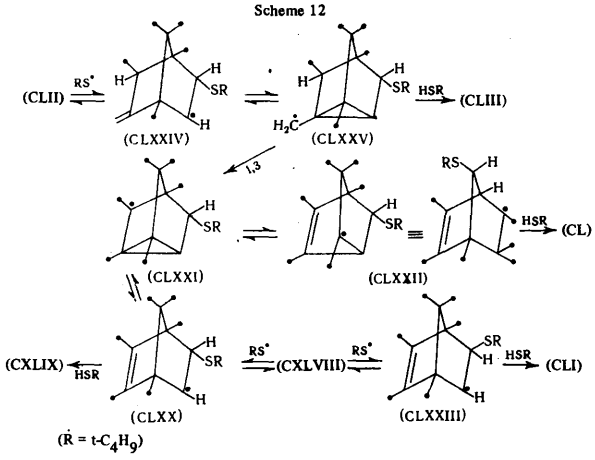


(CLXVIII) (CLXVII) (CLXIX)

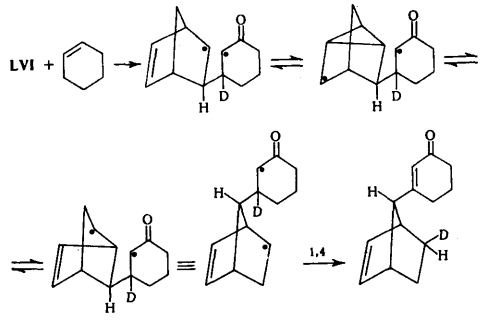
Confirmation of the proposed scheme of rearrangement is also the formation of the same 7-*syn*-sulphide (CL) in the thiylation of HMNBD and methylenepentamethylnorbornene (CLII), which can evidently proceed solely through the

formation of a common intermediate nortricyclene radical (CLXXI) (Scheme 12).[89,90] The presence in the reaction mixture of a nortricyclene product corresponding to radical (CLXXV) and the absence of a sulphide corresponding to the radical (CLXXI) is evidently connected with steric hindrance at the chain transfer stage, with participation of the latter:

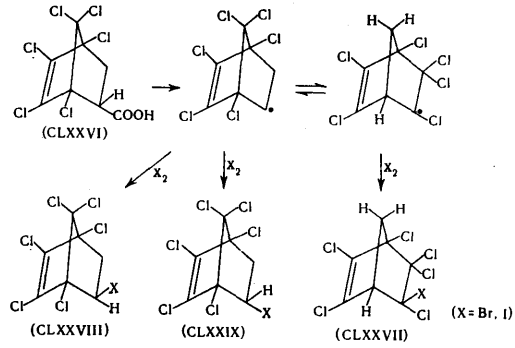
Scheme 12



Interestingly, for the formation of 7-*syn*-sulphide (CL) from the diene (CLII) 1,3-migration of the hydrogen with a corresponding shift of the radical centre in the radical (CLXXV) is postulated. The possibility of such a migration is confirmed, for example, by results obtained by McCullough and Rasmussen[107], who describe the *exo*-stereospecific 1,4-migration of hydrogen in the photochemical reaction of NBD with cyclohexen-2-one or 3-methylcyclohexen-2-one.



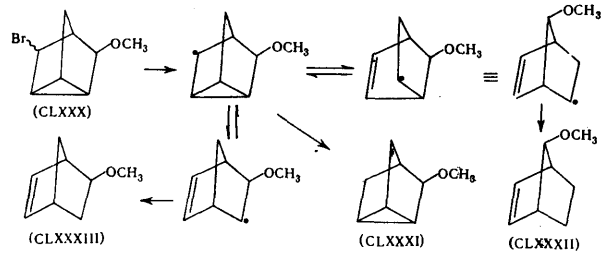
Hence in radical reactions of addition to polysubstituted NBD equilibrium is established between the intermediately formed radicals according to Scheme 9. The position of the equilibrium is determined by the competition between the steric and electronic interactions of the substituents of the reagents and also by the experimental conditions. Another example of this is Davies and Mason's modified Hunsdiecker reaction[2] for 1,4,5,6,7,7-hexachloronorborn-2-ene-5-carboxylic acid (CLXXVI) and its methyl analogue. In both instances when bromine is used the corresponding rearranged products (CLXXVII) are formed. Evidently, participation in the reaction of a slower chain carrier (in comparison with iodine) ensures the possibility of isomerisation:



Interestingly, the ratio of *exo*- to *endo*-halides (CLXXVIII) : (CLXXIX) when iodine is used is higher than for bromine, which also evidently confirms the importance of the electronic factor in this instance.

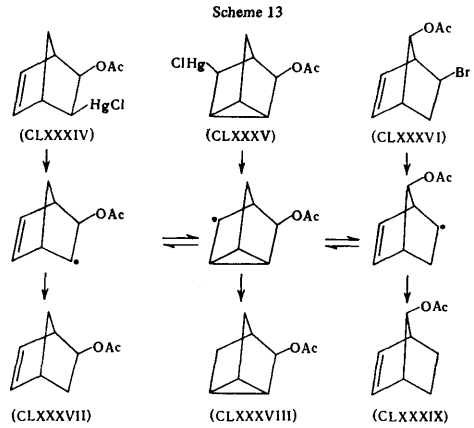
A rearrangement of the Wagner–Meerwein type has been reported very recently in the reaction of unsubstituted NBD with tetrafluorohydrazine[46] and cyclohexen-2-one[107].

In investigating the reaction of Grignard reagents with methoxy-substituted nortricyclyl bromide (CLXXX)†, Davies and coworkers observed both the norbornene ethers (CLXXXII) and (CLXXXIII) in the reaction mixture as well as the corresponding nortricyclene (CLXXXI):[2]



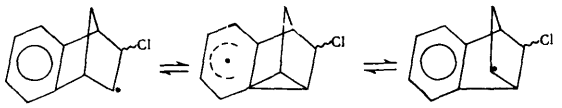
Similar results were obtained in the reduction of acetoxy-substituted mercury chlorides (CLXXXIV), (CLXXXV) or bromides (CLXXXVI) with sodium tetrahydroborate, or tri-n-butyl- or triphenyl-tin hydride or deuteride[108]. Irrespective of the initial acetate an equilibrium mixture of the three products (CLXXXVII)–(CLXXXIX) was obtained (see Scheme 13):

Scheme 13



The radical rearrangement with 1,2-shift of the phenyl group was observed in the reaction of benzonorbornadiene (XXIV) with nitryl chloride[67]:

† $CoCl_2$ catalyst.



Interestingly, in this instance the isomers ratio *endo/syn* ≃ 20 : 1, and *exo/anti* ≃ 1.3 : 1, which also clearly shows steric control in the radicals formed as intermediates.

From the above examples, it becomes evident that under different experimental conditions, in particular when addenda with a low transfer constant participate in the reaction, the lifetime of the intermediate radicals can be sufficient for the establishment of equilibrium according to Scheme 9 (p. 524).

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Hence a rather complex and still extremely contradictory interrelation of the steric and electronic effects of the substituents, which determine the direction of both stages of 1,2-addition and also the position of the equilibrium between the radicals formed, is observed in the reactions examined. Therefore the continuation of investigations in this field using modern methods of characterisation is extremely interesting and useful for finding both general and particular rules in free radical chemistry.

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Chemical Effects of Laser Radiation

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This review deals with the chemical effects observed under the influence of laser light. The operating principle of the laser, the main types of laser, and the properties of laser radiation are briefly described. The application of laser techniques to the production and investigation of short-lived excited states is discussed. One-photon and multi-photon processes induced by laser radiation are considered. Several examples of the specificity of the reactions initiated by laser light are given. 140 references.

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I. INTRODUCTION

In the hands of scientists and engineers, lasers have proved an important new tool to study interactions with matter. The physical principles of laser action were formulated as a result of the fundamental researches on quantum electronics carried out in the USSR (by Basov and Prokhorov's team) and in the USA (by Townes and Schawlow's team). In 1958 Schawlow and Townes [1] drew attention to the possibility of producing an optical quantum generator (laser) based on stimulated (or induced) radiation processes†. The first solid-state laser, using ruby, was constructed by Maiman [2] in 1960, and one year later Javan, Bennett, and Herriott assembled the first gas (helium–neon) laser [3]. At about this time, suggestions that laser light could be used to study chemical processes began to appear in the literature [4,5]. The most attractive properties of laser light for this purpose are its high intensity and monochromaticity, and also its accurate collimation, which enables the laser energy to be transmitted over long distances or concentrated into small, isolated regions of matter. The radiation of many lasers lies in the i.r. region of the spectrum, i.e. in a region where absorption is accompanied by the excitation of intramolecular vibrations. The availability of high-intensity, monochromatic light sources for this spectral region gave a new impetus to infrared photochemistry, i.e. to the excitation of specific molecular vibrations, and to the selective initiation and control of chemical reactions.

Many papers (both theoretical and experimental) have been written in recent years on the effect of laser radiation on matter and on the chemical reactions induced by laser light. Some overall trends are becoming apparent, and we can attempt to generalise some of the published results.

II. PROPERTIES OF LASER LIGHT. VARIOUS TYPES OF LASER

Lasers are devices for the generation or amplification of light by stimulated emission. Consider a vessel exposed to a flux of incident light. The atoms and molecules in the vessel will absorb light and undergo transitions. The transition from an excited level to the ground level can occur either spontaneously or by induced (stimulated) processes (see Fig. 1). The number of absorbtions and of induced emissions per unit time in unit volume is given by

$$\Delta N_{ik} = B_{ik}u_\nu N_i \quad (1)$$

$$\Delta N_{ki} = B_{ki}u_\nu N_k \quad (2)$$

where, as shown by Einstein in 1917,

$$B_{ik} = B_{ki} \quad (3)$$

(u_ν is the photon flux; N_i and N_k are the numbers of atoms in the i-th and the k-th level per unit volume; B_{ik} and B_{ki} are the Einstein coefficients).

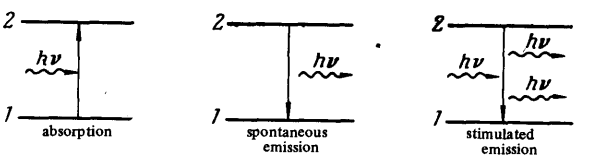


Figure 1. Model of absorption, spontaneous emission, and stimulated emission processes: *1*) ground level, *2*) excited level.

The fall in intensity of the light beam per unit volume along the direction of the incident beam is given by the formula

$$-\Delta U = B_{ik}N_i u_\nu \Delta E - B_{ki}N_k u_\nu \Delta E \quad (4)$$

where $\Delta E = h\nu = E_k - E_i$ (E_k and E_i are the energies of the k-th and the i-th level; ν is the frequency corresponding to the transition).

Using Eqn. (3),

$$-\Delta U = u_\nu B_{ik}N_i \Delta E\left(1 - \frac{N_k}{N_i}\right) \quad (5)$$

Under conditions of thermodynamic equilibrium

$$\frac{N_k}{N_i} = e^{-\frac{\Delta E}{kT}} \quad (6)$$

† This principle for the amplification of light had been suggested earlier (in 1940) by V.A. Fabrikant.

and, since $\Delta E > 0$, the exponential factor in the expression

$$-\Delta U = u_\nu B_{ik} N_i \Delta E \left(1 - e^{-\frac{\Delta E}{kT}}\right) \quad (7)$$

is always less than unity and therefore the stream of radiation must lose energy at any finite temperature (in the limit of $T \to \infty$, $\Delta U \to 0$). The condition for light amplification (or "negative absorption") is

$$\frac{N_k}{N_i} > 1 \quad (8)$$

This condition can be satisfied only by non-equilibrium processes. A population of energy levels corresponding to the inequality (8) is termed a population inversion. The more substantial the population inversion, the greater is the amplification of the light beam. Let us consider the ways in which population inversion can be induced. Assume that the atomic or molecular system can exist in three energy levels *0*, *1*, and *2* (see Fig. 2). Population inversion arises when the probability of a $1 \to 0$ transition is less than the probability of a $2 \to 1$ transition under conditions such that the rate of the $2 \to 0$ transition is sufficiently low.

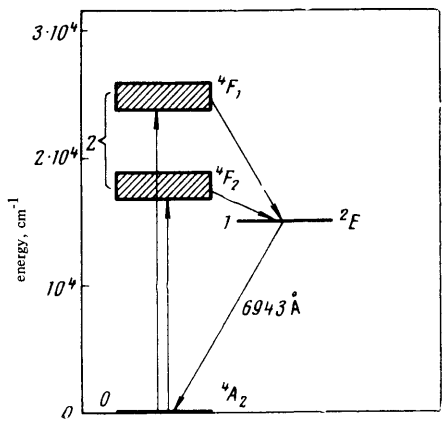


Figure 2. Energy levels of ruby ($Cr^{3+} \cdot Al_2O_3$).

Lasers consist of an active medium (i.e. the substance whose optical transitions are used to generate light), a pump (to excite the system), and suitable resonators (mirrors) to cause excitation of specific vibrations in the active medium. The active medium can be solid, gaseous, or liquid. Pumping, i.e. the production of a population inversion, is achieved in a variety of ways, depending on the type of laser: solid-state lasers are pumped optically, semiconductor lasers by electrical impulses, and gas lasers are usually pumped by electrical discharges. The resonator usually consists of a system of two plane-parallel mirrors.

Fig. 2 represents the system of energy levels for the ruby laser. Irradiation of the ruby crystal from a xenon flash tube causes inversion of the population of the ^2E level. The radiation density u_ν increases as a result of multiple reflections from the silvered end-faces of the crystal, and stimulated emission appears. The intensity of emission increases very rapidly until level *1* becomes depleted. The duration of the light pulse ("spike") is 10^{-6} s, and the total duration of the stream of separate spikes is of the order of 10^{-3} s. This operating regime for a pulsed laser is termed free generation.

Lasers can also be operated in a different regime: the so-called modulated Q-factor or giant pulse regime, or in English terminology the Q-switched regime[6]. By inserting a shutter between the crystal and one of the mirrors, the photon flux in the active medium of the laser is decreased, thus decreasing the number of stimulated transitions per unit time and hence enhancing the population inversion. A very powerful light pulse is obtained when the optical shutter is momentarily opened. Although the total energy of the giant pulse is about an order of magnitude lower than that obtained in the free generation regime, the length of the pulse can be as small as 10^{-8} s, and therefore power levels of hundreds of megawatts can be obtained. The optical shutter usually consists of a solution of a dye, which is decolorised by a very intense light beam (see Section III).

Even shorter (10^{-11}–10^{-12} s) and more powerful pulses have been generated as a result of recent advances in the Q-switching method. Picosecond pulses of laser light have been produced by the mode-locking method. The radiation from a solid-state laser consists of many modes or frequencies of vibration, close to the fundamental frequency. Some dyestuffs behave as amplitude modulators when irradiated: they amplify the frequencies of highest amplitude and they attenuate all the other frequencies. As a result, the many frequencies generated by the laser become phase-locked, and a series of narrow pulses (of length inversely proportional to the width of the corresponding frequency component) is produced[7,8] as a result of constructive and destructive interference.

The main types of laser are listed in Table 1 together with some properties of their radiation. The light emitted by lasers has some unique properties, not found in ordinary light sources (coherence, high monochromaticity, intensity, etc.). Not all of these are equally important from the point of view of initiating chemical reactions: the most valuable property of laser light in this respect is the intensity of the radiant energy available over a narrow range of frequencies. As Table 1 shows, the generated band-width in any laser is much narrower than the absorption band of the molecules. It is also possible to increase the density of laser radiation by focussing the beam. A monochromatic, low-divergence laser beam can be focussed into a spot 10^{-6}–10^{-4} cm^2 in area. Because of the coherence of laser radiation, interference can take place in the focal region: the amplitude of the radiation field will vanish, or increase by a factor of two, between points half a wavelength apart. Since many of the effects of laser radiation are non-linear, i.e. they vary as the square (or some higher power) of the intensity of radiation, interference can be expected to enhance some of the high-intensity effects of laser radiation. Such giant intensities of radiation are accompanied by substantial values of the electric and magnetic vector of the light wave. Thus, an electric field strength of 10^6 V cm^{-1} is set up when a pulse from a 1 MW ruby laser is focussed into a spot 0.2 mm in diameter. This level of field strength is comparable with the electric fields present within molecules. It follows that the electric field associated with the light waves can induce strong perturbations, leading to polarisation (and, in the limit, ionisation or dissociation) of the molecules.

When laser radiation is used to initiate chemical reactions, it would be desirable to have a smooth control over the wave length of the light (to suit the particular system)

Table 1. Main types of laser.

Active medium	Operating regime	Pump	Wave length	Monochromaticity, Δλ	Duration of emission, s	Power	Light flux[a] photons/cm^2 s	Comments	Ref.
Doped crystals and glasses									
Ruby (Cr^{3+}/Al_2O_3)	pulse[b]	optical	6943 Å	<1 Å	10^{-3}	1—100 kW	$3\cdot10^{21}$—$3\cdot10^{23}$	efficiency <1%	9
	Q-switch[c]			0.08—0.5 Å	10^{-8}	10—100 MW	$3\cdot10^{26}$—$3\cdot10^{29}$		
Nd^{3+}/glass	pulse		1.06 μm	100 Å	10^{-3}	1—100 kW	$5\cdot10^{21}$—$5\cdot10^{23}$		
	Q-switch			20—100 Å	10^{-8}	10—100 MW	$5\cdot10^{26}$—$5\cdot10^{29}$		
Semiconductor lasers									
GaAs	pulse	current pulses	9020 Å	5—10 Å	10^{-6}—10^{-7}	1—60 W at 10^4—10^5 pulses s^{-1}	$4\cdot10^{18}$—$3\cdot10^{20}$	at 300° K	10
	pulse		8430 Å	5—10 Å				at 77° K	
Gas lasers									
He-Ne	continuous[d]	discharge	6328 Å	10^{-4} Å or less	—	1—100 MW	$3\cdot10^{15}$—$3\cdot10^{17}$		11
			1.15 μm						
CO_2	continuous[d]	discharge or optical	10.6 μm	0.01 Å	—	50 W—8 kW	$2\cdot10^{21}$—$4\cdot10^{23}$	50-80 W per metre of discharge tube	12
N_2	*Q*-switch	discharge	3371 Å	0.01 Å	10^{-8}	50 kW	$8\cdot10^{22}$		13
He—Cd	continuous	discharge	3250 Å	—	—	5—50 MW	$8\cdot10^{15}$—$8\cdot10^{16}$		14
			4416 Å						15
Dye lasers	*Q*-switch	single laser pulse or optical	4000—12000 Å	0.6—300 Å	10^{-8}	1—10 MW	$2\cdot10^{27}$—$6\cdot10^{28}$	efficiency from 0.001% to 90%	16

[a] Flux calculated for an unfocussed beam of 1 cm^2 diameter.
[b] Pulsed, free generation regime.
[c] Pulsed, *Q*-switched regime.
[d] Continuous regime.

while retaining its high power and monochromaticity. Laser emission consists of discrete lines, usually in the i.r. region of the spectrum or close to the red end of the visible region. However, radiation in the u.v. region or close to the u.v. limit of the visible region would be much more appropriate in chemical applications (photon energy 4—7 eV). Only two gas lasers emit in this region of the spectrum: the N_2 pulsed laser[13], which has a relatively low power, and the recently discovered helium—cadmium laser, which can be operated in the continuous wave regime[14]. Laser radiation in the u.v. region can be obtained also by frequency doubling, which involves transmitting strong laser pulses through certain crystals (KH_2PO_4, $NH_4H_2PO_4$). In this way we can obtain light with λ = 3471 Å (by doubling the frequency of the ruby laser) or λ = 2650 Å (by twice doubling the frequency of the Nd^{3+} laser). Thus, by using the harmonics of laser light, we can increase the number of available discrete wave length and produce powers of the order of 0.1 MW in the short-wave region. Lasers based on organic dyes[15,16] offer an even better choice of wave lengths in the region of interest. The emission from these lasers can be controlled over fairly wide wavelength limits (several hundreds of Ångstroms). Dye lasers were discovered quite recently (in 1967), but the number of dyes in which laser action has been observed already exceeds the number of active media used in all other types of laser. In principle, the number of dyes capable of laser action is almost infinite, and it should be possible to synthesise dyes having the required properties (frequency, amplification coefficient) and to use a special laser for each of a large number of narrow frequency ranges. Thus, with the help of lasers based on solutions of organic dyes we expect to progress from a discrete and limited choice of frequencies (obtained from solid-state lasers) to a practically free choice of frequencies in the visible and near infrared regions of the spectrum. Generation from a 4-methylumbelliferone laser beginning at 3850 Å, i.e. in the u.v. region, has recently been reported[17].

III. MECHANISM OF THE EFFECT OF LASER RADIATION

1. Effects Associated with Electronic Excitation

a. One-photon effects

Direct excitation to the triplet state. When a substance having a singlet ground state is irradiated with light of relatively low frequency, direct excitation of triplet levels is not observed, because the extinction coefficients of light with a frequency corresponding to these transitions are 10^5—10^6 times smaller than the extinction coefficients for allowed transitions. Although the lowest triplet level of most molecules is located between the ground and the first excited singlet level (Fig. 3), the electronic spectra of molecules show their first absorption at frequencies corresponding to the $S_1 \leftarrow S_0$ transition. With ordinary photochemical excitation by light of low intensity, triplet states can arise only by $T_0 \leftarrow S_1$ transitions from excited singlet states (Fig. 3).

However, direct population of triplet levels can be induced by using laser light. In spite of the low probability of $T_0 \leftarrow S_0$ transitions, sufficiently intense radiation can make these transitions observable. Direct triplet excitation has been observed in a number of aromatic hydrocarbons and dyes with low-lying excited states[18-21] (see also a discussion[22] of the criteria for the direct formation of triplet states). The most convenient material for a study of this effect is anthracene, because the frequency of the transition to the triplet state in this material (14 750 cm^{-1}) is close to the frequency of radiation from the ruby laser (14 400 cm^{-1}). Phosphorescence has been observed in anthracene irradiated with light from a ruby laser[23] operated in the *Q*-switched mode. Since the quantum energy of the ruby laser is lower (by 350 cm^{-1}) than the excitation energy of anthracene, direct absorption can occur with a small activation energy, which may even

exceed 350 cm^{-1}, if a vibrationally excited triplet of anthracene is formed during absorption.

In molecular oxygen the ground level is triplet. However, transitions to the singlet, vibrationally excited $O_2(^1\Delta_g + v)$ level can be induced [24] by Nd^{3+} laser light

$$O_2(^3\Sigma_g^-) \rightarrow O_2(^1\Delta_{g+v})$$

and in this way the reactions of singlet oxygen can be initiated.

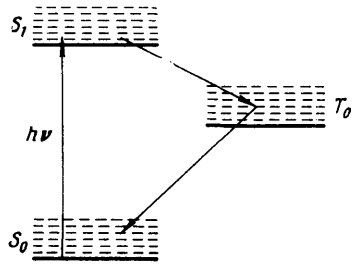


Figure 3. Energy levels of an organic molecule (the broken lines denote vibrational sublevels).

The one-photon mechanism of transition to a triplet state acting as an intermediate in a chemical reaction has been convincingly demonstrated [25] in one system only: the gas-phase photochemical bromination of perfluoro-olefins, initiated by light from a ruby laser. (The rate of the dark reaction is very low for these compounds.) During normal photobromination with light of wavelength below 6800 Å the Br_2 molecule dissociates into atoms and the reaction proceeds by a radical-chain mechanism. The energy of a light quantum corresponding to $\lambda = 6940$ Å is not sufficient for direct photodissociation of Br_2, but this quantum can excite a transition from the ground to the lowest excited state ($^3\Pi_{1u} \leftarrow {}^1\Sigma_{g^+}$). The vibrational energy of this state of the Br_2 molecule can be altered also by varying the radiation frequency [26] within several cm^{-1}. In this way, the addition to a double bond of bromine molecules in the triplet state and in exactly known vibrational states has been investigated. It has been shown that the reaction rate is very sensitive to the wavelength (within the absorption band) and is directly proportional to the intensity of the incident light at constant wavelength. Thus, the reaction is not caused by direct dissociation of the Br_2 molecules, corresponding to the appearance of a continuum in the spectrum. At the same time, participation of atomic bromine is suggested by the inhibiting effect of traces of NO. Mass spectrometric analysis of the products obtained in bromination experiments with labelled $^{79}Br-{}^{79}Br$ and $^{81}Br-{}^{81}Br$ molecules confirmed the absence of isotopic enrichment of the reaction products, which would be expected if the addition of Br_2 occurred by a molecular mechanism. The primary photobromination product, $Br_2(^3\Pi_{1u})$, has a closely spaced set of vibrational levels, the difference in energy between successive levels being less than kT at room temperature. Hence, the probability of vibrational energy transfer is high. Since the dissociation energy of this state of the Br_2 molecule is only 6 kcal $mole^{-1}$, the $Br_2(^3\Pi_{1u})$ molecule can acquire, by collision, the vibrational energy necessary for dissociation into Br atoms, which then enter into the chain reaction leading to the brominated product. The contribution to the reaction from the molecular mechanism is negligibly small.

Excitation into singlet states. The main feature of the excitation of singlet levels by giant laser pulses is the fact that the pulses are very intense and of short duration (shorter than, or comparable with, the mean life time of the singlet excited states). Because of the high intensity, excited levels can be highly populated. As a result, the spectral properties of the material are changed, and observation of the absorption spectra of excited singlets becomes possible. The short duration of the laser pulse enables us to monitor processes occurring in nanoseconds [27], and even picoseconds, provided that the reaction is accompanied by fast emission [28]. The frequencies of transitions into excited singlet states of organic molecules lie in the u.v. region. Since lasers which emit at these frequencies are not powerful enough, one-photon excitation to singlet states is usually carried out by utilising the higher harmonics of the light from very powerful pulsed lasers. Excited singlets, and their reactions, have been investigated by an extension of Norrish and Porter's [29] flash photolysis and spectroscopy method. An intense flash of light creates macroscopic concentrations of the primary photochemical dissociation product in the irradiated material: free atoms, radicals, or molecules in excited states. The excited system can be investigated either spectroscopically or kinetically. In the former case a second (test) pulse of light is transmitted through the system after a predetermined interval, and the absorption spectrum of the short-lived products is recorded. In the kinetic method, light of wavelength corresponding to the absorption maximum of the short-lived product is continuously passed through the cell, and changes in transmission are monitored for a predetermined period following excitation. The classical flash photolysis method uses pulses of 10^{-6} s duration, obtained from a discharge tube, which limits the application of the method to processes with rates $<10^6$ s^{-1}. Processes 100–1000 times faster can be studied by using laser-pulse excitation. The apparatus used by Porter and Topp [30,31] to record the absorption spectra of the excited singlets of aromatic compounds is shown in Fig. 4. The spectra were measured a known time after excitation by a giant pulse of the first harmonic of a ruby laser (3470Å). Part of the light, selected by a beam splitter, was focussed on a cell containing the solution of the experimental compound. The other part of the beam passed through the splitter, was reflected by a mirror back to the splitter, and to a cell containing the scintillator intended to generate a continuum in the spectral region of interest. The test pulse passed through the cell into the spectrograph, where the spectrum of the singlet excited states produced by the laser pulse was recorded. The time delay is determined by the distance between the beam splitter and the mirror: for example, a distance of ~3.5 m will produce a delay of 25 ns. For kinetic measurements, the test source of light can be a flash from a discharge tube of duration (several milliseconds) large compared to that of the excitation pulse from the laser. In practice, it is possible to use a small part of the light output of the lamp used for optically pumping the laser. It is important that the intensity of this light source remains practically constant during the measurement.

Novak and Windsor [32] used a slightly different method to generate their test pulse. They used a prism to isolate the beam of primary laser radiation, which is usually lost when a crystal of KH_2PO_4 is used for frequency doubling, and focussed it on to a cell containing an inert gas. The luminescence produced by the dielectric breakdown of this gas, having a continuous spectrum, could be used as the test pulse. Time resolution was obtained by directing the test radiation to a fast-response photocathode after it had passed through the cell. Obviously, the time delay can be controlled, as in the previous apparatus [31], by varying the distance between the prism and the inert gas cell with the help of a mirror. Lastly, by using a monochromator, the absorption spectra of excited singlets can be investigated from the time-resolved absorbance curves for several different wavelengths. This method has been used by a number of workers [33-38].

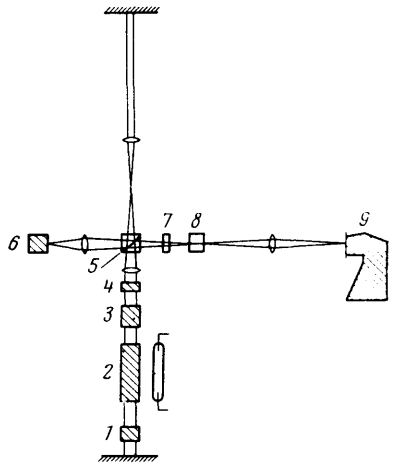


Figure 4. Apparatus for spectral measurements on short-lived products in the nanosecond region: *1*) Q-switch; *2*) ruby laser; *3*) $NH_4H_2PO_4$ crystal; *4*) filter; *5*) beam splitter; *6*) source of test pulses; *7*) attenuator; *8*) cell containing experimental compound; *9*) spectrograph.

Using this method, Porter and Topp [31] obtained the $S_X \leftarrow S_1$ absorption spectra for many aromatic hydrocarbons, and they were able to measure the mean life time of the first excited singlet. The latter quantity can also be measured independently from the rate of decay of fluorescence: in most cases the results obtained by the two methods were practically identical. The interpretation of singlet–singlet absorption spectra is complicated by the accumulation of the T_0 triplet in solution as the excited S_1 singlet disappears, so that the observed spectrum is not a simple one. With some hydrocarbons (pyrene, coronene) the apparent lifetime of the excited singlet is found to be much greater than the duration of the laser pulse, and therefore the spectra observed at very short delay times are characteristic of the excited singlet only. The isolation of the $S_X \leftarrow S_1$ absorption spectrum from the $T_X \leftarrow T_0$ background, which increases with time, is further complicated [33,34] by the great similarity between these spectra. This similarity has been reported for many hydrocarbons: naphthalene and benzanthracene [33,34], anthracene [36], biphenyl [39], pyrene, and coronene [31], and therefore it must be a general phenomenon, as theoretically predicted [40]. However, absorption from S_1 and T_0 levels has different polarisations [36,41]. The absorption spectra of excited singlets have been observed also for halogenated hydrocarbons [35,42].

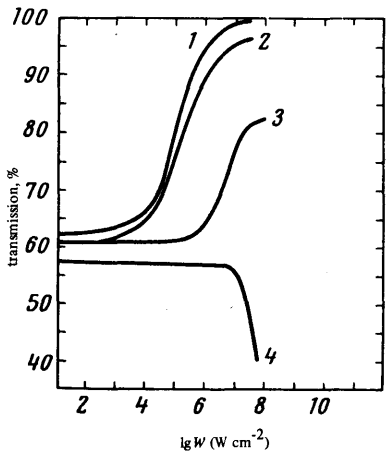


Figure 5. Transmission of dye solutions against intensity of laser radiation [30]: *1*) phthalocyanine in chloronaphthalene solution; *2*) vanadyl phthalocyanine in toluene; *3*) cryptocyanine in isopropanol; *4*) Sudan Black in acetic acid.

With dyes, whose electronic absorption spectra lie in the visible region, one-photon excitation of singlet levels can be induced by the radiation of the ruby laser. These processes are involved in the bleaching of the dyes used as passive optical shutters in Q-switching. Under the influence of a high-intensity beam the population of ground state dye molecules decreases, and as a result deviations from Beer's law are observed and the transmittance of the solution increases with light intensity. This behaviour is shown by solutions of phthalocyanine and cryptocyanine (see Fig. 5). At least two different mechanisms for this process can be suggested. According to the first [43,44], the dye acts as a two-level system, and the transition saturates when the populations of the ground and the excited state are equalised and the rates of absorption and stimulated emission are also equalised. However, it has been shown [45] that for most dyes at experimentally accessible photon fluxes the rate of stimulated radiative transitions from an excited level is smaller than the rate of intersystem crossing, as a result of which the triplet levels become populated. Thus, the dye should be treated as a multilevel system. The condition necessary for bleaching is that the cross-section for absorption of light of the laser generation frequency by molecules raised to the excited level should be less than the absorption cross-section for the ground state. In the opposite case—as with the dye Sudan Black, see Fig. 5—an increase in absorbance is observed. However, these phenomena can be explained only by assuming multi-photon excitation.

b. Multi-photon processes

Many of the effects of laser radiation are produced by multi-photon processes. Such processes are important in two respects. When laser radiation gives rise to excitation, ionisation, or chemical reaction, the process usually involves the absorption of more than one quantum, since the quantum energy of currently available lasers is several times smaller than bond dissociation energies, electronic excitation energies, or ionisation potentials. The rate of a multi-photon process is proportional to I^n, where $n > 1$. Hence, the larger n, the faster does the relative importance of multi-photon processes increase with intensity of illumination. Cross-sections for n-photon absorption are listed in Table 2: it can be seen that even at a flux of 10^{30} photons cm^{-2} s^{-1} the probability of two-photon excitation is less than the probability of one-photon excitation. However, the role of multi-photon processes may be enhanced by the non-linear self-focussing effect [47].

Table 2. Cross-sections for n-photon absorption.

n	Cross-section
1	10^{-17}–10^{-18} cm^2 $molecule^{-1}$
2	10^{-48}–10^{-54} cm^4 s $photon^{-1}$ $molecule^{-1}$
3	10^{-75}–10^{-85} cm^6 s^2 $photon^{-2}$ $molecule^{-1}$
4	10^{-115} cm^8 s^3 $photon^{-3}$ $molecule^{-1}$

Multi-photon (in particular, two-photon) processes were first observed in classical photochemistry, i.e. at relatively low light intensities [48]. In this case multi-photon processes can be favoured by producing high concentrations of metastable triplet states: the necessary increase in the life time of the triplet states is achieved by freezing the irradiated compound in a solid matrix. Two-photon excitation includes intersystem crossing and triplet–triplet absorption. Several reactions of the excited T_1 triplet have been observed: solvent interactions, decomposition, and photoionisation. The rate of a two-photon process is $r \propto I^2$, or more precisely $r \propto I_{\nu_1} I_{\nu_2}$. It is an interesting peculiarity of two-photon photochemical reactions that they require simultaneous irradiation with light of frequencies ν_1 and ν_2. The quantum yields of multi-photon processes are small: for two-photon processes, they are of the order of 10^{-2} for light intensities of 10^{14}–10^{17} photons cm^{-2} s^{-1}. However, at higher light intensities their yield (and therefore also the relative importance of multi-photon processes in competition with one-photon processes) is expected to increase. By using pulsed incoherent light sources, or better still lasers, multi-photon processes can be induced without special precautions to ensure long life times of the metastable states. In this case densely populated triplet levels are obtained not by lowering the probability of transitions from the triplet level, but by a high rate of generation of triplets under the influence of intense light. We shall now examine in detail some multi-photon processes induced by laser radiation.

Multi-photon excitation. Multi-photon (mostly, two-photon) excitation of aromatic molecules by a giant laser pulse has been observed by many workers [23,49–52]. In most cases, the excitation was detected by fluorescence or absorption, which depend (for two-photon processes) on the square of the intensity of the exciting light. A fluorescence yield proportional to the square of the intensity of a ruby laser has been reported [53] for benzoquinone, naphthaquinone, anthraquinone, N-ethylacridone, and many other aromatic molecules. All these molecules do not absorb (by the normal one-photon mechanism) light of wavelength 6490 Å, but they can be excited by u.v. light of wavelength close to one-half that of the radiation from the ruby laser. If a two-photon transition takes place, the experimental compound contains excitation levels of energy double that of the quantum. Hence, we may think of two-photon and multi-photon spectroscopy as a method of determining electronic excitation levels [54]. Resonance conditions are fairly easy to satisfy, because the electronic absorption bands of organic molecules usually contain vibrational fine structure and therefore are relatively broad. Hence, two-photon transitions will give rise to a vibrationally excited singlet state, as for example in the excitation of anthracene by light from a ruby laser [23]. An important feature of two-photon transitions is the fact that they obey quantum-mechanical selection rules different from those of ordinary one-photon transitions. Transitions involving a change in the parity of the initial and the final states are allowed in the one-photon excitation of molecules with a centre of symmetry, whereas in two-photon excitation transitions without parity changes are allowed [55,56]. Thus, states which are not accessible to ordinary optical excitation can be excited by using two-photon transitions. These transitions have been observed, for example, in coronene, 1,2-benzanthracene, and other aromatic hydrocarbons [32].

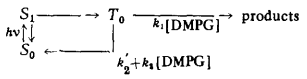
Since two-photon transitions have been observed with ordinary incoherent light sources as well as with lasers, the role of the coherence and monochromaticity of laser light has been questioned. Weiss and coworkers [57] compared the two-photon excitation cross-sections of naphthalene and anthracene with a laser and a xenon flash tube respectively. They found very similar values. A theoretical analysis [58] also led to the conclusion that the effect of coherence is negligible.

The degree of polarisation of the exciting light may have a stronger influence on the cross-section for two-photon absorption [59]. It has been shown [60] that the transition probabilities in anthracene and in 9,10-dichloroanthracene are several times greater in linearly polarised than in circularly polarised exciting light. The vibrational sub-level of the final excited state also depends on the polarisation of the light.

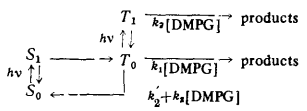
Multi-photon ionisation. Multi-photon ionisation in gases under the influence of laser radiation has been studied in detail [60–63]. Much less is known about multi-photon ionisation (photoconductivity) in the liquid phase. It has been shown [64] that light pulses from a nitrogen laser can generate photoconductivity, by a two-step mechanism, in solutions of N,N,N',N'-tetramethyl-p-phenylenediamine in non-polar solvents. The intermediate products may consist of triplet and singlet excited states, and possibly also charge-transfer complexes (CTC). Another paper [65] deals with the role of the solvent in the photoionisation of the same compound. The reaction $Fe^{2+} \rightarrow Fe^{3+}$ also appears to involve a metastable intermediate produced by a two-photon mechanism [66].

Chemical reactions induced by multi-photon excitation. The excitation which precedes

two-photon chemical reactions can occur either with formation of metastable (triplet) states or by the simultaneous absorption of two photons. It is suggested[56] that the latter process includes the formation of an intermediate virtual state. The mechanism of two-photon chemical reactions of the first type is similar to that of ordinary two-photon photochemical processes[48]. The photolysis of Methylene Blue by giant pulses from a ruby laser, studied by Tanaka and coworkers[67], is a good example of reactions of this type. The photo-reduction of Methylene Blue by ordinary light involves interaction between the reducing agent and the lowest triplet state of the dye. α-Dimethylphenylglycine (DMPG) was the reducing agent used. At low intensities of laser radiation the reaction follows the scheme



where the ratio $\frac{k_1 + k_2}{k_2'}$ is identical to the values found in ordinary photolysis. However, an increase in light intensity is accompanied by an apparent increase in the value of k_1. This increase was ascribed to the onset of triplet–triplet absorption in Methylene Blue, producing an excited triplet which takes part in the reaction and increases the rate of photo-reduction:

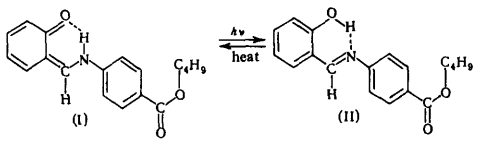


The above scheme is identical to two-photon excitation in ordinary photolysis‡. In the present case two-photon excitation arises because of the high rate of population of S_1 under conditions leading to sufficiently fast $T_0 \leftarrow S_1$ intersystem crossing, and also because the levels T_0–T_1 and S_0–S_1 are equidistant. The fact that in laser photolysis the metastable level can be excited only by a photon of energy equal to that used to excite the ground level limits the number of systems capable of undergoing chemical change under the influence of laser radiation. In this sense, the initiation of two-photon processes with two ordinary light sources of different wavelengths is a more flexible procedure. In principle, chemical reactions can be induced by using two laser lines of different wavelength (for example, with a gas laser, which radiates at different frequencies), or with a laser synchronised to a flash tube[70]. However, no system has yet been investigated by these methods.

Very high populations of triplet levels have been observed in studies of the *cis–trans*-isomerisation of substituted indigo dyes initiated by laser light[71]. A sharp decrease in transmission occurs at a radiation intensity of 10^{26} photons cm^{-2} s^{-1}: it is ascribed to the high population of a level with a higher absorption at 6940 Å than the ground level. The authors estimate that 62% of the molecules of *N,N*-dimethylindigo pass into the triplet state, whereas only 6% are present in the form of excited singlets.

‡ It should be noted that the mechanism of excitation of Methylene Blue by giant pulses from a ruby laser is much more complicated. In aqueous solutions, the dye exists in a partly associated form, as dimers[68]. Laser radiation gives rise[69] to a triplet of the monomer and a triplet of the dimer, which forms an additional excited state (probably a charge-transfer complex).

Prokhorov and coworkers[53] studied a number of multiphoton chemical reactions induced by laser radiation. Some azomethine dyes can undergo tunnelling hydrogen transfer under the influence of u.v. light:



accompanied by a change in the electronic configuration of the molecule and detected by a shift in the maximum of the fluorescence band. Fluorescence characteristic of compound (II) was observed by irradiating (I) with light from a ruby laser operated in the *Q*-switched mode. Since $I_{fluor.} \sim I^2_{exc.}$, the hydrogen transfer process must involve two-photon excitation. Free radicals produced by giant pulses from a ruby laser in triphenylmethane, α-nitronaphthalene, and other aromatic compounds frozen at 77°K have been detected by ESR. The triphenylmethyl radical $(C_6H_5)_3C^{\cdot}$, formed when $(C_6H_5)_3CH$ is irradiated with ordinary light with a quantum energy of 5.5 eV, was detected during irradiation of $(C_6H_5)_3CH$ with ruby laser light. It is evident that a three-photon mechanism must be involved, since $I_{fluor.} \sim I^3_{exc.}$, and the energy of three quanta of ruby radiation is close to 5.5 eV.

Porter and Steinfeld[72] studied the photolysis of phthalocyanine vapour at 420–430°C, a temperature at which the compound is stable. A pulse from a ruby laser with an energy of 40 J (equivalent to a power of 50 kW) did not cause decomposition, whereas a giant pulse of energy ~2 J but corresponding to a power of 100 MW produced decomposition of approximately 50% of the material in the path of the beam. The steep variation of reaction yield with intensity is evidence for a multi-photon mechanism. A reaction product with an absorption maximum in the u.v. region, characteristic of indole derivatives, was observed. The existence of a metastable or resonance level, excited by laser light, seemed probable in all the reactions considered.

Two-photon reactions have been observed also in systems where the electronic excitation of the reactants involved the simultaneous absorption of two quanta. Porter[73] exploited the two-photon initiation of the hydrogen–chlorine reaction in a lecture demonstration. When a mixture of $Cl_2 + H_2$ was illuminated with light from a ruby laser in the free generation regime (30 J) no reaction was observed, since both hydrogen and chlorine are transparent to red light, but an explosive reaction was induced by introducing a solution of cryptocyanine dye in the laser cell (even though the energy of the laser pulse had been decreased by a factor of 10). The explosion was initiated by the two-photon dissociation of chlorine, since the energy of two quanta of ruby laser light (3.57 eV) falls within the range of electronic absorption of chlorine (3.0–5.2 eV). The reaction $Cl_2 + CH_4$ involves a similar mechanism[74]. All possible chloro-substituted methanes are found among the reaction products, which points to a radical mechanism. Rousseau and coworkers[75] observed two-photon excitation and decomposition of AgCl under the influence of ruby laser light. AgCl is transparent to light of λ = 693 nm, but it absorbs at 347 nm. The reaction produces colloidal silver, identified by its absorption spectrum; it is accompanied by luminescence ($\tau = 10^{-4}$ s), with $I_{lum.} \sim I^2_{exc.}$ Light from a He–Ne laser (633 nm) of much lower intensity produced no reaction at the same (fully absorbed) energy.

2. Effects Associated With Vibrational Excitation

Lasers are powerful sources of radiation in the near and medium i.r. region. The absorption of radiation of frequency 10^2-10^4 cm^{-1} produces vibrational excitation in molecules. If the irradiated material is a sufficiently strong absorber at the frequency generated by the laser, it will display high, non-equilibrium occupancies of its vibrational levels. Deactivation of these excited states can occur either radiatively (by i.r. fluorescence), or by a non-radiative mechanism involving various relaxation processes. As long as the radiated power of the laser is not too high, very high vibrational temperatures can be reached without raising the translational temperature, i.e. without heating the material. With the most powerful lasers, infrared heating of the material can occur. The difference between this process and normal heating is that the whole of the absorbed energy is transferred to vibrations in the first instance, before being redistributed among other degrees of freedom. Ultimately, excitation of all the vibrational, rotational, and translational degrees of freedom can be expected, with the possibility of decomposition of the molecule. If the system can equilibrate between all degrees of freedom before decomposition sets in, the laser-induced reaction will not differ in any way from normal thermal decomposition at moderately high temperatures. However, if the chemical reaction begins before all the relaxation processes have gone to completion it may exhibit entirely different kinetic parameters (rate constants, activation energies). This is particularly true when absorption of a quantum raises the molecule to an excited vibrational level close to the dissociation threshold, and there is a finite probability of further thermal activation leading to dissociation (see, for example, Ref. 25). An alternative path to non-equilibrium chemical reactions involves multi-photon vibrational excitation. Examples of both types of process are discussed below.

Vibrational excitation by laser radiation. Measurement of the time dependence of the i.r. fluorescence from molecules which have been excited by laser radiation is a powerful new method of studying energy transfer processes in gases. Upwards of 20 compounds have been examined by this method, including methane, ethane, ethylene, and CO_2. The main results are discussed in recent reviews [76,77]. Recent developments in laser technology, by making available picosecond pulses, have enabled intramolecular vibrational relaxation to be studied [78] in complex molecules over times of the order of 7.5×10^{-12} s, i.e. over a few tens of vibrations.

Decomposition under the influence of laser radiation. As we have already pointed out, vibrational excitation can lead to decomposition of the irradiated compound at sufficiently high radiated powers. This type of decomposition has been observed by irradiating various hydrocarbons with light from a CO_2 laser [79,80]. Further work [81] showed that the decomposition of ethylene, propene, allene, and divinyl becomes appreciable only at pressures above a definite threshold. Thus, the decomposition of ethylene begins at pressures above 120 mmHg, and at pressures above 220 mmHg it is accompanied by strong self-heating, formation of carbon and resins, and visible luminescence. This steep pressure dependence arises from the pressure-induced broadening of the absorption bands. The greater the broadening, the more fully is the laser radiation absorbed by the compound. The distribution of reaction products is almost the same as in the thermal reactions of the hydrocarbons.

Decomposition of CO_2 is responsible for the relatively low power available from the sealed gas laser (in which circulation of the gas mixture is not provided) [82,83]. It has been shown [82] that the extent of conversion of CO_2 is large because the equilibrium $CO_2 \rightleftharpoons CO + \frac{1}{2}O_2$ in the system is displaced towards the right by adsorption or chemical reaction of the products (O_2 or O) with the electrodes or the walls of the discharge tube.

Multi-photon vibrational excitation and dissociation. With powerful modern lasers,

$$(2-3)\hbar\omega \approx D \text{ and } \omega \approx 10\omega_e$$

where $\hbar\omega$ is the quantum energy, and D and ω_e are "typical" values of the dissociation energy and natural vibration frequency of a chemical bond. It follows that direct photodissociation (without a predissociation step) can occur by a multi-photon mechanism with resonance transitions through several vibrational levels. The theory of "oscillating" molecular vibrations and photodissociation in a powerful field of laser radiation has been discussed by Askar'yan [84,85] and by Bunkin and coworkers [86].

There are two possible regimes of vibrational excitation and dissociation of molecules under the influence of laser light. The first occurs when the force acting on a molecule in an intense light field is linearly related to the field and has a frequency equal to that of the light field. This state of affairs is usually found with polar molecules. The molecules are set oscillating in the field when their mean dipole moment interacts with the electric component of the radiation field. The probability of two- and three-photon purely vibrational transitions (i.e. not involving a change in the electronic state) has been evaluated [86] for diatomic molecules in the anharmonic oscillator approximation. Molecular vibrations can interact with the field only as a result of their anharmonicity, which ensures that transitions with $|\Delta n| > 1$ are allowed. The probability of the process depends essentially on whether the discrete vibrational spectrum includes resonant transitions defined by the condition

$$(\omega - \omega_{n,0})^2 \ll \left(\frac{\mu\varepsilon}{\hbar}\right)^2$$

where $\omega_{n,0} = \frac{1}{\hbar}(E_n - E_0)$; ϵ is the electric field strength of the electromagnetic wave; μ is the dipole moment. It is evident from this formula that the resonance conditions is most easily satisfied by highly polar molecules in a field of high intensity. With a field of 3×10^7 V cm^{-1}, resonant transitions are more probable than non-resonant transition by a factor of 10^3. The difference is even greater at higher fields. Three-photon transitions without resonance are improbable at 10^7 V cm^{-1}, but at $\epsilon = 3 \times 10^8$ V cm^{-1} their probability is quite large.

The second excitation regime describes the situation when the force for excitation has a frequency different from that of the light wave. A force of this type may arise from atom polarisability, i.e. from the excitation of homopolar as well as heteropolar molecules. This force is proportional to the square of the field, and therefore it can only give rise to new spectral absorption lines in very strong light fields [84,85].

Evidence of initiation of a chemical reaction by the above mechanism is given in two papers only. Eisenthal and coworkers [87] studied the effect of ruby laser pulses (0.1–5 MW cm^{-2}) on biphenyl. The power density of

these pulses corresponded to a peak field strength of $10^{-4}-10^{5}$ V cm^{-1}. The observed fast luminescence spectrum was different from the fluorescence and the phosphorescence spectrum of the compound, and its intensity was proportional to the cube of the light intensity. Hence it was concluded that three-photon vibrational excitation and dissociation into two phenyl radicals can take place in laser light. The luminescence is produced by dissociation products with an excess of energy of ~30 kcal mole^{-1}. A similar mechanism is probably involved also in the photodissociation of dibenzofuran, dibenzthiophen, and also dibenzyl, for which a two-photon mechanism has been proposed.

Prokhorov and coworkers[53] observed the decomposition of α-nitronaphthalene irradiated with light from a dysprosium laser ($h\nu$ = 0.5 eV). This reaction probably involves stepwise excitation to vibrational sublevels of the electronic ground state, followed by dissociation of the bond (~1.1 eV bond strength).

IV. HIGH-TEMPERATURE REACTIONS

When solids are irradiated with laser pulses, instantaneous heating and evaporation occur, accompanied by plasma formation at the highest powers. Hence, lasers have been used for the mass-spectrometric[88] and emission-spectrometric[89] analysis of solids, and also in pyrolytic gas chromatography[90].

Hydrocarbons have been synthesised[74] from carbon (heated by a giant laser pulse) and hydrogen: the products included acetylene (90%), methane, ethylene, allene, methylacetylene, and diacetylene. Subsequent work[91,92] showed that the formation of acetylene (which can be observed also with normal laser pulses) is the result of interaction between C_2 and hydrogen or hydrocarbons in the gas phase. Some other reactions can also be ascribed to the diatomic C_2 radical[93]. Laser heating of silicon and germanium in a hydrogen atmosphere, and of carbon in an atmosphere of chlorine, has yielded SiH_4, GeH_4, and CCl_4 respectively[74]. A method for producing diamond from graphite in a laser beam has been patented[94].

The gas phase formed when solids are impulsively heated with laser radiation often differs in composition from the vapour evolved on slow heating. This type of phenomenon has been observed[95] with the oxides, sulphides, selenides, and tellurides of arsenic, antimony, and bismuth. The gas phase obtained by laser vaporisation is characterised by particles of the type Bi_3X: a probable explanation is that critical conditions are approached in the region subjected to instantaneous heating.

As already pointed out, dielectric breakdown can occur in transparent liquids and gases exposed to strong optical fields. Multi-photon processes play an important role in dielectric breakdown[60]. However, once a plasma has been formed, the medium becomes opaque to the laser radiation, and thereafter it can be heated to very high temperatures by the laser beam. Breakdown can initiate the fixation of atmospheric nitrogen[74] and the formation of acetylene from methane[96], but attempts to prepare ammonia by this method from a stoichiometric mixture of nitrogen and hydrogen have been unsuccessful[74]. Breakdown due to pulses from a ruby laser was shown[97] to produce C_2, C, C^+, C^{2+}, Cl, and O^+ in organic vapours (CCl_4, $CHCl_3$, CH_3COCH_3, CH_3OH, and n-C_6H_{14}). The vibrational state of C_2 was different in CCl_4 and $CHCl_3$ vapours. Chloroform and carbon tetrachloride gave C_2Cl_4, C_2Cl_6, C_6Cl_6, and octachloronaphthalene. Methanol gave only high-molecular products.

V. CHEMICAL EFFECTS OF LASER LIGHT IN VARIOUS SYSTEMS

We have considered the various types of excitation produced by laser radiation, and the corresponding mechanisms by which chemical reactions can be induced by laser light. Often the mechanism of a particular reaction is not known, and in some cases the observed changes can be ascribed to more than one factor. Systems of this type are best described without attempting to associate them with any particular mechanism.

1. Decomposition of Organic Compounds

Wiley and Weeravagu[98] studied the chemical effects of focussed light from a ruby laser operated in the free generation regime (pulse energy 3.5 J) on various solid or frozen aromatic compounds. According to the distribution of reaction products, all the compounds examined can be classified into three types (see Table 3). The first is characterised by the formation of acetylene in much larger amounts than methane. Compounds of the second group give comparable yields of methane and acetylene.

Table 3. Decomposition products of organic compounds[98].

Compound	Products, vol.%				
	CH_4	C_2H_2	C_2H_4	C_4H_2	$C_4H_4+C_4H_6$
Biphenyl	7	84	6	Tr*	3
Naphthalene	4	87	4	Tr	5
Anthracene	4	85	3	Tr	8
Phenanthrene	2	91	1	Tr	6
Benzoic acid	3	85	1	Tr	11
Benzil	15	65	19	1	—
Anthraquinone	3	86	2	Tr	9
Methyl Yellow	28	57	8	7	Tr
Toluene	38	51	10	1	—
p-Xylene	42	48	9	1	—
Mesitylene	46	40	13	1	—
Methylene Blue	44	43	8	3	2
Benzene	56	16	21	1.5	—
N,N-Dimethylaniline	77	2	12	5	—
N,N-Diethylaniline	51	9	26	7	—

*Traces.

Lastly, irradiation of some compounds (benzene, *N,N*-dimethylalanine, and *N,N*-diethylalanine) yields much larger amounts of methane than of acetylene. In addition to CH_4 and C_2H_2, appreciable amounts of ethylene, vinylacetylene, and diacetylene are produced in many cases.

The unexpected distribution of reaction products, summarised in Table 3, allows us to exclude a purely thermal decomposition mechanism at the focus of the laser beam. On the other hand, the high yields of methane from compounds such as benzene and benzil, which do not contain methyl or methylene groups, and also the CH_4/C_2H_2 ratios for pairs of compounds such as benzene–biphenyl and benzene–benzoic acid, make it very difficult to interpret the results. As Table 3 shows, chemically and structurally very different compounds fall in the same group.

The authors suggest that the reactions of hot atoms or radicals (CH, CH_2 or CH_3) formed "under specific focussing conditions of the laser beam" may be responsible for the formation of large amounts of methane and acetylene. Although reactions of atomic carbon sometimes give the same products[98] as the decomposition of aromatic compounds under the influence of laser light, the formation of particles like C or CH requires such large energy expenditure as to be inadmissible, except by a multi-photon mechanism, whose probability is low, however, at the relatively low intensities of a laser beam in the free generation regime. Whereas the above results suggest some measure of specificity in the effect of ruby laser light on solid aromatic compounds—in particular on frozen benzene—other results by Bragin and coworkers[100,101] show that laser radiation can initiate non-specific pyrolysis reactions in liquid benzene (and other aromatic compounds), with hydrogen and carbon as the only products. Liquid benzene was irradiated with unmodulated pulses of laser radiation, of energy in the range 1–8 J (i.e. of the same order of magnitude as the luminous fluxes used by Wiley and Weeravagu[98]). The wavelength of the laser light did not appear to play any part, but a sharp energy threshold of the laser pulses was identified below which no decomposition occurred. Above the energy threshold the formation of solid reaction products was accompanied by generation of shock waves. The threshold energy depended on whether a finely divided suspension was present in the liquid benzene, but not on its chemical nature. These observations, together with the anomalously high quantum yield (0.33), forced the authors to the conclusion[101] that the reaction is initiated by the temperature rise of the microscopic solid particles always present in a liquid, and proceeds by a chain mechanism. However, this mechanism fails to explain why the reaction follows an entirely different course in solid benzene irradiated with laser light, with a specific rather than thermal mechanism (as shown by the nature of the products). On the other hand, if laser radiation can initiate the pyrolysis of benzene, it is not clear why acetylene was not detected among the products although it is the commonest product of high-temperature decompositions of hydrocarbons. Studies of the laser photolysis of benzene[38,102] (λ = 3471 and 2645 Å) have revealed an intermediate with an absorption maximum close to 5000 Å and a life time of 2×10^{-8} s. This absorption was originally ascribed to the $^1E_{1u} \leftarrow {}^1B_{2u}$ singlet–singlet transition, but a more careful comparison with pulse radiolysis data[103] led to the conclusion that the particle responsible for this absorption is an excimer of benzene, formed by a two-photon mechanism. The excimer is formed from highly excited states of benzene with an energy of ~7 eV. At the same time, stable products are formed, and they accumulate in solution after prolonged irradiation (trienes, and fulvene derivatives). It is probable that laser radiation causes opening of the aromatic ring, which may explain the formation of CH_4 in Wiley's experiments[98]. The benzene biradical may be an intermediate in this reaction[103].

The data reviewed by Wolfgang[99], and also some recent experimental results[104,105] on the effect of laser radiation on a number of gaseous unsaturated hydrocarbons, suggest that hydrogen transfer reactions may be involved. We have detected[104] ethylene and ethane in acetylene irradiated with light from a Nd^{3+} laser (10^{-3} s, 1–10 J). As Table 4 shows, C_2 hydrocarbons are predominant among the products of this reaction.

We were unable to detect any higher hydrocarbons, in particular benzene—a familiar product of the photolysis of acetylene. Significant amounts of hydrogen, carbon black, and pyrolytic carbon were also absent. It is evident, from the composition of the products, that the radiation from a neodymium laser has a specific effect on acetylene, quite unrelated either to pyrolysis or to ordinary photolysis. The vibrational spectrum of acetylene includes a strong $3\nu_3$ overtone whose frequency (9640 cm^{-1}) is close to that of neodymium laser light (9400 cm^{-1}).[106] If this fortuitous agreement between the frequency of the laser radiation and the natural vibration frequency of the irradiated compound is responsible for the chemical reaction, we may expect both the absorption and the reaction to disappear if an isotopic frequency shift is introduced by replacing C_2H_2 by C_2D_2. However, we find that C_2D_2 also undergoes chemical reaction when irradiated with neodymium laser light, but in this case the product consists mainly of ethane. Irradiation of an equimolar mixture of C_2H_2 and C_2D_2 leads to isotope exchange with formation of C_2HD. The products obtained by irradiating ethylene with neodymium laser light included methane, acetylene, and divinyl in the ratio 3 : 1 : 1. The high relative yield of methane is remarkable, since neither pyrolysis nor ordinary photolysis of ethylene gives significant amounts of methane. Wiley and Reich[105] also obtained unexpectedly high yields of methane in their work on the irradiation of acetylene with light from a ruby laser in the free generation regime (Table 5).

Table 4. Products obtained from acetylene by the action of radiation from a neodymium laser in the free generation regime[104].

Starting material	Gaseous products, vol.%				
	ethane	ethylene	divinyl	vinylacetylene	diacetylene
C_2H_2	—	71.7	0.5	13.7	13.2
C_2D_2	71	2.0	5.5	21.3	—

Table 5. Products obtained from gaseous hydrocarbons by the action of radiation from a ruby laser in the free generation regime[105].

Hydrocarbon	Products				
	CH_4	C_2H_2	C_2H_4	C_2H_6	Higher
Cyclopropane	26.5	none	11.5	62	none
Ethylene	4.3	none	—	95.7	none
Acetylene	59.3	none	40.7	—	none
Ethane	32.1	—	not measured	67.9	none
Butane	25.4	1.2	26.9	43.4	3.6*

*Propene.

The material balance of these reactions suggests that in some cases (C_2H_4) large amounts of hydrogen must have been formed, in others (C_3H_6, C_2H_2) carbon must have been formed, or polymers with a low hydrogen content.

2. Polymerisation

Pulses of laser light can initiate polymerisation reactions. In the earliest experiments[107] polymerisation was

obtained in the presence of a dye sensitiser. When acrylamide was irradiated with argon laser light (4880 Å) in the presence of a sensitiser (4,5-dibromofluorescein + *N*,*N*,*N*′,*N*′-tetramethylethylenediamine) the polymerisation yield was 10^3 per absorbed photon[108]. The polymerisation of vinyl acetate, initiated by giant laser pulses (λ = 3472 Å) in the presence of 2-azo-bis-isobutyronitrile, is described in the Patent literature[109]. Polymerisation without sensitisers was first reported by Pao and Rentzepis[110], who irradiated styrene frozen at 77°K with light from a ruby laser (0.3 MW). A two-photon mechanism was suggested. The yield of polymer was 0.01% per pulse. The i.r. spectrum of the polymer was indistinguishable from that of polystyrene, and its molecular weight was 3.6×10^5. Because styrene does not absorb strongly at 3470 Å, it can only be polymerised in a rigid matrix (not in the liquid phase). Other monomers which are better absorbers at this frequency (e.g. *p*-isopropylstyrene) were successfully polymerised at room temperature. Polymerisation of the chloro-derivatives of styrene was easier still.

The possibility of polymerising styrene with giant ruby laser pulses was later confirmed by Apletalin and coworkers[111]. However, these workers described the process not in terms of two-photon excitation of the lower electronic levels, but in terms of multi-photon dissociation (probably by Bunkin's mechanism[86]) and ionisation, giving rise to a breakdown phenomenon accompanied by visible luminescence with a continuous spectrum.

3. Disintegration and Degradation of High-molecular Compounds

In opaque polymers, the energy of laser pulses is absorbed in a very small volume, and therefore the material is locally heated to very high temperatures (see Section IV). The mechanical degradation processes observed when powerful laser pulses are focussed within transparent polymers are very much harder to interpret[60]. Mechanical disintegration is evidently associated with chemical degradation of the polymer, which may result in the appearance of paramagnetic centres in the polymer[112]. These changes are sometimes preceded by phase transformations (melting and recrystallisation of some of the structural elements of the polymer)[113]. A study[114] of the decomposition of poly(methyl methacrylate), PMMA, under the influence of ruby and neodymium laser pulses has shown that gases are formed by a two-photon or a three-photon process, depending on the photon energy. The composition of the gaseous decomposition products of PMMA included CO, CO_2, and CH_4, whereas normal thermal degradation of PMMA yields only the monomer (at low temperatures) or a complex mixture of secondary reaction products—mainly acetylene and ethylene—at higher temperatures[115]. Hence, we can dismiss the purely thermal mechanism of degradation of transparent polymers exposed to laser radiation.

Many investigations[116-120] have been devoted to the action of laser radiation on opaque polymers (phenolic resins, elastomers) and on coal. The gaseous degradation products were found to consist predominantly of acetylene and hydrogen. The composition of the reaction products was quite different from the composition of the products of low-temperature (500–900°) degradation of these materials, and also from the composition of the products obtained by the action of a xenon flash tube[119]. A study of the laser degradation of coal in a time-of-flight mass spectrometer has shown that the primary products are H atoms and methyl radicals. The strongest peak in the mass spectrum was due to acetylene[121].

(Added in proof)

Several relevant papers have appeared since this review was submitted for publication. The most interesting results relate to the possibility of selectively initiating chemical reactions by monochromatic laser light, using resonant excitation of selected intramolecular vibrations. It has been shown[122] that the dissociation of BCl_3 under the influence of CO_2 laser light occurs by a cascade mechanism (i.e. by an *n*-photon mechanism with $n \gg 1$), and high vibrationally excited states, close to the dissociation threshold, have been observed spectroscopically. Mixtures of BCl_3 and H_2 react explosively when irradiated. The initiation of chemical reactions by excitation of molecular vibrations has been demonstrated in a number of other systems[124-126], including N_2F_4 in mixtures with N_2, H_2, and CH_4, and also CH_3OH mixed with CD_3OD. This work has shown that in many cases the anharmonicity of vibrations is not an insuperable obstacle to selective bond breaking. Two-stage excitation is proposed[127] for systems in which the vibrational–translational relaxation processes can compete with resonant excitation processes at levels not high enough to reach the dissociation threshold. Using this method, the photodissociation of HCl and the photoionisation of rubidium vapour have been demonstrated[128].

Barashev and Tal'roze[129] have developed a criterion for distinguishing photochemical from purely thermal effects of laser radiation on matter. A group of papers[130-132] deals with a theoretical analysis of the initiation of chemical reactions by laser light. Several reviews of the properties and applications of various types of laser have appeared: dye lasers[133], lasers based on compounds of the rare-earth elements[134], and pulsed gas lasers[135]. Further work on the laser photolysis of benzene has been reported[136]. Lastly, the laser photolysis of acetophenone[137], thiocyclobutanes and thiocyclopentanes[138], the two-photon gas-phase decomposition of azoethane[139], and the photoionisation of water[140] have been described.

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Use of Reversed Gas Chromatography in the Investigation of Polymeric Compounds

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The principal aspects of the use of gas chromatography for investigating polymers when they are employed as a stationary phase (the reversed gas chromatographic method) are considered: the identification of polymers, the determination of their molecular weights, the study of the thermodynamics of the dissolution of low-molecular-weight substances in polymers, the determination of the temperatures of the phase transformations, degrees of crystallinity, kinetics of crystallisation processes, and the chemical changes taking place in the polymers.
The theoretical principles of the use of reversed gas chromatography and the peculiarities of the gas-chromatographic behaviour of polymers determined by the structure and their phase and physical states are discussed. 67 References.

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I. INTRODUCTION

The classical version of the gas-chromatographic method cannot be used directly for investigating involatile high-molecular-weight compounds. Destructive gas chromatography is an indirect method, since it is based upon the correlation between the characteristics of the polymeric system being studied and the spectrum of products for its pyrolysis or from other chemical changes.

Another, qualitatively different, approach to the investigation of high-molecular-weight compounds is possible—the use of reversed gas chromatography (RGC). In RGC the system being studied is, unlike the classical version, the stationary phase, on which known volatile compounds (standards) are separated. RGC is based on the use of the direct interaction of the standard chromatographable compounds with the polymeric system being studied and the establishment of a definite connection between the chromatographic characteristics of the standard compounds and the composition, structure, and other properties of the polymeric system used as the stationary phase. Therefore the RGC method can be regarded as a direct method of investigation of high-molecular-weight compounds.

Martin[1] was the first to report the value of gas–liquid chromatography (GLC) in the study of the thermodynamics of the interaction of volatile substances with an involatile phase. The terminology "reversed gas chromatography" was proposed in 1966.[2,3]

Initially RGC was regarded as a method of solving separate, rather general problems: identification[4,5], determination of phase transformations[6,7], study of kinetics[8,9], etc. The wider concept of RGC as a physicochemical and analytical method of investigation of involatile systems was proposed by one of us[2,3].

The possibility in principle of using RGC as an independent analytical method for identification was first stated by Zhukovitskii and Turkel'taub[4]: "In individual instances the test substance can be used as a stationary phase, with the aim of identifying the components and finding the presence of impurities of a definite nature. For example, the presence of polar impurities in a non-polar solvent has a marked effect on the retention time for polar impurities".

The RGC method can be used for investigating both liquid and solid substances. In the investigation of polymers as stationary phases in each specific instance preliminary consideration must be given to the mechanism of the chromatographic process (absorption, adsorption, mixed), which is determined by the possibility of using recently developed theories of gas–liquid or gas–adsorption chromatography to obtain the physicochemical characteristics of polymeric specimens.

Owing to the widespread use of polymers in the practice of modern gas chromatography as liquid stationary phases (silicone oils, polyglycols, polyethers, rubber) and as solid adsorbents and carriers (porapaks of various grades, polyurethanes, polyalkenes, etc.) much material has accumulated on the retention volumes of various volatile compounds on polymeric phases. An analysis of these results can give valuable information in the study of many specific problems. The aim of the present review, however, is to find the main regions and prospective uses of RGC in the investigation of polymeric compounds.

II. IDENTIFICATION OF POLYMERS

Experimental verification of the applicability of reversed chromatography for identification purposes showed that this method permits group identification of the compounds used as stationary phase[5]. As an example, Fig. 1 gives the relative retention times for substances of different polarities (methanol, heptane, toluene) in a triangular coordinate system, when normal alkanes, aliphatic alcohols, and acids are used as stationary liquid phase. It was found that each of these homologous series is characterised by a sharply defined range of values of the retention times of standard compounds. We note that this method makes it possible even to distinguish some isomeric compounds. Thus the spectra of standard

volatile compounds are different for 1,3-butylene glycol and 1,4-butylene glycol, and also for primary and secondary octyl alcohols. The results given show the rather high sensitivity of the method of reversed chromatography. Similar results can also be obtained for polymeric systems.

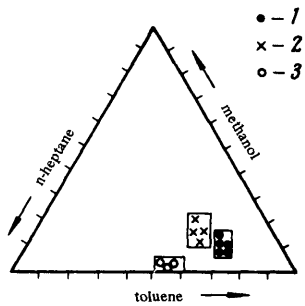

Figure 1. Diagram for group identification by three standard components: *1*) aliphatic acids; *2*) normal aliphatic alcohols; *3*) n-alkanes.

The large body of information that has accumulated in gas chromatography on the use of polymers as stationary liquid phases for separating mixtures of volatile compounds (for example, see McReynolds [10] and Lewis [11]) suggests that polymers can also be identified by RGC. Thus according to Devyatykh and coworkers [12] the retention volume for phosphine on a column with silicone oil 702 is 1.75 cm^3, with silicone oil VKZh-94 B it is 1.58 cm^3, and with silicone oil PFMS-4 it is 2.52 cm^3. Another example is of two polymeric compounds of the same type—poly(propylene glycol) with $\bar{M}_n$ = 1760 and poly(ethylene glycol) with $\bar{M}_n$ = 1540, which are characterised by markedly different retention values [10], which allows the RGC method to be used for their identification (see Table 1). RGC results for the identification of compounds are presented more conveniently on a logarithmic scale as spectra of relative retention volumes (or times) for volatile standard compounds (see Fig. 2). As Fig. 2 shows, polymers of rather similar structure are characterised by markedly different spectra. This form of presenting experimental results can be used in the future for compiling an atlas of spectra of standard volatile compounds on polymeric substances.

The RGC method has been developed in most detail for the characterisation (identification) of the asphaltenes (molecular weight 500–1000).[5] The so-called specific coefficients of interaction of volatile standard compounds with the stationary liquid phase I_g were used as characteristics of the asphaltenes:

$$I_g = 100 \lg (V_R^0/V_{RA}^0) = 100 \lg (V_g/V_{gA}) \quad (1)$$

where V_R^0 or V_g are the retention volumes of volatile standard on a column with asphalt, V_{RA} or V_{gA} the retention volumes of a hypothetical alkane, having the same molecular weight as the volatile standard being used. Recent investigation [13] showed the adequate constancy of I_g with respect to the principal parameters of the experiment.

Dorrence and Petersen [14] showed the advisability of using chemical reactions with the stationary liquid phase being investigated by RGC. To study the functional groups in the asphaltenes the specimen being studied in the column was subjected to silylation, as a result of which the active hydrogen atoms in the hydroxyl and carboxyl groups were replaced by trimethylsilyl radicals. Treatment of the asphaltene with *NN*-bis(trimethylsilyl)acetamide at 160°C led to a marked decrease in the specific interaction coefficients with selected volatile standards (phenol and propionic acid). This method can be used to characterise the functional groups of various polymeric compounds.

Table 1. Specific retention volumes of volatile compounds on polyglycols being used as stationary liquid phases (120°C; solid carrier: Celite 545).[10]

Polymeric stationary liquid phase	Specific retention volumes of the volatile compounds, ml g^{-1}								
	methanol	furan	hexane	ethyl acetate	cyclohexane	benzene	butanol	water	heptanol
Poly(propylene glycol) 1760	7.6	7.8	8.0	15.3	14.5	24.3	44.9	9.8	321
Poly(ethylene glycol) 1540	15.1	9.0	2.9	15.5	6.6	23.7	60.2	35.0	316

In conclusion, we note that when a packed column is used for the RGC method ~0.4 g of the test compound is required, but the amount is reduced to 3–4 mg when a capillary column is employed [5]. The use of the microversion of reversed chromatography is especially important for polymers which are difficult to prepare and in general for difficultly accessible compounds.

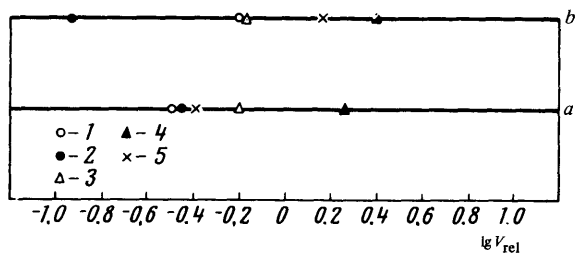

Figure 2. Chromatographic spectra of standard compounds on identifiable polymers: *a*) poly(propylene glycol) 1760; *b*) poly(ethylene glycol) 1540; *1*) methanol; *2*) hexane; *3*) ethyl acetate; *4*) butanol; *5*) water.

In view of the fact that the task of identification of the polymers sometimes reduces to the determination of their molecular weights, which is of interest in itself, we will examine how the retention of volatile compounds varies with the molecular weight of the polymer.

III. DETERMINATION OF THE MOLECULAR WEIGHT OF POLYMERS

A change in the molecular weight of a polymer leads to a change in many of its properties, and in particular in its chromatographic properties.

Evidently, the retention volume can be regarded as a colligative property of solutions, since its value is determined ultimately by the vapour pressure of the substances dissolved in the stationary liquid phase.

Like the other colligative properties of solutions (vapour pressure, freezing point depression, etc.), the retention volume of a dissolved substance depends upon the number of particles per unit volume of solution, and consequently on the molecular weight of the solvent [15] (the number-average molecular weight for a polydisperse polymeric liquid phase):

$$V_g^{(i)} = \frac{RT}{\overline{M}_n f_i^0 \gamma_i^\infty} \qquad (2)$$

where $V_g^{(i)}$ is the specific retention volume of the ith substance at column temperature T; f_i^0 and γ_i^∞ are the fugacity of the pure ith substance and its activity coefficient at infinite dilution in the stationary phase; $\overline{M}_n$ is the molecular weight of the stationary liquid, and R the gas constant.

However, as a strict analysis of the theory of dilute solutions [16] shows, only the molecular weight of the dissolved substance can be determined from the colligative properties of solutions, but not that of the solvent. This also applies to the retention volume. Actually, from the quantity Vg, which is readily determinable by experiment, only the product $\gamma_i^\infty \overline{M}_n$ can be calculated from Eqn. (1), and in all independent methods of determining γ_i^∞ a knowledge of the molecular weight of the solvent is always necessary.

Hence Eqn. (2) cannot be used for calculating the molecular weight of the stationary liquid. Nevertheless this equation is often used to determine γ_i^∞ and here $\overline{M}_n$ is usually taken as equal to the molecular weight of the monomeric form of the solvent, even when the latter is a strongly associated liquid.

Generally speaking, the values of γ_i^∞ or their variation with M_n needed for evaluating the molecular weight of the solvent by Eqn. (2), can be calculated theoretically. However, current theory of solutions does not in many instances yet permit the thermodynamic functions of the solution to be calculated with sufficient accuracy just from the molecular characteristics of the initial pure components, especially for polar associated substances. Usually, the theoretical expressions for the activity coefficients include parameters, the a priori evaluation of which is extremely difficult [17].

Consequently, semiempirical methods are often used for evaluating the quantities γ_i^∞ needed for the calculation of M_n by Eqn. (2).

Martire and Purnell [18] started from the well known Flory–Huggins [19] equation for the activity coefficient of the solvent in solutions of polymers and postulated its validity for limitingly concentrated (in relation to polymers) solutions:

$$\ln \gamma_i^\infty = \ln \frac{V_i^0}{V_p} + 1 - \frac{V_i^0}{V_p} + \chi, \qquad (3)$$

where V_P and V_i^0 are the molar volumes of the solvent (polymer) and of a low-molecular-weight solute respectively and χ is the Flory–Huggins interaction parameter. Then by assuming that within a polymer-homologous series the parameter χ is almost independent of $\overline{M}_n$ of its members, it is easy to use Eqns. (2) and (3) to calculate the molecular weight of the polymeric phase, if the retention volumes of a standard substance on this phase (index b) and on the same polymer with a known molecular weight (index a) are determined:

$$\frac{1}{\overline{M}_n^{(a)}} = \frac{\rho_a}{\rho_b \overline{M}_n^{(a)}} + \frac{\ln [(V_g^{(i)})_b / (V_g^{(i)})_a] + \ln (\rho_b / \rho_a)}{\rho_b V_i^0}, \qquad (4)$$

where ρ_a and ρ_b are the densities of phases a and b, and $\overline{M}_n^{(a)}$ and $\overline{M}_n^{(b)}$ are the number-average molecular weights of the polymers of phases a and b. Another, more convenient, modification of this method is the determination of the molecular weight of the polymeric stationary phase from the relative retention volumes of two substances of similar nature (often neighbouring members of a single homologous series), measured on phases a and b:

$$\frac{1}{\overline{M}_n^{(b)}} = \frac{\rho_b}{\rho_b \overline{M}_n^{(a)}} + \frac{\ln (R_a / R_b)}{\rho_b \Delta V_i^0}, \qquad (5)$$

where R_a and R_b are the relative retention volumes of two selected standard dissolved substances X and Y ($V_g^{(Y)} = 1$) on phases a and b:

$$\Delta V_i^0 = (V_i^0)_Y - (V_i^0)_X.$$

This method is usable for comparatively low-molecular-weight polymers—liquid silicones, polyglycols, and hydrocarbon oils with $\overline{M}_n \leqslant 1500$. The accuracy of the proposed method decreases as the molecular weight is raised.

The Flory–Huggins equation (3) and the assumption that χ is independent of the molecular weight of the polymer at a sufficiently high value are valid only in the absence of a specific interaction of the dissolved substance with the solvent. Hence the volatile compounds (solutes) used should preferably be saturated hydrocarbons.

Martire and Purnell [18] gave as an example the determination of the molecular weight of poly(propylene glycol) 1200 with the use of n-heptane and n-octane as volatile compounds and poly(propylene glycol) 400 as liquid phase of known molecular weight. The molecular weight of the poly(propylene glycol) calculated by Eqn. (5), was 1220 (according to the cryoscopic method, $\overline{M}_n = 1260$).

The use of the chromatographic method for determining the molecular weight of the stationary phase can naturally also be effected on a purely empirical basis by a preliminary calibration, that is, obtaining the graphical dependences of the retention volume on the molecular weight of the members of the polymer homologous series being studied.

The possibility of using this method was considered in several papers, for example, that of Kogan and Fedotova [20]. In this it was noted that with increase in the molecular weight of the oligomers containing –OH and –SH terminal polar groups and employed as the stationary phase the retention volumes of the non-polar compounds increase somewhat, whereas those of polar compounds (water, alcohols, ketones, ethers, etc.) fall considerably.

The effect of the molecular weight of poly(ethylene glycols) of the general formula $HO[CH_2CH_2O]_nCH_2CH_2OH$ on the retention indices of compounds of various types was also examined by Evans and Smith [21]. The most pronounced dependence of the retention volumes on the molecular weight of the polymeric stationary phases is observed for compounds capable of specific interaction with the terminal polar groups of polymers, for example, with the formation of hydrogen bonds. It was found that the retention volumes of such compounds depend linearly on the concentration of terminal functional groups in the polymeric molecule, that is, on the quantity $1/\overline{M}_n$, [22,23] where $\overline{M}_n$ is the molecular weight of the polymer.

The observed relations can be explained on the basis of the lattice theory of polymer solutions [19], which postulates

that long polymeric chains can be regarded as consisting of a set of segments—sections of the chain which are capable, because of the flexibility of the chain, of exchanging sites with the molecules of the second component of the solution and which occupy one cell of the quasicrystalline lattice of the liquid.

If we have a polymer with terminal polar functional groups the latter can, in accordance with the above ideas, be regarded as molecules of another component of the solution, since in their chemical behaviour (specific interaction with polar dissolved substances) they differ from all the other segments of the polymeric chains.

These predictions are justified, for example, by the fact that the reactivity of the terminal functional groups of macromolecules is often close to that of the same group in small molecules and does not depend on the size of the molecule [24].

In this instance a polymer with terminal functional groups, capable of reacting specifically with certain volatile compounds, can be regarded as a binary solution consisting of functional groups (solute) and of the remaining segments of the polymeric chains (solvent).

On the other hand, it is well known that when the stationary phase is a solution of a dissolved substance B, which reacts specifically with compound A, which is being passed through the column, then the distribution coefficient of compound A (K_A) depends on the concentration of substance B in the following manner [25]:

$$K_A = K_A^0(1 + K_x x_B), \qquad (6)$$

where K_X is the thermodynamic characteristic of the interaction of substances A and B, equal to the equilibrium constant of the reaction of complex formation A + B $\rightleftharpoons$ A.B, x_B the mole fraction of substance B in the stationary phase, and K_A^0 the distribution coefficient when $x_B \to 0$.

In the example being considered the functional groups play the part of the complex-forming agent B, and their mole fraction is $2m/\bar{M}_n$, where m is the molecular weight of the segment.

Hence

$$K_A = K_A^0\left(1 + K_x\frac{2m}{\bar{M}_n}\right) \qquad (7)$$

It is noteworthy that K_A^0 is in general also a function of the molecular weight owing to the contribution of the configuration term to the activity coefficient of the dissolved low-molecular-weight substance:

$$\left(\ln \gamma_{\text{config.}}^{\infty} = \ln\frac{V_i^0}{V_p} + 1 - \frac{V^0}{V_p}\right).$$

In this connection the relative retention volumes of the volatile compounds which react specifically with the functional groups of the polymers compared to the compounds incapable of such reaction (for example, saturated hydrocarbons) with approximately the same molar volume, will take into account to a considerable extent the change in the configuration entropy:

$$V_{\text{rel.}} = \frac{V_g^{(A)}}{V_g^{(\text{hyd})}} = \frac{K_A}{K_{\text{hyd}}} = \frac{K_A^0}{K_{\text{hyd}}}\left(1 + K_x\frac{2m}{\bar{M}_n}\right) \qquad (8)$$

Here K_{hyd} is the distribution coefficient of a hydrocarbon with a molar volume close to that of substance A.

Hence the relative retention volume for the standard volatile compounds which interact specifically with the terminal functional groups of the polymer is itself a more accurate linear function of $1/\bar{M}_n$.

On the basis of such ideas, a linear relation between V_{rel} and $1/\bar{M}_n$ was found earlier [23], but use of this equation did not reflect a specific interaction in the systems being considered. However, an equation of type (8) is valid only for such systems. Actually, as various investigations [18-20] have shown, V_g for saturated hydrocarbons varies with the molecular weight of the stationary phases by a different law.

It is interesting to note that Evans and Smith [21] observed a linear relation between the Kovačs retention indices (I) of polar compounds passing through a column and $1/\bar{M}_n$ for poly(ethylene glycols). The Kovačs index is known to depend linearly on the logarithm of the relative retention volume of the substance. Evidently, the linear dependence of I on $1/\bar{M}_n$ is the result of the fact that the quantity $K_X x_B$ in Eqn.(8) is rather low in comparison with 1 [$x_B < 0.2$; at a comparatively high temperature (100°C) the probability of the formation of hydrogen bonds becomes very slight and consequently K_X is small and probably even less than 1]. Then $\ln(1 + K_X x_B) \simeq K_X x_B$. A detailed experimental study of relations of the type of Eqn.(8) was made [22] in which specimens of poly(diethylene glycol maleate adipate) of various molecular weights were used as stationary phase and the chromatographed mixture contained ethanol, propanol, and benzene (internal standard).

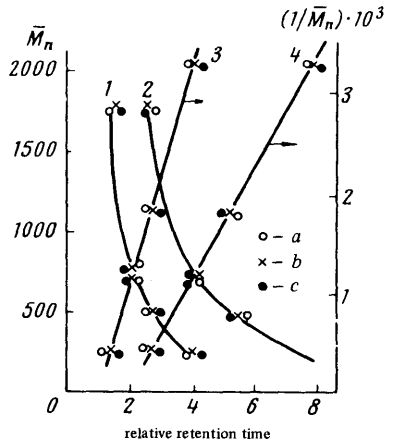

Figure 3. Variation of the relative retention times of ethanol (*1*, *3*) and propanol (*2*, *4*) (standard: benzene) with the molecular weight ($\bar{M}_n$) and the quantity $1/\bar{M}_n$ for poly(ethylene glycol maleate adipate): *a*), *b*), and *c*) series of experiments.

To reduce the adsorption effect of the carrier on the retention of polar alcohols the polyether being tested was carried on sodium chloride (0.25–0.5 mm fraction), proportion 1% of the carrier weight (column 200 × 0.4 cm, temperature of investigation 30°C). Fig. 3 shows the results for three series of experiments on the form of the variation of the relative retention time for ethanol and propanol with the molecular weight $\bar{M}_n$ and with $1/\bar{M}_n$. As Fig. 3 shows, the relative retention time of the volatile compounds which interact specifically with the terminal groups of the polymer depend linearly on the reciprocal

of its molecular weight. Naturally, to increase the sensitivity of the method the standard compounds used must be those having a strong specific interaction with the polar terminal groups of the polymer, that is, be characterised by very high values of K_X.

It was interesting to examine the effect of temperature on the parameters of Eqn.(8). It was to be expected that the first term of this equation should not depend significantly upon temperature, since it is linked with the non-specific interaction of the molecules of the volatile substances with the central fragments of the polymer molecule. For example, the second term of Eqn.(8), which reflects the specific interaction of a polar compound with the terminal groups of the polymer should depend on the temperature. To check these qualitative ideas, published results [10] were used to calculate the relative retention volumes of methanol (internal standard: decane) on poly(ethylene glycols) with molecular masses in the range from 300 to 6000 at 100° and 120°C. Fig.4 shows the variation of the relative retention volume with the reciprocal of the molecular mass. In accordance with Eqn.(8), this relation is linear, with the first terms being almost the same for the two temperatures, but the second term decreasing as the temperature is raised.

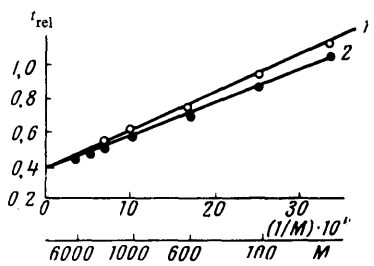

Figure 4. Variation of the relative retention volume of methyl alcohol with the reciprocal of the molecular weight of poly(ethylene glycol). Temperature, °C: *1*) 100; *2*) 120.

The relations found between the retention quantities for polymers with terminal functional groups which differ markedly from the main chain of the macromolecule can be used for polymers with number-average molecular weights up to 30 000–50 000.

The practical use of the chromatographic method is connected with the use of polymers of known molecular weight for a preliminary calibration. Several essentially positive features of the method are noteworthy. The carrying out of the experiment in a stream of carrier gas, the possibility of pre-heating the specimen, and performing the experiment at elevated temperatures considerably reduce the number of possible low-molecular-weight impurities, which usually impede the determination of the number-average molecular weight. Furthermore, the method is sensitive mainly to impurities which are capable of specific interactions with volatile substances of the standard mixture. We note that the possibility of determining the molecular weight of a series of oligomers with polar functional groups—poly(propylene glycols), poly(diethylene glycol adipates,) and thiokols—has been confirmed [20].

Kogan and Fedotova [20] have demonstrated another possible practical use of the variation of the retention of volatile substances with the molecular mass of oligomers. They showed that this relation can be used to select effective solvents for the fractionation of oligomers, since the solubility of the polymers and the retention volumes of the solvents are symbathically interconnected. For fractionation of oligomers a solvent must be chosen, the solubility in which of the members of the polymer homologous series shows the greatest dependence upon molecular weight. The use for this purpose of solvents and precipitants chosen on the basis of RGC results has given good results.

IV. INVESTIGATION OF THE THERMODYNAMICS OF THE INTERACTION OF VOLATILE COMPOUNDS WITH POLYMERIC COMPOUNDS

Even in the very beginning of the development of gas–liquid chromatography, one of its originators (Martin) noted the wide prospects of the use of the method for determining thermodynamic characteristics. He wrote [1]: "The method [of gas chromatography] provided perhaps the easiest of all means of studying the thermodynamics of the interaction of a volatile solute with a non-volatile solvent, and its potential value for providing this type of data should be very great". Thus position is also valid for polymeric compounds used as stationary phases.

An investigation by the gas-chromatographic method of the thermodynamic parameters for the interaction of low-molecular-weight compounds with polymers requires the calculation of a series of specific features for the behaviour of high-molecular-weight substances.

First of all it is necessary to note that the complexity of the molecular structure of polymeric materials leads to a variety of states in which the stationary polymeric phases can be found. Thus the polymers can be in two phase states—crystalline and amorphous, distinguished by differing degrees of ordering: long-range order in the arrangement of the links and chains for crystalline polymers and short-range order characteristic for liquid and amorphous solid polymers.

Solid polymers can also be partly crystalline, when crystalline and amorphous regions coexist in the polymer. In certain respects such a polymer can be regarded as an ordinary mixture of impermeable crystals and quasi-liquid amorphous medium [26].

Depending upon the temperature, amorphous polymers can be found in three physical states: vitreous, highly elastic, and visco-fluid distinguished by different degree of mobility of the structural elements of the macromolecules. The vitreous state is characterised solely by vibrational motion of the atoms which form the chain, in consequence of which the polymeric chain acquires the ability to buckle; the visco-fluid state by the mobility of all the macromolecules as a whole [27].

The mechanism of the retention (sorption) by polymeric molecules of low-molecular-weight compounds is determined by the phase and physical state of the polymers.

When the polymeric stationary phase is at a temperature below the glass temperature (T_g) the molecules of the specimen are not able to penetrate through the entire mass of the polymeric phase, and the retention here is determined by absorption on the polymeric surface, that is, gas-adsorption chromatography is involved. A similar situation is observed for crystalline polymers in the temperature range below the melting point.

Amorphous polymers at temperatures above T_g are capable both of dissolving low-molecular-weight compounds and of adsorbing them at the polymer–gas and polymer–solid carrier interfaces. When the high-molecular-weight phase is a partly crystalline polymer, then in the temperature range $T_g < T < T_f$ there is also the possibility of adsorption of the vapours of substances at the interfaces between the crystalline and amorphous regions.

In gas chromatography experimental methods for the determination of the contributions of each of the retention mechanisms to the total retention volume have been developed, and particularly methods of calculating retention due to dissolution of the substances in the stationary phase [28–30].

A knowledge of the retention volume due to dissolution of a substance permits the most important thermodynamic characteristics of the dissolution process to be calculated, namely, the distribution coefficient $k = V_g\rho$ (where ρ is the density of the stationary liquid phase), the activity coefficient γ_i [at infinite dilution, according to Eqn.(2)], and the changes in the excess partial molar thermodynamic functions of the solute [25]:

$$\Delta\bar{H} = R\frac{\partial \ln \gamma_i}{\partial\left(\frac{1}{T}\right)},\quad \Delta\bar{S} = -R\frac{\partial (T\ln\gamma_i)}{\partial T},\quad \Delta\bar{G} = -RT\ln\gamma_i.$$

Even the first studies of the thermodynamics of dissolution showed completely satisfactory agreement between the distribution coefficients for polymeric stationary phases determined by static and chromatographic methods. As an example, Table 2 gives results obtained by Anderson and Napier [31] for the distribution coefficients of benzene and cyclohexane in the gas–cresyl ester of poly(ethylene glycol) system.

Table 2. Distribution coefficients determined by static and gas-chromatographic methods for cresyl poly-(ethylene glycol) ether [31].

Compound	conditions					
	80°		100°		131°	
	GLC	static method	GLC	static method	GLC	static method
Benzene	71.6	73.0	43.4	44.1	23.4	20.1
Cyclohexane	18.9	19.9	13.5	15.0	9.3	7.8

The thermodynamic functions for the dissolution of volatile organic compounds were determined for several polymeric phases: Reopleks 400, poly(ethylene glycol) 600, Ftorsilikon FS-16, Silikon DS-550, [32] polyglycols [33,34], silicones [35], and solutions of magnesium chloride in poly-(ethylene glycol)-400. [36]

Problems in the use of gas chromatography for studying the thermodynamics of the interaction of a volatile substance with a polymeric phase were examined specially by Smidsrød and Guillet [37], who used Eqn.(2) to calculate from chromatographic results the coefficients γ_i^∞ for acetic acid, butanol, *o*-chloronaphthalene, naphthalene, and hexadecane in poly(*N*-isopropylacrylamide).

The excess thermodynamic functions for mixing at temperatures above the flow points of the polymer (Table 3) were calculated from the temperature dependences of γ_i^∞.

In calculating the activity coefficient from the chromatographic results by Eqn.(2), Smidsrød and Guillet [37] use the number-average molecular weight of the polymer; however, they note that for polymers some parameter determined by the size of the segment of the polymeric chain should be introduced instead of M_n. This indeterminacy disappears for the relative activity coefficients, which can also give valuable information in investigations of interactions of low-molecular-weight compounds with polymers [38].

Table 3. Excess thermodynamic functions for the mixing of volatile compounds of various types in poly(*N*-isopropylacrylamide), [38] temperature 200°C.

Compound	$\Delta\bar{G}$, cal mole^{-1}	$\Delta\bar{H}$, cal mole^{-1}	$\Delta\bar{S}$, cal deg^{-1} mole^{-1}
Acetic acid	−6740	−2400	+ 9.2
Butanol	−5390	+1100	+13.7
Naphthalene	−4360	+3900	+17.5
1-Chloronaphthalene	−4010	+3606	+11.3
n-Hexadecane	−1760	+2200	+ 8.4

The determination of the activity coefficients of low-molecular-weight compounds in polymers, especially under conditions of infinite dilution, is of considerable interest, especially for the theory of polymer solutions.

Thus the Flory–Huggins theory of regular solutions of polymers [19], which is based on a lattice model of liquids, allows the free energy of mixing in the dissolution of a long-chain polymeric molecule in a low-molecular-weight solvent to be calculated; for the case where the volume fraction of the polymer tends to 1 it yields Eqn.(3) for the activity coefficient of the substance dissolved in the polymer.

The first three terms on the right-hand side of Eqn.(3) are determined by the contribution from the changes in configurational or combinatorial entropy of mixing, due to the structure of the macromolecule (a flexible long chain, the segments of which are mobile and can exchange lattice sites with molecules of low-molecular-weight substances). Such a structure leads to large positive changes in entropy on the formation of polymer solutions and explains the characteristic negative departure from Raoult's law for the vapour pressure of the low-molecular-weight component of the solution.

The interaction parameter χ entering into Eqn.(3) reflects, in accordance with the theory of regular solutions, the contribution to the change in total free energy of dissolution of the change in free energy due to contact between the molecules of the components of the system. In the earlier stage of development of the theory of polymer solutions the interaction parameter χ was given the value of the van Laar enthalpy of mixing [19]:

$$\chi = \frac{V_i^0(\delta_i - \delta_p)^2}{RT}, \qquad (9)$$

where δ_p and δ_i are parameters of the solubility of the polymer and low-molecular-weight components of the solution respectively, in which δ_i is connected with the cohesion energy density $\Delta E_i^v/V_i^0$ by the relation

$$\delta_i = \left(\frac{\Delta E_i^v}{V_i^0}\right)^{1/2},$$

where ΔE_i^v is the heat of vaporisation of the pure ith component, and V_i^0 the molar volume of the ith component. However, the parameter χ is now regarded as a reduced

residual chemical potential consisting of enthalpy and entropy terms[39]:

$$\chi = \chi_H + \chi_S, \tag{10}$$

$$\chi_H = -T\left(\frac{\partial \chi}{\partial T}\right), \quad \chi_S = \frac{\partial(\chi T)}{\partial T}. \tag{11}$$

From the theory of regular solutions, the parameter χ is independent of the concentration of the solution. However, for many systems χ is a function of the composition of the solution and usually increases with the polymer concentration. Thus for the polyisobutylene–benzene system at 25°C the parameter χ rises from 0.50 in the range of infinitely dilute solutions to 1.1 for $v_p \to 1$ (v_p is the volume fraction of the polymer)[39]. χ is exceptionally important in investigating solutions of polymers: it determines the solubility of the polymer, the critical compositions and temperature of the solutions as a function of the length of the molecule. Gas chromatographic measurements and application of Eqn.(2) enable the activity coefficient γ_i^∞ of the solute to be determined, and consequently the parameter χ for $v_p \to 1$:

$$\chi_{v_p \to 1} = \ln \gamma_i^\infty - \left(\ln \frac{V_i^0}{V_p} + 1 - \frac{V_i^0}{V_p}\right). \tag{12}$$

Values of χ_H and χ_S can be estimated from the temperature dependence of χ and Eqn.(11). Gas chromatography also allows the value of χ at finite concentrations of a low-molecular-weight solute to be calculated[40]. If the solution can be regarded as regular, it is easy to use Eqn.(9) and the values of χ to find the density of the energy of cohesion, an important characteristic of polymers. The change in χ with concentration and also the high value of the entropy constituent χ_S cannot be explained by the simple theory of regular solutions. There are now several other theories of solutions of polymers: Prigogine's theory of corresponding states[41] which takes account of the change in volume during dissolution; a theory using ideas of the theory of corresponding states and employing the equations of state of the pure components in the calculation of the characteristics (Flory theory)[39,42]; and various others.

Gas chromatography exhibits wide possibilities for the experimental verification of these theories.

A recent paper by Patterson and coworkers[43] examined the possibility of evaluating the interaction parameter χ as the most important thermodynamic characteristic of solutions of polymers directly from the retention volumes and not from γ_i^∞ to determine which it is necessary to know the number-average molecular weight of the polymeric liquid phase ($\overline{M}_n$). In this paper it was shown that:

$$\ln\left(\gamma_i^\infty \frac{\overline{M}_n}{M_i}\right) = \ln\left(\frac{a_i}{w_i}\right)^\infty = \ln\frac{v_i}{v_p} + \left(1 - \frac{V_i}{\overline{M}_p v_p}\right) + \chi =$$

$$= \ln\left[\frac{RT}{p_i^0 v_g^{(i)} M_i}\right] - \frac{p_i^0}{RT}(B_{ii} - V_i), \tag{13}$$

where v_i and v_p are the specific volumes of solute and polymer respectively; a_i and w_i the activity and weight fraction of solute; M_i is the molecular weight of the solute, p_i^0 the vapour pressure of the pure solute at temperature T; $p_i^0/RT(B_{ii} - V_i)$ a term allowing for the non-ideality of the gas phase, and B_{ii} the second virial coefficient of the pure ith solute. Consequently,

$$\chi = \ln\left[\frac{RTv_p}{p_i^0 V_g^{(i)} V_i}\right] - \left(1 - \frac{V_i}{\overline{M}_n v_p}\right) - \frac{p_i^0(B_{ii} - V_i)}{RT}. \tag{14}$$

At sufficiently large $\overline{M}_n$ the term $V_i/\overline{M}_n V_p$ can be neglected and then χ can be calculated without knowledge of the molecular weight of the polymer or its dispersion.

It was shown[45] that the change in the excess partial molar enthalpy of dissolution ($\Delta\overline{H}_i^\infty$) can be recalculated from the temperature dependence of χ after allowing for the temperature dependence of the molar volumes of the solute and polymer:

$$\Delta\overline{H}_i^\infty = RT^2(\alpha_p - \alpha_i) + R\left[\frac{\partial \chi}{\partial\left(\frac{1}{T}\right)}\right], \tag{15}$$

where α_i and α_p are the coefficients of thermal expansion of the components of the solution in the liquid state. The first term in $\Delta\overline{H}_i^\infty$, determined by the difference in the thermal expansion of the low-molecular-weight solute and the polymer, is ~100 cal at 300°K.

Use of the Flory theory of solutions of polymers[42] leads to values of χ which differ greatly from the corresponding values calculated from the Flory–Huggins equation within the framework of the theory of regular solutions. It was found that the combinatorial part of the free energy of mixing is independent of the temperature and consequently

$$\Delta\overline{H}_i^\infty = R\left[\frac{\partial \chi^*}{\partial\left(\frac{1}{T}\right)}\right], \tag{16}$$

where χ^* is the interaction parameter calculated on the basis of the Flory theory.

Gas chromatography can be used extensively in the investigation of cross-linked polymers. From the statistical theory of the swelling of cross-linked polymers[19], at $v_p \to 1$,

$$\ln \gamma_i^\infty = \ln\frac{V_i^0}{V_p} + 1 - \frac{V_i^0}{V_p} + \chi + \frac{\rho_p V_i^0}{2M_c} \tag{17}$$

where V_p is the molar volume of the polymer before cross-linking, ρ_p the density of the polymer, M_c the molecular weight of the segment of the chain between the nodes of the lattice.

The parameter M_c, which is a characteristic of the density of the lattice and determines its strength, can thus be calculated from results of the chromatographic determination of γ_i^∞.

An investigation of the thermodynamics of the interaction of cross-linked polymers with low-molecular-weight compounds is of great interest in connection with the extensive use in chromatographic analysis of polymeric sorbents such as, for example, Porapak[44–46].

However, the use of gas chromatography for investigating solutions of polymers requires the investigation of a series of specific problems.

Primarily this is a problem of finding the gas–polymeric phase equilibrium under dynamic chromatographic conditions. The very high viscosity of the polymers, from 10^3 to 10^{13} P, should, at first glance, lead to the very slow diffusion of small molecules in the polymeric film, much slower than through a film of ordinary liquid.

However, only relatively non-coordinated movements of small segments of the polymeric chain are necessary for the diffusion of small molecules in a polymeric mass. In this connection the diffusion coefficients of low-molecular-weight substances are determined by the mobility of the segments and the packing density of the chains; here the molecular weight of the polymer is almost without effect on the rate of diffusion and the permeability through a film of polymer[26]. As a result, despite the enormous viscosity of the polymers the diffusion coefficients of small molecules in them are only one or two orders of

magnitude less than in ordinary liquids. Thus the diffusion coefficient of benzene in natural rubber is $D_{50^\circ} = 3 \times 10^{-7}$ cm^2 s^{-1},[26] and for CO_2 in poly(methylsiloxane) rubber $D_{20^\circ} = 3.8 \times 10^{-5}$ cm^2 s^{-1}.[27]

The high efficiency of the widely used chromatographic columns with polymeric liquid phases, for example, with silicone rubbers or poly(ethylene glycols) also shows that gas–polymer equilibrium is established rather rapidly under gas chromatographic conditions. However, in each instance of the study of the thermodynamics of polymer solutions by gas chromatography it is evidently necessary to prove that the measured retention volumes correspond to gas–polymer equilibrium. For example, it can be shown that the distribution coefficients K are independent of the carrier gas velocity.

An investigation of the rate of mass transfer in polymeric films is also of independent interest, since the permeability of the polymeric films for small molecules provides the basis of the technique of membrane separation of mixtures of substances[47].

Gas chromatography can be used to investigate the rate of mass transfer in liquid or amorphous films, from the variation of the height of the equivalent theoretical plate (HETP) with the velocity of the carrier gas[48].

The HETP equation allows the quantity d_L^2/D_L to be determined (where d_L is the thickness of the film of stationary liquid phase, and D_L the diffusion coefficient of the substance in the film); it is proportional to the so-called permeability lag time[26]. When d_L can be evaluated independently, the diffusion coefficient of the substance D_L can readily be determined from the lag time. The permeability P can be estimated from measurements of the distribution coefficients (K), which can be found from the retention volumes, and from the diffusion coefficients[26]:

$$P \equiv D_L \frac{K}{RT} . \qquad (18)$$

Incidentally, the parameter P can also be obtained directly from the component HETP, characterised by the erosion of the peak as a result of the resistance to mass exchange in the liquid phase (C_L):[48]

$$C_L \simeq \frac{K\frac{q_s}{q_m}}{\left(1+K\frac{q_s}{q_m}\right)^2}\frac{d_L^2}{D_L} \approx \frac{d_L^2}{K\frac{q_s}{q_m}D_L} \qquad (19)$$

for

$$K\frac{q_s}{q_m} \gg 1,$$

where q_S and q_m are the sections of the stationary and gas phases in the column respectively.

The use of gas chromatography in investigating diffusion in polymers and their permeability has a number of definite advantages over the usual methods of determining these quantities. These advantages are mainly connected with the rapidity and ease of the experiment, the availability of standard apparatus, and evidently, the adequate accuracy.

Another important feature is the above-mentioned variety of mechanisms of retention by polymeric phases, which act simultaneously in a chromatographic column.

As is known, important information about the retention mechanisms and the possibility of estimating the contribution of each mechanism to the total retention are given by the variation of the specific retention volumes with the amount of stationary phase in the column[28,29].

In the determination of retention volumes on polymeric phases an appreciable dependence of the retention volume on the size of the specimen even for very small specimens is often observed. Thus, Lavoie and Guillet[49] observed a dependence of V_g on the size of the specimen in the range 0.1–1 μl and evidently only for specimens of ~0.01 μl does Henry's law cease to be obeyed, from which the independence of V_g and the size of the specimen also follows.

The non-linearity of the distribution isotherms even in the range of very small concentrations (low volume fraction of the low-molecular-weight component, but nevertheless the mole fraction can be very large) can in many instances be explained by the sorbed molecules (especially the vapours of poor solvents) having a tendency to form aggregates inside the polymers[26]. It is therefore to be expected that the worse the dissolving ability of the sorbate, the narrower the range of concentrations where the distribution isotherm is close to linear. This conclusion is confirmed, for example, by results[37] where the greatest dependence of the retention volume on the size of the specimen was observed for the peaks of hexadecane, which is a very bad solvent for the polymeric phase, poly(*N*-isopropylacrylamide).

The values of V_g used to calculate the thermodynamic characteristics of the distribution, have been obtained by extrapolating to zero size the experimental relations between V_g and the size of the specimen.

Methods have now been developed for the chromatographic investigation of the thermodynamic parameters for the distribution at the terminal concentrations of sorbed substances and in particular methods of determining distribution isotherms[40] and the specific surfaces of the stationary phase[25], which can undoubtedly be also used for polymeric phases.

These methods are undoubtedly widely used in studying the permeability, swelling, and plasticising of polymers.

V. STUDY OF PHASE TRANSFORMATIONS

A phase transformation converts the initial stationary phase into a new non-stationary phase (new sorbent), which is in general characterised by physicochemical properties different from those of the initial phase. This should be reflected by a change in the chromatographic characteristics of volatile standard substances in the range of the phase transformation of the stationary phase. Therefore the RGC method can be used for studying phase transformations in polymers. In studying phase transformations it is desirable to use as chromatographic characteristics not only the retention volume or time, but also the width of the peak of a volatile standard compound[7].

The marked dependence of the retention parameters on temperature in the range of fusion of the stationary liquid phase was noted long ago[50–55]. However, usually the investigators were interested not in studying the phase transformation phenomenon but in its effect or use in analytical chromatography. Thus the pronounced decrease in the retention of the compounds being analysed on eicosane when the column is cooled to a temperature below its melting point has been used[50] as a method of rapid elution from the column of heavy hydrocarbons after the analysis of the lighter components.

Evidently the first studies in which the chromatographic properties of stationary phases were specially investigated in the range of their phase transformations were those of liquid crystals (as stationary liquid phases)[6,56,57]. The stationary liquid phases found in a liquid-crystalline state are very selective for the separation of the isomers of organic compounds (for example, *o*-, *m*-, and *p*-cresols).

At the temperatures of the phase transformations from the crystalline state to the mesomorphic liquid-crystal, and also in going from the mesomorphic to the isotropic liquid state sharp anomalous changes in the specific retention volume are observed.

As shown by Alishoev and coworkers [7] the RGC method can also be used successfully in studying the phase transformations on going from one crystalline modification to another by the example of carbon tetrachloride. Subsequently this method was used successfully by Guran and Rodgers for investigating phase transformations in crystals of thallium nitrate [58], Cu_2HgI_4, and Ag_2HgI_4. [59] In all the above instances the results of the gas-chromatographic experiment agree well with those on phase transformations obtained by other methods.

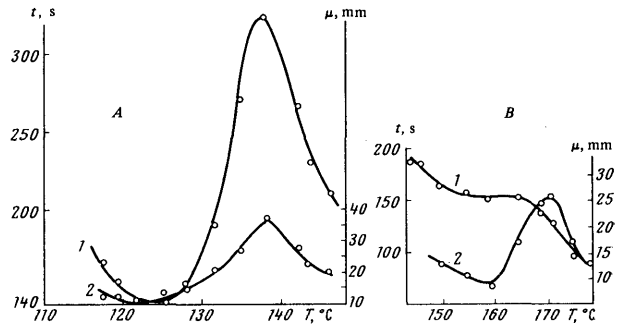

Figure 5. Variation of the retention time (*1*) and peak width (*2*) with the column temperature: *A*) the n-tetradecane–polyethylene system; *B*) the cetene–polypropene system.

According to Berezkin and coworkers [60], the RGC method was first used specially for studying phase transformations in polymers by Alishoev and coworkers [7], who investigated stereoregular polymers with a high degree of crystallinity: polyethylene and polypropylene. A mechanical mixture of powders of the test polymer (1%) with glass spheres was put in a column (100 × 0.4 cm) which was connected to a chromatograph and heated at a rate of 0.2–0.5 deg min^{-1}. Periodically a specimen of standard substance was introduced into the column and its chromatogram recorded. The results of the experiments were presented as graphs of the retention time and peak width of the standard substance (for polyethylene–tetradecane and polypropylene–cetene) against column temperature (Fig. 5). [7] In the instances investigated the retention time and peak width curves show a maximum (a plateau on the cetene retention time curve for polypropylene) in the temperature range of the phase transformation. The appearance of maxima is due to a change in the distribution constant and diffusion coefficients of the standard volatile substance as a result of the phase transformation. In the deposition of polypropylene on glass spheres from its solution in decalin at 110°C or from a melt in an inert atmosphere the plateau on the curve in this coordinate system associated with the phase transformation almost disappears. Similar behaviour is noted in studying phase transformations of thallium(I) nitrate crystals [58].

Guillet and coworkers [37,49,61–63] have made a large contribution to the development of the RGC method in studying phase transformations in high-molecular-weight compounds and their quantitative interpretation.

In these studies the variation of $\lg V_g$ with the reciprocal of the temperature was examined for polymeric stationary phases. Fig. 6 shows the most general type of this relation for the semicrystalline polymer [64]. Such behaviour is characteristic, for example, of polypropylene and crystalline polystyrene when hydrocarbons (n-alkanes) are used as solutes.

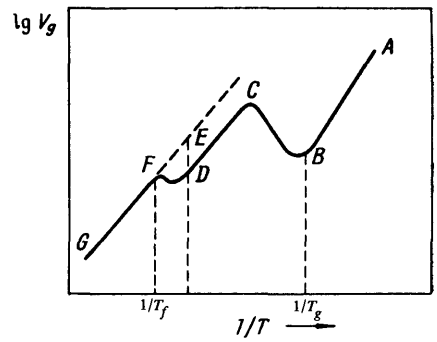

Figure 6. Variation of the retention volume with the reciprocal of the absolute temperature of the column for semicrystalline polymers.

In the range corresponding to the part *AB* of the curve the polymer is at temperatures below the glass point. The retention is here determined by adsorption on the surface of the vitreous polymer, since the molecules of the specimen cannot penetrate into the body of the polymeric film.

The linear dependence of $\lg V_g$ on $1/T$ is observed up to the glass point (T_g) (point *B*). An increase in the retention volume at the phase transformation point, also observed for phase transformations of the first type [55], is, as already noted, due to a fundamental change in the structure of the stationary phase. A further rise in temperature leads to passage of the curve through a minimum and to an increase in $\lg V_g$ along the part *BC*. Guillet [62] explains this increase as follows. The region *BC* corresponds to non-equilibrium adsorption of the vapour on the polymeric phase. The molecules start to penetrate into the body of the phase but the diffusion rate is so small that only at point *C* does the adsorption of vapour reach the entire thickness of the film in the contact time. This prediction could readily be checked from results on the variation of V_g with gas velocity. However, the studies of the behaviour of stationary phases close to the transformation point do not include such results.

The possibility of chain flexibility (progressive movement of the segments) in the amorphous ranges of polymers is known to increase with the temperature. In addition, an increase in the temperature leads to breakdown of ordered supermolecular structures (blocks) and the molecules acquire the conformation of disordered convoluted and tangled balls [64]. In other words, raising the temperature leads to a decrease in the mean cohesion energy of the molecules of amorphous polymers, which should, in turn,

lead to a decrease in the activity coefficient of the solutes—compare, for example, Eqns.(9) and (3). It seems that these changes in the cohesion energy are most pronounced in the region BC of the curve (Fig. 6).

Thus the increase in V_g with temperature is explained by the fact that in the range BC as the temperature is raised the activity coefficients γ^{∞} of the solutes decrease more sharply than the vapour pressure of the vapour of the pure solutes p_1^0 or f_1^0 of Eqn.(2) increases.

The definition and depth of the minimum on the curve (Fig. 6) depend on the nature and dimensions of the molecules of the volatile solutes. Thus it has been shown [38] that for butanol and acetic acid the graph of $\lg V_g$ against $1/T$ for the stationary phase poly(*N*-isopropylacrylamide) is a straight line over the entire temperature range. Possibly the formation of strong hydrogen bonds by the molecules of the alcohol and acid with the amide group of the polymer makes the mechanism of their dissolution in the polymer differ from that for hydrocarbons.

Nevertheless it should be noted that the nature of the inflection on the graph of $\lg V_g$ against $1/T$ close to the glass temperature and the dependence of its form on the nature and size of the sorbate molecules are still far from explained.

At point C, an amorphous polymer or an amorphous part of a semicrystalline polymer evidently reaches a state which is identical with that of ordinary liquids. Thus, for poly(*N*-isopropylacrylamide) point C is close to its flow point. Thus along the segment CD in addition to possible adsorption at the surface and at the boundaries of the amorphous and crystalline regions, dissolution of the vapours of the volatile compounds takes place over the entire volume of the amorphous part of the polymer. In this region the thermodynamic functions of the dissolution can be determined.

Close to point F the crystalline part of the polymer melts. In this region a characteristic maximum is usually observed on the curve (Fig. 6). [55,63] The range FG corresponds to the state when the entire mass of the polymer participates in the dissolution of the molecules of the specimen. Since it is thought that on the segment CD the crystalline regions of the polymer do not participate in the retention of the solute molecules, it is possible to estimate the degree of crystallinity of the specimen in the temperature range CD. Actually, extrapolation of the line FG in the range of temperatures below T_f allow the retention volume which would correspond to a hypothetical amorphous state of the entire polymer at $T < T_f$ to be estimated. Then the degree of crystallinity can be calculated from the formula:

$$\text{degree of crystallinity} = \frac{(V_g)_E - (V_g)_D}{(V_g)_E} \cdot 100 \qquad (20)$$

(see Fig. 6).

In this the possibility of adsorption of the volatile standards at the boundary between the crystalline and amorphous parts or at the gas–polymer and polymer–solid carrier surfaces is not taken into account.

Guillet has termed the method of investigating the structure and physical state of polymers from the temperature dependence of the retention volumes the method of "molecular specimens" [62].

This method has been used for determining the degree of crystallinity of high-density polyethylene at various temperatures [63]. Fig. 7 shows the variation of its degree of crystallinity with temperature obtained gas-chromatographically and by differential thermal analysis. As Fig. 7 shows, the agreement between the two methods is completely satisfactory.

As the form of the curve in Fig. 6 shows, the variation of $\lg V_g$ with $1/T$ can be used to determine the glass point of the polymers.

Table 4 [49] shows values of T_g obtained by differential thermal analysis and by reversed chromatography. The agreement between the two methods is completely satisfactory and evidently in determining T_g of the polymer by gas-chromatography it is desirable to use as characteristic quantity the temperature (T_1) of the first departure from linearity on the curve of the logarithm of the retention volume against the reciprocal of the temperature.

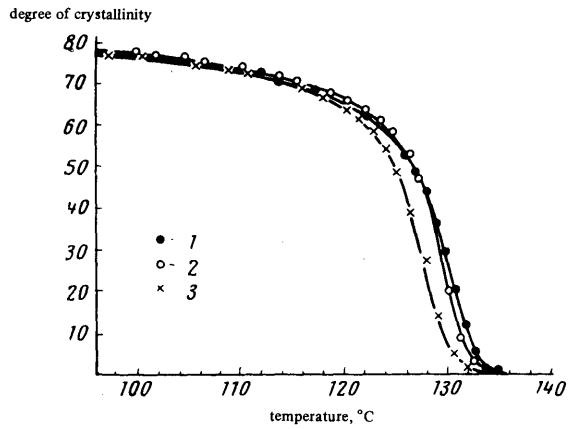

Figure 7. Variation of the degree of crystallinity of high-density polyethylene with the temperature: *1*) Calorimetric results; *2*) and *3*) results obtained by the method of molecular specimens; *2*) on cooling at a rate of 1.0 deg min^{-1} and heating at 0.5 deg min^{-1}; *3*) on cooling according to the ballistic rule and heating at 0.5 deg min^{-1}.

Table 4. Determination of the glass temperature by the reverse gas chromatographic method [49].

Characteristic	Poly (vinyl chloride)		Polystyrene	Poly(methyl methacrylate)
	A	B		
Molecular weight	68 000	35 500	31 000	48 000
Standard volatile component	dodecane	dodecane	dodecane	hexadecane
Glass temperature, °C (DTA)	75±2	75±2	95±2	100±2
Temperature for the first departure from linearity, T_1, °C	81	81	88	97
Temperature of first minimum, T_2, °C	91	91	100	105

The RGC method has also been used successfully for studying the kinetics of the crystallisation of organic substances from the melt. The use of this method for polymeric compounds has been described by Guillet and

coworkers[63], and for monomeric compounds by Andreev and coworkers[65].

The features of the reversed chromatography method in the study of phase transformations are the relative simplicity of the apparatus and experimental procedure, the possibility of rapid measurement of the chromatographic characteristics for volatile standard substances of various types and the use of small amounts of the polymers being tested. Another advantage of the RGC method in comparison with widely used methods based on measuring the heat of phase transformation is the possibility of studying slow phase transformations.

VI. INVESTIGATION OF THE KINETICS OF THE REACTIONS OF POLYMERS

In studying the kinetics of chemical reactions by the RGC method the reaction is effected in a chromatographic column where the reaction mixture is used as stationary phase for a standard mixture of volatile non-reacting compounds. The change in the composition of the reaction mixture with time is determined by periodic measurement of the elution characteristics of the volatile standards. The determination of the composition of the reacting system with time is based on the use of a relation of the type

$$c_i = f(V_j), \qquad (21)$$

where c_i is the concentration of one of the components in the reaction mixture, V_j the retention volume of one of the standards. The concept of "component" also embraces the functional groups of the polymer being tested.

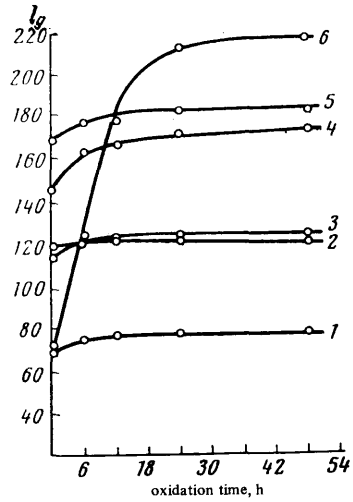

Figure 8. Change in the interaction coefficients during the oxidation of asphaltene: *1*) butanol; *2*) propionic acid; *3*) pyrrole; *4*) phenol; *5*) formamide; *6*) 1-methylpyrrolidone.

This method requires small amounts of the test substances and is characterised by the following advantages: a thin film of the phase allows the kinetic regime to be realised readily, an investigation of the kinetics of the reaction can be made without removal of specimens, and it is possible to investigate the kinetics of reaction systems which cannot be analysed chromatographically. The method was proposed by Berezkin and coworkers[60] and used for studying the kinetics of oxidation of benzaldehyde into benzoic acid[66]. It was shown that the oxidation of benzaldehyde by atmospheric oxygen (air is a carrier gas) proceeds formally by a first-order reaction, and the rate constant obtained in a chromatographic experiment differs from that obtained in a bubbling reactor by no more than 3%.

This method was subsequently used by Davis and Petersen for studying the oxidation of asphaltene[67]. Fig. 8 shows the change in the specific interaction coefficient — see Eqn. (1) —for various volatile standards as a function of the time of oxidation of the asphaltene with air at 130°C.

Undoubtedly, the RGC method is extremely convenient for studying the kinetics of the reactions of polymeric compounds.

In conclusion, we wish to emphasise that although the development of the RGC method is far from ended the experience that has already been accumulated is sufficient for the wide use of this method in polymer chemistry for solving the most diverse problems.

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Reactions of RȮ, RṠ, and RȮ$_2$ Radicals with Phosphites and Phosphines

D.G.Pobedimskii, N.A.Mukmeneva, and P.A.Kirpichnikov

The review deals with studies designed to elucidate the detailed mechanism and quantitative relations in the kinetics of the reactions of RȮ, RṠ, and RȮ$_2$ radicals with phosphites and phosphines. It is shown how the isotope tracer method has been used to prove the irreversible formation of the phosphoranyl radical—the primary intermediate in these radical reactions. The results of the study of the competition between the addition of RȮ and RṠ radicals to phosphites and phosphines on the one hand and their other reaction pathways (abstraction of a hydrogen atom from hydrocarbons, addition to a double bond, and monomolecular decomposition) on the other have been analysed. The last section discusses the mechanism of the inhibiting effect of aromatic phosphites in the thermo-oxidative degradation of polyolefins within the framework of the hypothesis that they terminate kinetic oxidation chains by radical exchange.
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I. INTRODUCTION

Organophosphorus compounds are involved in many free radical reactions[1-6]. The autoxidation of compounds such as phosphites and phosphines has a radical chain mechanism and constitutes a large and important class of organic reactions. The aim of the present review is to examine and analyse the kinetics and mechanisms of the elementary steps of the interaction of RȮ, RṠ, and RȮ$_2$ radicals with phosphites and phosphines, i.e. to examine all the reactions constituting the basis for the autoxidation processes of these compounds. There is in addition a practical aspect of the studies of these elementary radical reactions associated with the participation of phosphites in polymer stabilisation processes.

II. REACTIONS OF RȮ AND RṠ RADICALS

The reactions of RȮ radicals play an important role in the transfer of kinetic chains in the autoxidation of phosphites and phosphines. Before discussing the kinetics, we shall first examine the mechanism of the transfer reaction.

Trialkyl phosphites $(R'O)_3P$ readily interact with t-BuȮ radicals, forming the corresponding derivatives containing the phosphoryl group $\rangle P=O$:

$$(R'O)_3P + t\text{-}BuO^{\cdot} \rightarrow (R'O)_3P{=}O + t\text{-}Bu^{\cdot}.$$

These reactions take place with a high enthalpy change (the P=O bond energies are in the range 120 — 150 kcal mole^{-1} [5]). For example, the heats of reaction t-BuȮ

radicals with ethyl and butyl phosphites, which we estimated as the differences between the heats of formation of the final products and the initial reactants, are respectively 74 and 46.5 kcal mole^{-1}; the known values of ΔH_f^0 were employed[7-10].

Walling and Rabinowitz[11] studied by gas – liquid chromatography (GLC) and mass spectrometry the products of the interaction of triethyl phosphite with various oxy-radicals: in all cases triethyl phosphate and hydrocarbons were detected. The results of the quantitative analysis of the products are presented in Table 1.

Table 1. Products of the reactions of RȮ radicals with triethyl phosphite (in the absence of oxygen)[11].

Source of RȮ radicals	Type of RȮ radicals	Conditions of radical generation	No. of moles of phosphite per mole of peroxide	No. of moles of phosphate per mole of peroxide	No. of moles of hydrocarbon per mole of peroxide
Dicumenyl peroxide	$PhC(CH_3)_2\dot{O}$	Ultraviolet irradiation, 25°, 125°	5.4	2.16	0.46 (dicumene)
Ditto	ditto	ditto	5.4	1.87	0.71 (dicumene)
Di-t-butyl peroxide	$(CH_3)_3C\dot{O}$	Ultraviolet irradiation, 25°	3.6	2.08	0.31 (isobutane); 0.20 (isobutene); 0.035 (2,2,4-trimethylpentane); 0.080 (tetramethylbutane); 0.020 (2,2,4-trimethylpentane)
ditto	ditto	120°	3.4	2.2	Isobutane, isobutene tetramethylbutane (not determined quantitatively)

Table 1 shows that, firstly, the yield of phosphate is on average 2.0 moles per mole of peroxide and, secondly, the yield is independent of the source and type of RȮ radicals, the conditions of their generation, and also of phosphite concentration when the rates of thermal initiation by di-t-butyl and dicumenyl peroxides are almost equal (1.7×10^{15} and 2.2×10^{15} cm^{-3} s^{-1})†. This implies that phosphite molecules fully accept all the peroxy-radicals formed from the peroxide.

The following mechanism for the interaction of triethyl phosphite with RȮ radicals has been proposed on the basis of the composition of the reaction mixture[11]:

$$ROOR \rightarrow 2R\dot{O}, \quad (1)$$

$$R\dot{O} + R(OEt)_3 \rightarrow RO\dot{P}(OEt)_3, \quad (2)$$

$$RO\dot{P}(OEt)_3 \rightarrow \dot{R} + O{=}P(OEt)_3, \quad (3)$$

$$\dot{R} + \dot{R} \rightarrow \text{disproportionation products}, \quad (4)$$

$$\dot{R} + \dot{R} \rightarrow \text{recombination products}. \quad (5)$$

One may suppose that a similar mechanism will probably hold also for the reactions of tributyl phosphite with t-BuȮ radicals, where tributyl phosphate was detected as the main product by the ^{31}P NMR method[14].

Bentrude's data[15] derived from an analysis of the reaction product of another (aromatic) phosphite (triphenyl phosphite) conflict with this mechanism to some extent. Thus, in the stages involving the transfer of an oxygen atom [stages (2) and (3)], one should expect the formation of triphenyl phosphate; moreover, such a pathway is thermodynamically favourable (according to our estimate, the formation of the phosphate is exothermic to the extent of about 41 kcal mole^{-1}). However, in the experiment (130°C, di-t-butyl peroxide, chlorobenzene, no oxygen) only diphenyl phosphite, isobutene (1.0 and 0.5 mole per mole of triphenyl phosphite respectively), and phenol were detected[15]. This is because in the presence of triphenyl phosphite the elementary steps involving the substitution (exchange) of radicals mainly occur:

$$t\text{-}Bu\dot{O} + (PhO)_3P \rightarrow t\text{-}BuOP(OPh)_2 + Ph\dot{O}.$$

Furthermore, by hypothesis, the mixed phosphite, which is unstable under the experimental conditions, decomposes fully with formation of an olefin and diphenyl phosphite. This mechanism is confirmed also by the observation of the ESR spectrum of the phenoxy-radical under the conditions of the photolysis of di-t-butyl peroxide in the presence of triphenyl phosphite (–85°C, cyclopropane)[16].

The substitution of t-BuȮ radicals, accompanied by the dissociation of the P – C bond in the phosphoranyl radicals and less probable from the thermodynamic point of view, was also observed when these radicals were allowed to act on tri-n-butylphosphine (130°C, no oxygen)[17]. Quantitative study of the reaction products of the phosphine yielded an estimate of the probability of this reaction: the yield of t-butyl di-n-butylphosphinite, which can only be obtained in the substitution step

$$t\text{-}Bu\dot{O} + n\text{-}Bu_3P \rightarrow t\text{-}BuOP(n\text{-}Bu)_2 + n\text{-}B\dot{u},$$

amounts to about 80%; the fraction of phosphine oxide, formed in the step involving the transfer of an oxygen atom, is significantly lower (20%).

Thus there is a definite kinetic control of the relative amounts of the products of addition to phosphines and aromatic phosphites. At the present time it is difficult to interpret this phenomenon unambiguously; its possible causes may be different distributions of unpaired electron density in the P – O and P – C bonds of phosphoranyl radical and also the differences between the energies of the bonds undergoing dissociation.

In an interesting recent study[16], where the intermediate radical products of the oxidation by t-BuȮ radicals of a large class of trialkyl phosphines and trialkyl phosphites were investigated by ESR, showed that in all cases alkyl radicals are present. The authors demonstrated by special experiments that, in the absence of organophosphorus compounds, in the photolysis of di-t-butyl peroxide (between –70° and –90°C, cyclopropane), only t-BuȮ radicals are formed, while in the presence of such substances alkyl radicals are detected immediately; the ratio of the line intensities in the hyperfine structure and the proton hyperfine coupling constants (HCC) are consistent with this interpretation of the ESR spectra. Thus, in the reactions of triethyl-, tri-isopropyl-, tri-isobutyl-, and tricyclohexyl-phosphines, the observed ESR spectra were assigned respectively to $CH_3\dot{C}H_2$, $(CH_3)_2\dot{C}H$, $(CH_3)_2CH\dot{C}H_2$ and $\dot{C}_6H_{11}$ radicals, probably formed by a substitution mechanism‡:

$$R'_3P + \dot{O}C(CH_3)_3 \rightarrow R'_2P{-}OC(CH_3)_3 + \dot{R}'. \quad (6)$$

† According to the literature[12,13], the rate constants for the decomposition of the peroxides are $k = 10^{15.1} \exp(-36\,000/RT)$ for di-t-butyl peroxide and $k = 10^{14.6} \exp(-34\,500/RT)$ (s^{-1}) for dicumenyl peroxide.

‡ Adams and Ingersoll[18] succeeded in detecting by the ESR method the alkyl radicals $CH_3\dot{C}H_2$, $CH_3(CH_2)_2\dot{C}H_2$, and $CH_3(CH_2)_6\dot{C}H_2$ formed under simpler conditions: in the photolysis of iso-octane solutions of the same peroxide in a flow system (20°C, trialkylphosphines).

The behaviour of trialkyl phosphites (trimethyl, triethyl, and tri-isopropyl phosphites) in relation to t-BuO· radicals is fundamentally different from that of the trialkylphosphines: in all cases only the t-Bu· radicals were detected; they are probably formed by a mechanism in which an oxygen atom is transferred:

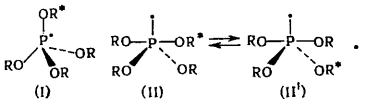
$$(R'O)_3P + \dot{O}C(CH_3)_3 \rightarrow (R'O)_3P{=}O + \dot{C}(CH_3)_3 \ . \qquad (7)$$

This result (see also Hudson and Hussain[19]) may be regarded as confirmation of the mechanism of the interaction of trialkyl phosphites with t-BuO· radicals proposed[11] on the basis of chemical analysis of non-radical products.

The problem arises whether the phosphoranyl radical [$R'_3\dot{P}OR$ or $(R'O)_3\dot{P}OR$] is a kinetically independent species or whether it is a form of transition state for the transfer of an oxygen atom or for substitution via mechanisms (6) and (7). Other experimental data, which allow a choice to be made, will be considered next.

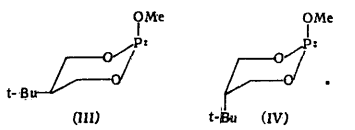
Bentrude and Wielesek[20], who studied the decomposition of di-t-butyl hyponitrite, labelled with the ^{14}C isotope in the methyl groups, in deoxygenated benzene solution at 65°C in the presence of tri-t-butyl phosphite, showed that the phosphite is quantitatively converted into phosphate. It was demonstrated that, firstly, the fraction of labelled phosphate is independent of the concentration of phosphite and of the phosphite/hyponitrite ratio, secondly, the ^{14}C label is hardly incorporated into the unreacted phosphite or phosphate added before the reaction, and, finally, the fraction of labelled phosphate is constant (about 75%).

These results are important; they imply that all t-Bu*O· radicals, which have emerged from the [Bu*-O· O· — Bu-t] cage, are entirely captured by acceptor (phosphite) molecules and that the formation of the phosphoranyl radical $[(t\text{-}BuO)_4\dot{P}]^*$ as an intermediate is irreversible. Bentrude and Wielesek[20] suggested that a statistical distribution of the ^{14}C label in the phosphoranyl radical becomes possible if the radical has the structure of an equilateral pyrimid (I) where all four alkoxy-groups are configurationally equivalent or it can obtain in a trigonal-bipyramidal structure (II) as a result of the pseudorotation of configurationally non-equivalent groups; by hypothesis, such rotation takes place at a frequency higher than that of the decomposition of radical (II):



(I) (II) (II')

However, it has been shown[21] that stereospecific transfer of an oxygen atom from t-BuO· radicals to a mixture of geometrical isomers—six-membered cyclic *cis*(III)- and *trans*-(IV)-phosphites—and also to the optically active methylphenyl-n-propylphosphine $\{[-\alpha]_D\}$ takes place with retention of the configuration at the phosphorus atom. The results of a stereochemical study of the free-radical oxidation at the tervalent phosphorus atom are presented in Table 2.



(III) (IV)

The retention of the configuration at the phosphorus atom in a radical reaction (stereospecificity, retention of the sign of optical rotation) implies that the pseudorotation of the substituents at the phosphorus atom in the radical with structure (II) is impossible, since it should lead to the inversion of the sign of optical rotation or to the isomerisation of the phosphite.

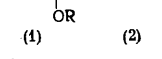
Thus a reasonable explanation of both the statistical distribution of the ^{14}C label and the retention of the configuration at the phosphorus atom in the oxidation by t-BuO· radicals can be obtained only within the framework of the model where the phosphoranyl radical has structure (I).

Table 2. Oxidation of an optically active phosphine and a mixture of isomeric phosphites by t-BuO· radicals.

Source of t-BuO· radicals	Optical activity of phosphine oxide	(III):(IV) ratio	(III)-oxide:(IV)-oxide ratio
t-BuO—N=N—OBu-t-	−16.7±0.2	15:85	21:79
(65°, CH_3CN, without O_2)		91:9	96:4

The formation of phosphoranyl radicals was first observed directly by Kochi and Krusik[16] and by Davies et al.[22] Thus, Kochi and Krusik[16] observed in the oxidation of trimethylphosphine by t-BuO· radicals (photolysis of di-t-butyl peroxide, cyclopropane, temperature between −70° and 90°C) an ESR spectrum with a doublet splitting of 619 G, which was assigned to hyperfine interaction involving the ^{31}P nuclei in the $t\text{-}BuO\dot{P}(CH_3)_3$ radical. According to Davies et al.[22], the addition of t-BuO· radicals to triethyl phosphite (photolysis of di-t-butyl peroxide, cyclopentane, −85°C) is accompanied by the appearance of the ESR spectrum of the phosphoranyl radical $t\text{-}BuO\dot{P}(OC_2H_5)_3$ with an HCC constant a_P = 891 G and g = 2.008; it is noteworthy that this was the first determination of the g-factor of the phosphoranyl radical.

Another striking example illustrating the possibility, in principle, of the formation of the phosphoranyl radical as a kinetically independent species is the observation[14] of the chemically induced nuclear polarisation of ^{31}P (CINP-31P), which arises in the thermal decomposition of di-t-butyl and dibenzoyl peroxides in the presence of triethyl, tributyl, or triphenyl phosphite (110 — 190°). Since the appearance of CINP in chemical reactions implies that they take place with formation of radical pairs[23,24], the negative sign of the chemically induced nuclear polarisation of ^{31}P suggests that the CINP in phosphate molecules is solely a result of the elementary step involving the disproportionation of the radical

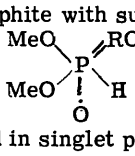


(1) (2)

in singlet radical pairs [$a_P > 0$; $\Delta g = (g_1 - g_2) > 0$; the g_2-factor of the majority of hydrocarbon radicals is 2.0024 — 2.0025,[25] while according to the literature[22] the g_1-factor of the phosphoranyl radical $t\text{-}BuO\dot{P}(OC_2H_5)_3$ is 2.008]§; previously this type of disproportionation of phosphoranyl radicals was examined by Davidson[26] on the basis of the chemical analysis of the non-radical products.

§ Disproportionation in triplet pairs is unlikely since it leads to the formation of a phosphate molecule in an electronically excited triplet state.

Thus the study of the chemically induced nuclear polarisation of ^{31}P is extremely promising from the standpoint of the identification or refining of the mechanism of the elementary radical reactions of organophosphorus compounds.

For example, analysis[27] of the sign of the CINP involving ^{31}P nuclei (emission) in the dicyclohexyl peroxydicarbonate (or dilauryl peroxide) — dimethyl phosphite systems (75 — 110°C, tetrachloroethane) led us to the conclusion that of the two kinetically equivalent mechanisms of the formation of the polarised product (phosphate)—via the abstraction of a hydrogen atom and the recombination of the $(MeO)_2\dot{P}{=}O$ and $R\dot{O}$ radicals ($a_P > 0$ $\Delta g > 0$; absorption by ^{31}P expected in "random" pairs) or via the "adhesion" of the $R\dot{O}$ radicals to the double bond of the phosphite with subsequent disproportionation of the radicals  and $O\dot{R}$ ($a_P > 0$, $\Delta g > 0$; emission expected in singlet pairs)—the second mechanism actually obtains.

The above analysis shows that the composition of the intermediate and final products of the reactions of $R\dot{O}$ radicals with phosphites and phosphines has been investigated fairly completely; only one other aspect of the mechanism needs to be refined, namely the reaction kinetics. However, so far there are no experimental data obtained by direct determination of the elementary rate constants; the only source of information on this problem is kinetic analysis of the competition between the reactions involving the abstraction of a hydrogen atom from the hydrocarbon by $R\dot{O}$ radicals and their addition to phosphites and phosphines.

Table 3. Ratios of the rate constants for the reactions of t-Bu$\dot{O}$ radicals with triethyl phosphite and triphenylphosphine (130°C, hydrocarbon).

Hydrocarbon	k_{ph}/k_{RH}	
	$(EtO)_3P$	Ph_3P
Cyclohexane	610±10	7.0±0.2
Cyclohexene	440±10	7.4±0.2
Cyclopentene	610±10	7.4±0.2
Cumene	730±10	10.3±0.5
2,3-Dimethylbutane	1100±100	9.8±0.7

Thus Walling and Pearson[28] investigated the competition between the addition to triethyl phosphite or triphenylphosphine of t-Bu$\dot{O}$ radicals (the radicals were generated by the thermal decomposition of di-t-butyl peroxide at 130°C in sealed tubes) and the abstraction by them of a hydrogen atom from various hydrocarbons (cyclohexane, cyclohexene, cyclopentene, cumene, and 2,3-dimethylbutane). The results of the kinetic analysis are presented in Table 3; the ratios of the rate constants for the reaction of the phosphite k_{ph} to that for the reaction of the hydrocarbon k_{RH} were estimated from the composition of the products—a phosphate and an alcohol).

Table 3 shows that triethyl phosphite reacts 82 ± 20 times faster with t-Bu$\dot{O}$ radicals than does triphenylphosphine and that even the abstraction of a hydrogen atom from hydrocarbons cannot compete effectively with these two reactions.

Since the study under consideration[28] is unique as regards the quantitative kinetics of the reactions of $R\dot{O}$ radicals with phosphines, we believe it is useful to supplement its results with an approximate calculation of the activation energy for the reaction of t-Bu$\dot{O}$ radicals with triethyl phosphite on the basis of the quantitative data of Walling and Pearson.

The activation energy for the competing reaction with cyclohexene is approximately 3 kcal mole^{-1}.[29] The main reaction (the addition to the phosphite) can occur at a rate comparable to that of the competing reaction only if its activation energy is equal to or somewhat less than 3 kcal mole^{-1}. The activation energy for the reaction of $(EtO)_3P$ with t-Bu$\dot{O}$ radicals can be estimated approximately in the following way. In Walling and Pearson's experiments[28], the concentration of peroxide molecules was 6×10^{23} cm^{-3} and the rate constant for the decomposition of the peroxide at 130°C was $k_{decomp} = 4.0 \times 10^{-5}$ s^{-1} (we obtained this value from other literature data[12,13]). Therefore the rate of initiation under these conditions is

$$W_i = 2 \cdot 4.0 \cdot 10^{-5} \cdot 6 \cdot 10^{23} = 4.8 \cdot 10^{19} \text{ cm}^{-3}\text{ s}^{-1},$$

so that the steady-state concentration of t-Bu$\dot{O}$ radicals may be determined as follows:

$$[\text{t-Bu}\dot{O}]_{st} = \frac{4.8 \cdot 10^{19}}{k_{RH}[RH] + k_{ph}[(EtO)_3P]} = \frac{4.8 \cdot 10^{19}}{A} \text{cm}^{-3}.$$

Next the rate constant k_{RH} for the abstraction of a hydrogen atom from cyclohexane, which we estimated from Walling's data[29], is

$$10^{-13}\exp\left(\frac{-3000}{RT}\right) = 2.4 \cdot 10^{-15} \text{ cm}^{-3}\text{ s}^{-1}$$

then the rate of abstraction becomes

$$W_{RH} = 2.4 \cdot 10^{-15}\frac{4.8 \cdot 10^{19}}{A} 12 \cdot 10^{23} = \frac{13.8}{A} \cdot 10^{28} \text{ cm}^{-3}\text{ s}^{-1},$$

where 12×10^{23} is the concentration of hydrocarbon molecules.

Since the concentration of phosphite molecules was 12×10^{23} cm^{-3}, then, in terms of the activation energy for the reaction of the phosphite E_{ph}, its rate at 130°C should be

$$W_{ph} = 10^{-13} \cdot 10^{-E_{ph}/4.57 \cdot 403} \cdot 12 \cdot 10^{23}\frac{4.8 \cdot 10^{19}}{A} =$$

$$= \frac{5.76}{A} 10^{30} \cdot 10^{-E_{ph}/4.57 \cdot 403} \text{ cm}^{-3}\text{ s}^{-1}.$$

For the reaction of the phosphite with t-Bu$\dot{O}$ radicals to proceed at an inappreciable rate, it must amount to not more than 1% of W_{RH}, i.e.

$$\frac{5.76}{A} 10^{30} \cdot 10^{-E_{ph}/4.57 \cdot 403} \leqslant \frac{13.8}{A} 10^{26}$$

or

$$10^{30} \cdot 10^{-E_{ph}/4.57 \cdot 403} \leqslant 2.4 \cdot 10^{26}.$$

Hence it follows that the activation energy for the reaction of triethyl phosphite with t-Bu$\dot{O}$ radicals is $E_{ph} \geqslant 3.62 \times 4.57 \times 403 = 6.7$ kcal mole^{-1}¶. Evidently this value of E_{ph} is higher than the activation energy for

¶ In the calculation of E_{ph} a typical value was adopted for the pre-exponential factor for the reaction of t-Bu$\dot{O}$ radicals with molecules, namely 10^{-13} cm^3 s^{-1};[30] it can be easily shown that with the pre-exponential factor equal to the bimolecular collision frequency ($10^{-10} - 10^{-11}$ cm^3 s^{-1}), E_{ph} should be even higher.

the reaction of the active hydrocarbon. Using it, it is possible to show that only in the presence of a 100-fold excess of the phosphite can the competing reaction with the hydrocarbon be supressed. This conclusion, albeit in fact inconsistent with the conclusions of Walling and Pearson, makes it necessary to treat with a certain amount of caution the earlier estimate of the relative reactivity of triethyl phosphite[28].

Walling and Pearson employed the method of competing reactions also for the determination of the relative reactivities of the triethyl phosphite — triphenyl phosphite, tri-n-butylphosphine — triphenylphosphine, and triethyl phosphite — tri-n-butylphosphine pairs in relation to t-BuȮ radicals. Kinetic analysis (the reactivities were estimated from the degree of consumption of the reactant) led to the following relative reactivity series for the compounds investigated (at 130°C):

$$Bu_3P : (EtO)_3P : (PhO)_3P : Ph_3P = 1.9 : 1.6 : 1 : 0.78\dagger .$$

It is useful to estimate the ratio of the rate constants for the reactions of triethyl and triphenyl phosphites (k_1/k_2) from an approximate calculation of the activation energies for the two reactions. Thus, for the overall decomposition of di-t-butyl peroxide in the presence of triphenyl phosphite, one can postulate a competition between the decomposition of the t-BuȮ radical:

$$(CH_3)_3C\dot{O} \xrightarrow{k_d} \dot{C}H_3 + CH_3COCH_3$$

and its addition to the phosphite:

$$(CH_3)_3C\dot{O} + (PhO)_3P \xrightarrow{k'_{ph}} (CH_3)_2C{=}CH_2 + HOP(OPh)_2 + Ph\dot{O} .$$

In Bentrude's experiments[15] (in this investigation a detailed study was made of the reaction products of triphenyl phosphite), the concentration of t-BuȮ radicals was (130°C, in chlorobenzene)

$$[t\text{-}Bu\dot{O}]_{st} = \frac{2 \cdot 4 \cdot 10^{-5} \cdot 2.4 \cdot 10^{20}}{k'_{ph}[(PhO)_3P] + k_d} = \frac{2 \cdot 10^{16}}{B} \quad cm^{-3}$$

where 4×10^{-5} s^{-1} is the rate constant for the decomposition of the peroxide and 2.4×10^{20} cm^{-3} is the concentration of peroxide molecules, while the rate constant for the decomposition of the radicals $k_d = 10^{11.5} \exp(-10\,600/RT) = 5.6 \times 10^5$ s^{-1}.[31] Therefore the rate of decomposition of t-BuȮ radicals is

$$W_d = 5.6 \cdot 10^5 \cdot \frac{2 \cdot 10^{16}}{B} = 1.1 \cdot \frac{10^{22}}{B} \quad cm^{-3}\,s^{-1}.$$

Since the concentration of triphenyl phosphite molecules was 5×10^{20} cm^{-3}, the rate of reaction of triphenyl phosphite with t-BuȮ radicals at 130°C should be

$$W'_{ph} = 10^{-13} \cdot 10^{-E'_{ph}/4.57 \cdot 403} \frac{2 \cdot 10^{16}}{B} \cdot 5 \cdot 10^{20} = \frac{1}{B} 10^{24} \cdot 10^{-E'_{ph}/4.57 \cdot 403} \quad cm^{-3}\,s^{-1}$$

Using the kinetic condition for the supression of competition by the phosphite which we derived above, one can show that

$$\frac{10^{24}}{B} \cdot 10^{-E'_{ph}/4.57 \cdot 403} \leqslant 1.1 \cdot \frac{10^{20}}{B} .$$

Hence it follows that the activation energy for the reaction of triphenyl phosphite $E'_{ph} \geqslant 3.96 \times 4.57 \times 403 = 7.3$ kcal mole^{-1}.

† It follows from the data in Table 3 that the relative reactivity of triphenylphosphine should be 0.020; this finding confirms yet again the contradictory nature of the results in Table 3.

Since this is lower than the activation energy for the decomposition of t-BuȮ radicals, triphenyl phosphite can accept these radicals to an appreciable extent‡. Next, assuming that the reactions of triethyl and triphenyl phosphites have the same pre-exponential factor (about 10^{-13} cm^3 s^{-1}), it is possible to estimate the ratio of the rate constants for these reactions; k_1/k_2 is found to be 2.1. This is close to the value of 1.6 found by Walling and Pearson[28] from experimental kinetic data for the joint consumption of triethyl and triphenyl phosphites in the decomposition of di-t-butyl peroxide, which illustrates the internal consistency of the estimates of activation energy quoted here.

In conclusion of the discussion of the kinetics of the reaction of RȮ radicals with phosphite and phosphines, one should also point out that the level of the quantitative kinetics of these radical reactions is fairly low. For the majority of elementary reactions, there are no quantitative data and treatment has to be restricted to approximate estimates of activation energies and rate constants. For example, by studying the rate of consumption of reactants under various experimental conditions (different rates of initiation, temperatures, radical sources, relative amounts of the reactants, etc.) and using the kinetic procedures of the method of competing reactions, it is possible to determine, in principle, the rate constants for elementary radical reactions. So far no experimental studies on these lines have been made.

We shall now consider the experimental data on the mechanism and kinetics of the reactions of RṠ radicals with phosphites and phosphines. Like those of the RȮ radicals, these reactions are of interest from the standpoint of the determination of the mechanism of the formation of phosphoranyl radicals; moreover, they are suitable for the generation of alkyl radicals of known structure from mercaptans and disulphides.

Walling et al.[11,32] established by gas — liquid chromatography that the main molecular products of such interaction are the phosphorothionates $(R'O)_3P{=}S$ and phosphine sulphides $R'_3P{=}S$ as well as hydrocarbons or sulphides; their formation is greatly accelerated by ultraviolet irradiation, azobisisobutyronitrile (AIBN), and di-t-butyl peroxide; this implies that the reaction involves kinetic chains. The following mechanism has been proposed on the basis of the composition of the reaction products of triethyl phosphite, for example:

$$R\dot{S} + P(OEt)_3 \rightarrow RS\dot{P}(OEt)_3 \rightarrow \dot{R} + S{=}P(OEt)_3 ,$$
$$\dot{R} + RSH \rightarrow RH + R\dot{S}$$

or

$$\dot{R} + RSSR \rightarrow RSR + R\dot{S} .$$

Many facts support the above mechanism of the interaction of RṠ radicals with phosphites or phosphines[11,32]. For example, Kochi and Krusik[16] detected by the ESR method the $(CH_3)_3\dot{C}$ radical, which is formed in the photolysis of di-t-butyl disulphide in the presence of tri-isopropylphosphine (−90°C, cyclopropane) probably by the reaction

$$(CH_3)_3C\dot{S} + [(CH_3)_2CH]_3P \rightarrow (CH_3)_3\dot{C} + [(CH_3)_2CH]_3P{=}S.$$

Subsequently Kavun et al.[33] demonstrated by the ESR method that the alkyl radicals formed in thermal decomposition of di(trichlorophenyl) disulphide (60 — 100°C, benzene, no oxygen) in the presence of triphenylphosphine combine with stable nitroxide radicals as acceptors; the

‡ Indeed hardly any acetone was detected in the mixture of products[15].

kinetic behaviour of the acceptor then reflects accurately the kinetics of the rate-limiting stage—monomolecular decomposition of the disulphide bond. The following mechanism has been proposed for the decomposition of a disulphide in the presence of a phosphine:

$$RSSR \rightarrow 2R\dot{S};$$
$$R\dot{S} + R'_3P \rightarrow RS\dot{P}R'_3 \rightarrow \dot{R} + S{=}PR'_3;$$
$$\dot{R} + \text{acceptor} \rightarrow \text{stable product}.$$

This mechanism is confirmed by the kinetics of reactions in which radicals combine with acceptors.

Finally Bentrude et al.[21] established that the stereospecific transfer of the sulphur atom from BuS· radicals to a mixture of geometrical isomers (III) and (IV) (see p. 557) takes place, as for t-BuO· radicals, with retention of the configuration at the phosphorus atom.

This result and also the direct detection of alkyl radicals and their combination with stable nitroxide radicals as acceptors illustrate the common features of the interaction of RO· and RS· radicals with phosphites and phosphines, which take place via the formation of an intermediate phosphoranyl radical; in this sense the reactions of RO· and RS· radicals have common properties and features.

Only one study has been made[28] on the kinetics of the reactions of RS· radicals, in which the ratio of the rate constants for the interaction of n-BuS· radicals (from n-BuSH) with triethyl phosphite and styrene, initiated by AIBN at 70°C, was measured. By hypothesis, the following reactions occur under experimental conditions:

$$\text{AIBN} \xrightarrow{k_0} \overbrace{\dot{r} + N_2 + \dot{r}} \begin{cases} \xrightarrow{fk_0} \dot{r} + N_2 + \dot{r} \\ \xrightarrow{(1-f)k_0} r{-}r + N_2 \end{cases},$$
$$\dot{r} + RSH \xrightarrow{k_1} rH + R\dot{S},$$
$$R\dot{S} + P(OEt)_3 \xrightarrow{k_2} \dot{R} + S{=}P(OEt)_3,$$
$$\dot{R} + RSH \xrightarrow{k_3} RH + R\dot{S},$$
$$R\dot{S} + CH_2{=}CHPh \xrightarrow{k_4} RSCH_2{-}\dot{C}HPh,$$
$$RSCH_2{-}\dot{C}HPh + RSH \xrightarrow{k_5} RSCH_2{-}CH_2Ph + R\dot{S},$$

where f is the probability of the emergence of the radicals from the "cage".

Since the sulphide $RSCH_2CH_2Ph$ was obtained only by the reaction with styrene and the phosphorothionate $S{=}P(OEt)_3$ by the reaction with a phosphite, the rate constant ratio k_4/k_2 is determined by analysing the products for an olefin and phosphite:

$$\frac{d[\text{olefin}]}{d[\text{phosphite}]} = \frac{d[\text{sulphide}]}{d[\text{phosphorothionate}]} = \frac{k_4[\text{olefin}]}{k_2[\text{phosphate}]}.$$

The average value of this ratio was found to be 3.2. On the basis of a study by Sivertz[34], who showed that RS· radicals add to the styrene molecule with a diffusional rate constant of 1.3×10^{-12} cm^3·s^{-1}, Walling and Pearson[28] determined the absolute rate constant $k_2 = 0.4 \times 10^{-12}$ cm^3 s^{-1}; this value implies that the reaction of RS· radicals with triethyl phosphite should occur with an almost zero activation energy.

It is noteworthy that there are no serious grounds for regarding this conclusion as unambiguous; this follows from the following considerations. Firstly, analysis of the experimental results of Walling and Pearson[28] in Table 4 showed that, with an approximately constant $[\text{styrene}]_0/[\text{phosphite}]_0$ ratio, the rate constant ratio k_4/k_2 varies in parallel with the increase of the concentration of the mercaptan (by a factor of 2); such an increase can probably be explained either by the fact that at the concentrations indicated in Table 4 there is not sufficient time for the mercaptan to accept all the cyanoisopropyl radicals ṙ emerging from the initiator "cage" into the bulk of the solvent or by the occurrence of side reactions where the olefin is alkylated, which were disregarded by the authors in the kinetic treatment of the experimental results.

Table 4. Ratios of the rate constants for the addition of n-BuS· radicals to triethyl phosphite (AIBN, 70°C, n-BuSH, styrene, no oxygen).

$10^3[\text{n-BuSH}]_0$, M	$\frac{k_4}{k_2}$	$\frac{[\text{olefin}]_0}{[\text{phosphite}]_0}$	$10^3[S{=}P(OEt)_3]$, M	$10^3[\text{sulphide}]$, M	$\frac{k_4}{k_2}\left(\frac{[\text{olefin}]}{[\text{phosphite}]}\right)_{av}$
4.1	1.9	1.0	1.6	2.5	1.71
4.3	2.3	0.8 av 0.9	1.3	1.9	2.07
9.5	4.9	0.9	0.43	1.02	4.4
4.5	2.3	0.47	1.9	1.5	1.22
9.5	4.4	0.6 av 0.53	0.52	1.37	2.33

Secondly, according to the same authors' estimate, the difference between the reactivities of n-BuS· and t-BuO· radicals in relation to various phosphites and phosphines is almost independent of the structure of the radicals and lies in the range 0.1 — 1.0; this means that the reaction of n-BuO· radicals, like that of t-BuO·, with phosphites probably involves an appreciable activation energy.

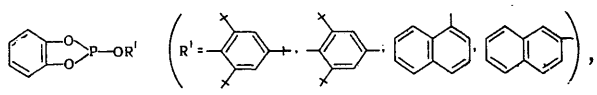
III. REACTIONS OF RO_2· RADICALS

In the previous section evidence was presented demonstrating that RO· and RS· radicals interact effectively with phosphites and phosphines under any conditions either by a radical exchange (substitution) mechanism or via a sulphur or oxygen atom transfer.

At first sight this has the consequence that the kinetics of the reactions of RO· and RO_2· radicals should be determined only by the reactivity of the phosphites (phosphines) and should not be sensitive to the type of the oxygen-containing radical. However, many facts contradict this conclusion.

In liquid-phase chain oxidation of hydrocarbons, the intensity of the chemiluminescence associated with the exothermic elementary step (recombination of peroxy-radicals) decreases appreciably in the presence of certain phenolic and amine inhibitors[35]; this is explained by postulating that the rate of linear chain termination by the inhibitor becomes higher than the rate of quadratic termination (via the recombination of RO_2· radicals). However, Khloplyankina et al.[36], who studied the AIBN-initiated oxidation of ethylbenzene at 60°C by a chemiluminescence method, showed that the introduction of tri-isopentyl phosphite, tri-isopentyl phosphate, and diethylphosphorous acid has almost no effect on the luminescence intensity I: their relative reactivities in the reaction with RO_2· were found to be respectively 1×10^{-5}, 2×10^{-3}, and 1×10^{-5}, i.e. the rate of this reaction is zero or very low.

When an aromatic phosphite,



is introduced into the reaction mixture, the chemiluminescence intensity decreases slightly. It was then found that the rates of consumption of these phosphites, calculated from the kinetic luminescence data, are on average higher by one- two powers of 10 than the specified rate of initiation, while the quantity $[d(I/I_0)/dt]_{max}$ (the maximum slope of the kinetic curve), which characterises the capacity of the inhibitor molecules to react with peroxy-radicals[35], remained almost constant and was usually equal to the corresponding quantity measured in experiments with free phenols (catechol and substituted phenols), which may be obtained by the hydrolysis of phosphites, i.e. may be present as impurities.

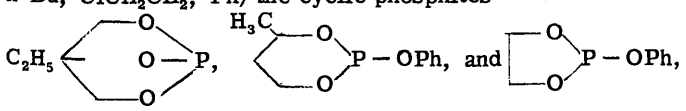
All these characteristics of the quenching of chemiluminescence by aromatic phosphites may be accounted for by adopting a mechanism in which a single kinetic oxidation chain is terminated either by 10 — 100 phosphite molecules or by a single phenol molecule (for an impurity/phosphite ratio of 0.1 — 0.01). The agreement between the slopes of the kinetic luminescence curves for the consumption of the phosphite and its hydrolysis products is evidence that the second mechanism obtains, i.e. aromatic phosphites, like aliphatic phosphites, hardly react with RO_2 radicals at 60°C.

Walling and Rabinowitz[11] were the first to draw attention to the fact that at higher temperatures (about 130°C) the oxidation of aliphatic phosphites by alkoxy-radicals in the presence of O_2 becomes autocatalytic (an excess super-stoichiometric amount of phosphate is formed). They also explained the autocatalysis on the hypothesis that at 130°C the peroxy-radicals, into which the alkyl radicals $\dot{R}$ (t-Bu$\dot{O}$) were converted at 130°C under the influence of molecular oxygen (see p. 556 for the mechanism of the formation of $\dot{R}$), rapidly oxidise new phosphite molecules, regenerating at the same time the active centres of the kinetic chains—the $R\dot{O}$ radicals:

$$\dot{R} + O_2 \rightarrow R\dot{O}_2,$$
$$R\dot{O}_2 + P(OR')_3 \rightarrow RO_2\dot{P}(OR')_3,$$
$$RO_2\dot{P}(OR')_3 \rightarrow O{=}P(OR')_3 + R\dot{O},$$
$$R\dot{O} \rightarrow \text{stages (2) and (3).}$$

It should be noted that this mechanism does not include the termination of the kinetic chains; the oxidation continues until the complete consumption of the phosphite.

An illustration of the mechanism of the autoxidation of phosphites with AIBN as an initiator is provided by the data of Bentrude[15], who measured the yields of trialkyl and triallyl phosphates in the oxidation by RO_2 radicals (benzene, 80°C, O_2) of phosphites $(R'O)_3P$ (where R' = Et, n-Bu, $ClCH_2CH_2$, Ph) the cyclic phosphites



and the mixed phosphite $(EtO)_2P(OPh)$: in all cases the yield was found to be close to 80 — 90% for the molar ratio phosphite/initiator = 10. It is noteworthy that, when di-t-butyl peroxide was employed as an initiator, the rate of initiation decreased under the experimental conditions (130°C, chlorobenzene) only by a factor of 2 (relative to AIBN), while the yield of cyclic and aromatic phosphates was less than 2.5 moles per mole of the peroxide; this can probably be accounted for by the occurrence of the competitive radical exchange reaction (see Section II).

The above example shows that, in order to conclude that a particular reaction is impossible (such a conclusion was arrived at by Neiman and Miller[37] for the reaction of RO_2 with phosphites on the basis of the results of Khloplyankina et al.[36]), it is insufficient to investigate this reaction at only one temperature; a comprehensive kinetic investigation is required.

Clearly the results of only one study[15] do not yield a complete picture of the kinetics of the reactions of $R\dot{O}_2$ with phosphites; in addition, it is necessary to have data which would make it possible to identify the oxidation conditions and to find the rate-limiting stage (from the effect of O_2 pressure, rate of initiation, phosphite concentration, etc. on the rate of formation of phosphates).

Buckler[17] observed the autocatalytic oxidation of tri-n-butylphosphine under the influence of O_2 to phosphine oxide and n-butyl di-n-butylphosphinite at 26°C in hexane solution in the absence of initiators. It was found that the catalysis is possible when the diffusion of oxygen is retarded and chain propagation

$$R\dot{O}_2 + PR_3 \rightarrow R\dot{O} + O{=}PR_3$$

is much faster than chain transfer

$$R\dot{O} + PR_3 \rightarrow \dot{R} + O{=}PR_3$$
$$R\dot{O} + PR_3 \rightarrow \dot{R} + ROPR_2.$$

Next it was discovered that the relative yields of phosphine oxide varies in parallel with the increasing polarity of the solvent. This finding implies that the polarisation of the P — O bond in the phosphoranyl radical $R - O\dot{P}R_3$ is probably the main cause of the formation of phosphine oxide (see also p. 556). Since in this investigation an initiator was not employed, the nature of the elementary chain initiation step remains obscure.

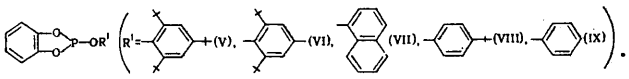
The above brief analysis shows that there are almost no quantitative data for the reactions of $R\dot{O}_2$ radicals with phosphites and phosphines although these reactions, like those of the $R\dot{O}$ and $R\dot{S}$ radicals, are important in the autoxidation of phosphites and phosphines and, as will be shown below, in polymer stabilisation processes. Quantitative kinetic criteria for such reactions are very necessary for practical purposes.

IV. THE ROLE OF RADICAL MECHANISMS IN THE OXIDATION OF POLYMERS INHIBITED BY PHOSPHITES

Hitherto the kinetics and mechanisms of the reactions of low-molecular-weight radicals $R\dot{O}$ and $R\dot{O}_2$ with phosphites and phosphines in the liquid phase were considered. The kinetics of the reactions of $R\dot{O}$ and $R\dot{O}_2$ macroradicals with phosphites are of exceptional interest for the theory of polymer stabilisation. Unfortunately, there are almost no quantitative data for the rates of these reactions in polymer melts and in the solid phase. Nevertheless, such data would be extremely significant. The point is that the idea of the involvement of aromatic phosphites in the termination of kinetic chains in the oxidation of polymers (in the melts) and the associated theory of the action of organophosphorus inhibitors (critical concentrations, linear relation between the induction period and phosphite concentration, etc.) are based on hypotheses concerning the reactions of low-molecular-weight $R\dot{O}$ and $R\dot{O}_2$ radicals (see Sections II and III); these hypotheses were developed by Levin[38,39] and confirmed by a number of investigators

in studies on the high-temperature (180 — 220°C) oxidation of polypropylene[38-43]. Initially we shall examine the available data in this field and then interpret them from the kinetic standpoint.

Levin and coworkers[39,40,43], who studied the oxidation of polypropylene at 200°C (i.e. in the melt) and at an oxygen pressure of 200 mmHg, observed a linear relation between the induction period in the oxidation process τ and the concentration of aromatic phosphites with the general formula



Comparison of several mechanisms for the inhibited oxidation of polypropylene in the presence of these phosphites shows that formally they all reduce to a linear relation between τ and the phosphite concentration.

Firstly, phosphites may inhibit degenerate branching:

$$\mathrm{RH} + \mathrm{O_2} \xrightarrow{W_0} \dot{\mathrm{R}} + \mathrm{H\dot{O}_2},$$

$$\dot{\mathrm{R}} + \mathrm{O_2} \xrightarrow{k_1} \mathrm{R\dot{O}_2},$$

$$\mathrm{R\dot{O}_2} + \mathrm{RH} \xrightarrow{k_2} \mathrm{ROOH} + \dot{\mathrm{R}},$$

$$\mathrm{R\dot{O}_2} + \mathrm{R\dot{O}_2} \xrightarrow{k_3} \text{stable products},$$

$$\mathrm{ROOH} + \mathrm{RH} \xrightarrow{\frac{O_2}{k_4}} \delta\mathrm{R\dot{O}_2},$$

$$\mathrm{ROOH} + \mathrm{P(OR')_3} \xrightarrow{k_5} \text{stable products}.$$

Kinetic analysis of this mechanism (where δ is the probability of degenerate chain branching) in the steady state (with respect to $\dot{R}$, $R\dot{O}_2$, and ROOH) leads to the following relation between the rate of consumption of the phosphite and its concentration:

$$-\frac{d[\mathrm{P(OR')_3}]}{dt} = \frac{k_2 k_5 [\mathrm{RH}]\, W_0^{1/2} [\mathrm{P(OR')_3}]}{k_3^{1/2}(k_4[\mathrm{RH}] + k_5[\mathrm{P(OR')_3}])}.$$

At fairly high phosphite concentrations, we obtain

$$-\frac{d[\mathrm{P(OR')_3}]}{dt} = \frac{k_2[\mathrm{RH}]\, W_0^{1/2}}{k_3^{1/2}}.$$

and

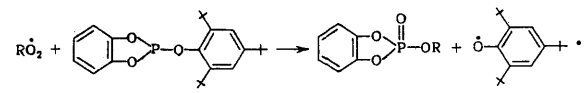
$$\tau = \frac{k_3^{1/2}}{k_2[\mathrm{RH}]\, W_0^{1/2}} [\mathrm{P(OR')_3}]_0.$$

i.e. τ varies linearly with $[P(OR')_3]_0$. In addition, it is possible to show that, under the experimental conditions (200°C, typical inhibitor concentration $10^{-1} - 10^{-2}$ mole kg^{-1}), the phosphite (V) is in fact capable of suppressing degenerate branching, since

$$\frac{W_5[\mathrm{ROOH}]}{W_4[\mathrm{ROOH}]} = \frac{0.4 \cdot 10^{-13} \exp(-14\,000/RT)(10^{-1} - 10^{-2})}{1.6 \cdot 10^{-13} \exp(-25\,000/RT) \cdot 23} = 1.2(10^3 - 10^4).$$

The rate constant for the bimolecular decomposition of polypropylene hydroperoxide was obtained by ourselves from the results of Pudov and Neiman[44] and the "liquid-phase" rate constant for the reaction of tri-t-butylphenyl *o*-phenylene phosphite with 1,1-diphenylethyl hydroperoxide (this hydroperoxide can serve as a model of polypropylene hydroperoxide) extrapolated to 200°C was taken from Mukmeneva[45]; the inhibitor and polymer concentrations were $10^{-1} - 10^{-2}$ and 23 mole kg^{-1}. However, the finding that the effectiveness of the phosphites (V) — (IX) investigated is not correlated with the rates at which they decompose 1,1-diphenylethyl hydroperoxide in the liquid phase at 25°C cannot be accounted for within the framework of this mechanism[39,45,46].

Secondly, phosphites can terminate kinetic oxidation chains probably by replacing the active macroradicals $R\dot{O}_2$ by relatively inactive resonance-stabilised phenoxy-radicals[38] (see also Section II):



In this case the general mechanism of the inhibited oxidation can be represented as follows:

$$\mathrm{RH} + \mathrm{O_2} \xrightarrow{W_0} \dot{\mathrm{R}} + \mathrm{H\dot{O}_2},$$

$$\dot{\mathrm{R}} + \mathrm{O_2} \xrightarrow{k_1} \mathrm{R\dot{O}_2},$$

$$\mathrm{R\dot{O}_2} + \mathrm{RH} \xrightarrow{k_2} \mathrm{ROOH} + \dot{\mathrm{R}},$$

$$\mathrm{R\dot{O}_2} + \mathrm{P(OR')_3} \xrightarrow{k_p} \mathrm{O{=}P(OR')_3(OR)} + \mathrm{Ar\dot{O}},$$

$$\mathrm{ROOH} + \mathrm{RH} \xrightarrow{\frac{O_2}{k_4}} \delta\mathrm{R\dot{O}_2}.$$

Assuming steady-state concentrations of $\dot{R}$, $R\dot{O}_2$, and ROOH, it is possible to obtain the following expression for the rate of consumption of phosphite:

$$-\frac{d[\mathrm{P(OR')_3}]}{dt} = \frac{k_p[\mathrm{P(OR')_3}]\, W_0}{\delta k_2[\mathrm{RH}] + k_p[\mathrm{P(OR')_3}]}.$$

At fairly low values of δ (it has been shown in a review[47] that, at oxygen pressures ranging from 0 to 200 mmHg, δ varies in the range $17 \times 10^{-3} - 0.8$, i.e. is less than unity), this expression simplifies:

$$-\frac{d[\mathrm{P(OR')_3}]}{dt} = W_0 \text{ and } \tau = \frac{1}{W_0}[\mathrm{P(OR')_3}]_0;$$

i.e. in this case τ depends linearly on $[P(OR')_3]_0$. This mechanism is confirmed by the critical concentrations of the phosphites investigated[40-42] (observed in kinetic experiments), i.e. concentrations above which the oxidation process passes from a non-steady state to a steady state (hypotheses concerning the critical concentrations of inhibitors of different types have been developed by Neiman and Shlyapnikov[48,49]). Evidently an unambiguous and direct demonstration of the elementary kinetic chain termination stage in oxidation by aromatic phosphites in the polymer melt and in the solid phase would be of fundamental importance for the theory of the stabilisation of polymers by these compounds; hitherto such a demonstration has not been achieved in any of the experimental studies.

Thirdly, a linear relation of the type $\tau \cong [P(OR')_3]_0/W_0$ may be obtained on the hypothesis[37] that aromatic phosphites inhibit the oxidation of polypropylene via their hydrolysis products, which are formed in the course of the oxidation process. Indeed, the formation of water molecules in the induction period of the oxidation reaction becomes the rate-limiting stage in this case and therefore the hydrolysis of the phosphite is of zero order with respect to the phosphite. However, from the standpoint of these hypotheses about phosphites as sources of catechol and other stabilisers, one cannot explain the finding that the phosphites investigated (except phosphites with the substituents and) have a critical concentration, while all theoretically conceivable products of their hydrolysis (phenols, catechol, *o*-phenylenephosphorous acid, phosphorous acid, and others) do not exhibit such a concentration[41].

Thus the existence of a linear relation between the induction period and the concentration of aromatic phosphites can be explained unambiguously by adopting the mechanism in which the kinetic oxidation chains are

terminated by radical exchange. This mechanism probably obtains in polymer melts; on the other hand, the presence of critical phosphite concentrations can serve as a kinetic criterion of its validity. Moreover, such a mechanism makes it possible to deal more rigorously and on a sounder basis with the selection of phosphites for which an inhibiting effect may be predicted.

It is noteworthy that the extensive data on the effectiveness of aromatic phosphites in polymer oxidation products in melts can be hardly used for solid-phase reactions of $R\dot{O}_2$ radicals with phosphites; this follows from the kinetic characteristics of solid-phase radical reactions (see the review on radical polymer degradation and stabilisation reactions[47]). We may note that, in order to determine the effectiveness of the phosphites in the termination of kinetic chains in the oxidation of a solid polymer (100 – 130°C), it is necessary to know not only the rate constant and the elementary mechanism of the interaction of the $R\dot{O}_2$ macroradical with the phosphite (which characterises the kinetic stage) but also the diffusion coefficient of the phosphite in the solid polymer (the macrodiffusion stage).

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This review has dealt with the most important radical reactions of phosphites and phosphines, their role in autoxidation processes in the liquid phase and in the inhibited oxidation of polymers in melts has been assessed, and their quantitative kinetic characteristics have been given.

It is noteworthy that the quantitative data for many reactions are extremely contradictory; frequently this applies not only to kinetic constants but even to the mechanisms. For example, the mechanism of the termination of kinetic chains in the oxidation of polypropylene by aromatic phosphites via radical exchange is valid provided that the phenoxy-radical is not involved in the propagation of the $Ph\dot{O} + RH \rightarrow PhOH + \dot{R}$ chains but recombines with a second peroxy-radical. Calculation shows that 200°C the rate via the first pathway for the disappearance of phenoxy-radicals is comparable with the rate via the second pathway; one can only suppose that phenoxy-radicals disappear via disproportionation to low-molecular-weight products. The solution of these problems constitutes an important step in the creation of a theoretical basis for the stabilisation of polymers by organophosphorus compounds.

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Association of Hydrocarbon Hydroperoxides

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The results of studies on the association of hydrocarbon hydroperoxides and the formation of their complexes with alcohols and aromatic, dienic, and olefinic hydrocarbons are reviewed. The role of the intermolecular hydrogen bond in the decomposition of hydrocarbon hydroperoxides is demonstrated.
The bibliography includes 53 references.

CONTENTS

1. Introduction
2. Self association of hydrocarbon hydroperoxides
3. Intramolecular hydrogen bonds in hydroperoxides
4. Intermolecular hydrogen bonds in "hydrocarbon hydroperoxide-proton acceptor" complexes
5. The role of the intermolecular hydrogen bond in the decomposition of hydrocarbon hydroperoxides

1. INTRODUCTION

The oxidation of hydrocarbons by molecular oxygen (autoxidation) constitutes an important method for the industrial preparation of valuable oxygen-containing compounds. Numerous studies on the liquid-phase oxidation of various hydrocarbons have now firmly established that hydroperoxides are the first stable products of their oxidation[1-5]. The molecules of organic substances with a hydroxy-group (alcohols, phenols, hydroperoxides, etc.) are known[6,7] to be capable of associating with one another and with the molecules of other compounds by hydrogen bonding, the presence of which has a significant effect on the reaction kinetics. The study of the association processes of hydroperoxides and their derivatives makes it possible to assess more fully the results obtained in the liquid-phase oxidation of hydrocarbons and also to suggest radical improvements to the process. Hydroperoxides play a fundamental role in polymer oxidation and degradation processes, promoting chain branching. A very important factor here is that the branching efficiency, i.e. the decomposition rate constants and the number of radicals formed per decomposition step, depends on the physicochemical state of the hydroperoxide. The association equilibrium constants enter into all the kinetic equations and therefore the knowledge of these constants and of the coordination numbers is always essential. In the present paper an attempt is made to review data obtained in the study of the association of hydrocarbon hydroperoxides by ^{1}H NMR and infrared spectroscopy.

2. SELF ASSOCIATION OF HYDROCARBON HYDROPEROXIDES

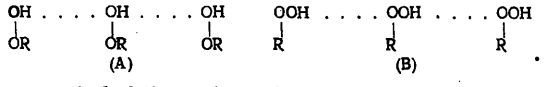
Up to 1950 only the infrared spectra of hydrogen and deuterium peroxides were investigated, the 870 cm^{-1} band being attributed to the O — O bond[8].

The infrared spectra of isopropylphenyl, tetralyl, cyclohexyl, and t-butyl hydroperoxides were recorded in 1951. Sherve et al.[9] attribute three frequencies to the vibrations of the C — O — O — H group: 840, 880 (OOH), and 3600 cm^{-1} ($OH_{stretch}$). The shift of the absorption maximum towards shorter wavelengths on dilution with carbon disulphide indicates the presence of hydrogen bonds in the system. Karyakin et al.[10] established that the vibrations of the hydroperoxy-group C — O — O — H are fairly active in the infrared and have the following characteristic frequencies (mean values):

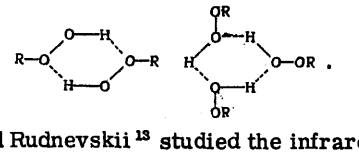
C—O—O—H_{def}	840	cm^{-1}
O—$O_{stretch}$	880	»
C—$O_{stretch}$	1151	»
O—H_{def}	1300	»
O—$H_{stretch}$	3450	»
First overtone	6800	» .

The presence of these frequencies in the infrared spectrum of any compound (primarily two of them: 840 and 3450 cm^{-1}) may serve as an indication that the given compound is a hydroperoxide.

Table 1 lists the vibration frequencies of the C — O — O — H group in various hydroperoxides. A number of studies have been made on the structure of hydroperoxide association complexes. Thus Minkoff[11] suggested on the basis of the stretching vibration frequencies of the OOH group that there are two types of association (A and B) in hydroperoxides (3.01 and 2.92 μm bands):



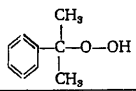
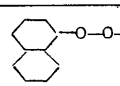
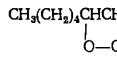
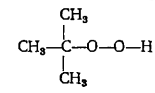
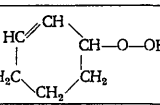
It was concluded that, depending on the nature of the monomer (free hydroperoxide molecules) and the concentration of the hydroperoxide in heptane solution, the isomers of the hydroperoxide exist in dimeric and trimeric forms[12]:



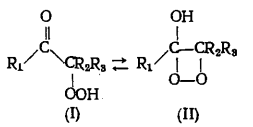
Zharkov and Rudnevskii[13] studied the infrared spectra of t-butyl hydroperoxide solutions in carbon tetrachloride in the range 3200 — 3600 cm^{-1}. They were the first to calculate for hydrocarbon hydroperoxides two association constants from the change in the intensity of the absorption band due to the OH group at 3540 cm^{-1}: the dimerisation constant and the constant for a higher degree of association, together with the dimerisation energy (6.3 ± 1.0 kcal $mole^{-1}$) and the energy of further association (2.8 ± 0.7 kcal $mole^{-1}$). The authors put forward a mechanism for the association of t-butyl hydroperoxide which includes the formation of a cyclic dimer via two hydrogen bonds

with subsequent linear association which probably takes place via the oxygen atoms of the hydroperoxy-groups in the cyclic dimer not involved in hydrogen bonding.

Table 1. C—O—O—H vibration frequencies in the infrared spectra of various hydroperoxides[10].

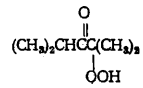
Hydroperoxide	Structural formula	Wave number, cm^{-1}					
		C—O—O—H def.	O—O stretch	C—O stretch.	O—H def.	O—H stretch	O—H first overtone
Isopropylphenyl hydroperoxide		837	881	1155	1325	3450	6740
Tetralyl hydroperoxide		833	885	1150	1300	3380	6840
Decalyl hydroperoxide		837	873	1155	1310	3400	6900
Hydroxymethyl hydroperoxide		840	880	no data	no data	3400	6800 6450
Heptyl hydroperoxide		862		1135	1300	3450	no data
t-Butyl hydroperoxide		846	888	1194	1365	3520	ditto
Cyclohexenyl hydroperoxide		838	856	1160	1305	3450	»
Hydrogen peroxide	H—O—O—H		870	—	1370	3417	»

In recent years the proton magnetic resonance method (^{1}H NMR) has been widely used in the study of hydrogen bonds[14-20]. The ^{1}H NMR chemical shifts of a number of alkyl hydroperoxides were first measured by Japanese investigators[7]. The proton resonance in the OOH group occurs at a lower field than the proton resonance in the CH_3 group approximately by 9.06 p.p.m. (at a working frequency of 27 030 MHz and H_0 = 6300 G). The signal of the hydroperoxy-proton is close to that of the carboxy-group in aliphatic acids (9.9 — 10.3 p.p.m.), occurring in a lower field than the OH proton signal in alcohols (3.7 — 4.44 p.p.m.). The shift of the signal due to the OOH proton as a function of concentration is attributed to the formation of a hydrogen bond. Richardson and Steed[18] studied the structure of α-ketohydroperoxides and also the intermolecular and intramolecular hydrogen bonds in these compounds. They established that the equilibrium in reaction (1) is fully displaced to the left:

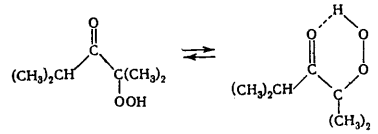


(I) (II) (1)

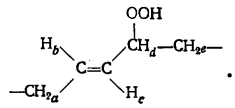
The proton magnetic resonance spectrum of the compound



shows that the proton linked to oxygen gives rise to a signal at low field (9.39 p.p.m. for an 11% solution in carbon tetrachloride), characteristic of the hydroperoxy-group. This finding led to the conclusion that the compound is most likely to exist in the hydroperoxy-form (I) [Eqn. (1)]. On the basis of the infrared spectra, the authors calculated the enthalpy (−1.45 kcal mole^{-1}), free energy (−0.12 kcal mole^{-1}), and entropy (−4.3 e.u.) of the monomer — dimer equilibrium for form (I). The low enthalpy for form (I) can be explained by the formation of a strong intermolecular hydrogen bond according to the following scheme:

 (2)

According to the infrared spectroscopic data, the energy of this bond is −1.86 kcal mole^{-1}. In the ^{1}H NMR spectra of the monohydroperoxides of oleic and linoleic acid esters[19], the hydroperoxy-group gives rise to a broad signal at 8.92 p.p.m. (30 — 40% solution in carbon tetrachloride) and the infrared spectrum shows a band due to the vibrations of the OH group at 3440 cm^{-1}. These hydroperoxides probably have the following structure:



The chemical shifts of the individual groups of protons and the spin — spin coupling constants are listed below:

δ_a, p.p.m.	δ_b, p.p.m.	δ_c, p.p.m.	δ_d, p.p.m.	δ_e, p.p.m.	J_{ab}, Hz	J_{bc}, Hz	J_{cd}, Hz	J_{ac}, Hz	J_{bd}, Hz
2.10	5.60	5.30	4.11	1.44	±6.25	±15.59	±8.04	±0.96	±1.17

The splitting constant (15.6 Hz) confirms that the (*b*) and (*c*) protons are in the *trans*-position. In the spectrum of 1-tetralyl hydroperoxide the signal due to the hydroperoxy-proton is at 8.65 p.p.m., while in the spectrum of the monohydroperoxide of methyl-linoleic acid prepared in different ways the signal is at 9.0 and 8.8 p.p.m. Kucher et al.[20] studied the dependence of the chemical shifts of the proton in the OOH group of isopropylphenyl hydroperoxide on its concentration in various solvents: carbon tetrachloride, isopropylbenzene, and nitrobenzene. Extrapolation of the concentration curve (in carbon tetrachloride) to infinite dilution yields the chemical shift δ = 6.55 p.p.m., while in the pure hydroperoxide δ = 8.62 p.p.m. The authors estimated the dimer ⇌ monomer equilibrium constants from the slope of the $\delta = f(c)$ concentration curve at infinite dilution and obtained a value of 19.5.

The self-association processes of isopropylphenyl, t-butyl, and t-pentyl hydroperoxides have been analysed on the basis of ^{1}H NMR data[21-23].

The thermodynamic parameters of the hydrogen bonds have been calculated from the temperature and concentration variation of the chemical shift of the proton in the

OOH group of hydroperoxides in an inert solvent (Table 2). It has been shown (see also Zharkov and Rudnevskii[13]) that the self-association of hydroperoxides takes place via the formation of cyclic dimers with subsequent linear association of the dimer with hydroperoxide molecules. The calculated enthalpies of formation of the hydrogen bond in hydroperoxides makes it possible to compare them in terms of the strength of the hydrogen bond with other classes of compounds and to devise a general mechanism of the self-association of hydroperoxide molecules. The hydrogen bond in hydroperoxides is weaker than in other compounds containing hydroxy-groups (alcohols, phenols, and acids).

Table 2. Thermodynamic parameters for the formation of hydrogen bonds by hydroperoxides[21,22].

Hydroperoxide	K_{dim} at 21°C (p.p.m.)$^{-1}$	$K_{subs.\ assn.}$ at 21°C, (p.p.m.)$^{-1}$	$-\Delta H_{dim}$, kcal mole^{-1}	$\Delta H_{subs.\ assn.}$ kcal mole^{-1}	$-\Delta S_{dim}$, cal mole^{-1} deg^{-1}	$-\Delta S_{subs.\ assn.}$, cal mole^{-1} deg^{-1}
t-Butyl hydroperoxide	19±2	180±20	6.6±1	3±1	17±2	0±3
t-Pentyl hydroperoxide	18±2	180±15	6.5±1	3±1	17±2	0±2
Isopropylphenyl hydroperoxide	15±2	146±15	7.7±1	2.2±1	21±3	2±3

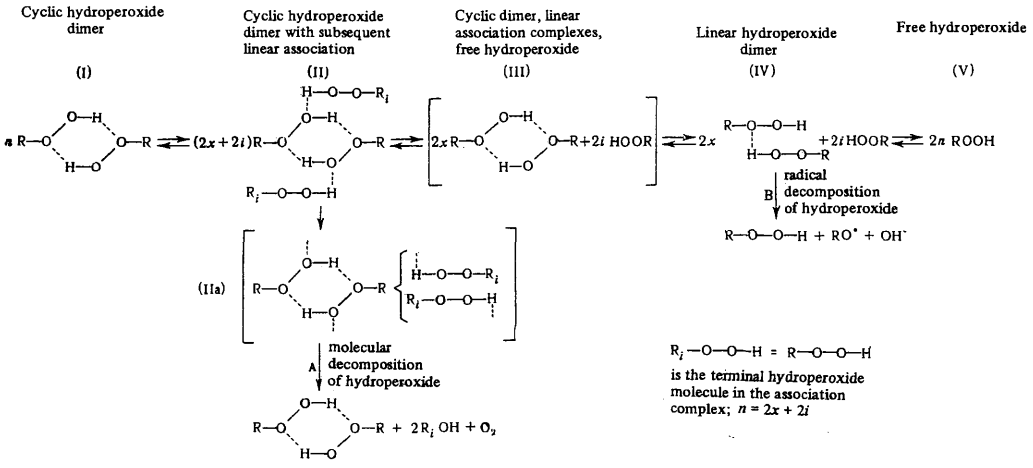
The mechanism of the self-association of hydroperoxide molecules devised by the authors is given below[23]. Generally speaking, one can suggest that at comparatively low temperatures the hydroperoxide exists in forms (I) — (V). However, examination of the relative equilibrium constants K_{12} for the monomer ⇌ cyclic dimer equilibrium [forms (V) and (I)] and the equilibrium constants for the subsequent linear association [forms (I) and (II)] at different temperatures showed that, with decrease of temperature, K_{12} increases faster than does K.[21,22] One should then expect that under certain conditions the constants will become equal (for example, near −40°C for isopropylphenyl hydroperoxide) and that at lower temperatures dimerisation will predominate [form (I)].[23]

With increase of temperature, one of the dimers of form (I) decomposes with formation of form (II). It was found that the enthalpy of formation of the overall hydrogen bond in the cyclic dimer is 6 — 8 kcal mole^{-1}, while that for the hydrogen bond formed in subsequent association is only 2 — 3 kcal mole^{-1}. In its turn form (II) can dissociate into a cyclic dimer and the linear association complex [forms (III) and (IV)]. The cyclic dimer decomposes further into form (IV) and then into form (V).

The formation of a hydrogen bond is known[24] to weaken the H — O and O — O covalent bonds in the molecule of the proton donor and to strengthen the bonds adjoining the oxygen atom in the acceptor molecule. Thus in the hydroperoxide molecule, which is a donor in form (IV), the weakest O — O bond is weakened further by the formation of an intermolecular hydrogen bond. This leads to a cleavage of only one hydroperoxide molecule in form (IV) via the familiar mechanism (see the above mechanism, reaction B) of the unimolecular decomposition of the hydroperoxide with formation of free radicals.

In the association complex comprising the cyclic hydroperoxide dimer with subsequent linear associations [form (II)], the terminal hydroperoxide molecules may be in the immediate vicinity of one another owing to their polar interaction. Moreover, in these molecules, as in form (IV), the O — O bonds are weakened. All these factors suggest that both hydroperoxide molecules decompose simultaneously without the formation of free radicals (reaction A), in agreement with the usually observed second order of the thermal decomposition reaction of hydroperoxides[26]. The second order decomposition reaction of hydroperoxides is observed at high hydroperoxide concentrations, i.e. when association complexes of type (II) predominate in solution. The main products of reaction A are an alcohol and molecular oxygen. The only products of the thermal decomposition of t-butyl hydroperoxide (95 — 100°C) are trimethylmethanol and oxygen[27]. Dimethylphenylmethanol and oxygen were also found in the products of the thermal decomposition of isopropylphenyl hydroperoxide[28].

The mechanisms of the unimolecular and bimolecular thermal decomposition of hydroperoxides discussed above lead to the conclusion that the hydroperoxide molecules, which behave as proton acceptors in forms (II) and (IV),



Mechanism of the self association and the uni- and the bi-molecular decomposition of hydrocarbon hydroperoxides in inert solvents.

function as reaction catalysts ("autocatalysis"). In the cyclic dimer the hydrogen bonds are stabilised in the six-membered ring where the covalent bonds are not weakened, since the effects of the hydrogen bonds cancel out. This leads to the conclusion that the cyclic hydroperoxide dimer is the most stable association complex from the standpoint of the thermal stability of hydroperoxides. The thermal stability of the hydroperoxide in form (I) is close to that of the free hydroperoxide [form (V)].

The relative stabilities of the cyclic dimers of various hydrocarbon hydroperoxides are determined by the energy of the hydrogen bonds in the hydroperoxide molecules involved in their formation. The higher the hydrogen bond energy, the more stable the ring. Thus the equilibrium between forms (I) and (IV) of the hydroperoxides forming stable rings is displaced to the left and in this case the probability of the formation of form (IV) is lower than for hydroperoxides forming less stable rings.

On this hypothesis, isopropylphenyl hydroperoxide (ΔH = 7.7 kcal mole^{-1}) should have a higher thermal stability than t-butyl hydroperoxide (ΔH_{12} = 6.6 kcal mole^{-1}) and t-pentyl hydroperoxide (ΔH_{12} = 6.5 kcal mole^{-1}). On the other hand, the higher the hydrogen bond strength in linear association complexes of form (II) ($\Delta\bar{H}$ = 3.0 kcal mole^{-1} for t-pentyl and t-butyl hydroperoxides and $\Delta\bar{H}$ = 2.2 kcal mole^{-1} for isopropylphenyl hydroperoxide), the greater the shift, other conditions being equal, of the equilibrium between forms (II) and (III) towards form (II), in which two $R_i-O-O-H$ molecules are in a position energetically favourable for decomposition and where in addition the O — O bonds are weakened owing to the stronger hydrogen bond.

From this standpoint, isopropylphenyl hydroperoxide should also have a higher thermal stability than t-pentyl and t-butyl hydroperoxides.

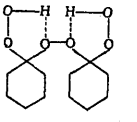
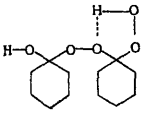
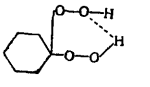
Conclusions concerning the different thermal stabilities of hydroperoxides based on the properties of the hydrogen bond are consistent with thermal stability data. Thus pure isopropylphenyl hydroperoxide is stable in saturated hydrocarbon solutions at 130 — 140°C,[28] while t-butyl hydroperoxide is cleaved at an appreciable rate at a temperature as low as 90°C.[29] It is also known[30] that t-pentyl hydroperoxide decomposes in octane at 110°C.

3. INTRAMOLECULAR HYDROGEN BONDS IN HYDROPEROXIDES

Hydroperoxides can form intramolecular hydrogen bonds in addition to addition to intermolecular complexes. The intramolecular hydrogen bond in isopropylphenyl hydroperoxide between the OOH group and the π electrons of the aromatic ring has been investigated by infrared spectroscopy[31]. In the infrared spectrum the OH absorption band consists of a doublet with maxima at 3497 and 3530 cm^{-1}. The 3530 cm^{-1} band was assigned to the vibrations of the free OH group and the 3497 cm^{-1} band to the vibrations of the bound OH group. The authors calculated from the temperature variation of the intensities of these bands that the energy of the intramolecular hydrogen bond was 0.9 ± 0.10 kcal mole^{-1}. The presence of an intramolecular hydrogen bond between the OOH group in isopropylphenyl hydroperoxide and the aromatic π electrons was confirmed[32].

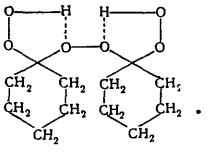
Terent'ev and Antanovskii studied the intramolecular hydrogen bonds in a number of hydroperoxides[33,34]. Table 3 lists the shifts $\Delta\nu$ of the band due to the C — O — O — H group on formation of an intramolecular hydrogen bond and the bond energies E_H. The authors calculated E_H for di-(1-hydroperoxycyclohexyl) peroxide from the intensity of the single absorption band at 3435 cm^{-1}, characteristic of its C — O — O — H group.

Table 3. The shifts $\Delta\nu$ of the bands due to the C — O — O — H group on formation of an intramolecular hydrogen bond and the intramolecular hydrogen bond energies[34] E_H.

Hydroperoxide	$\Delta\nu$, cm^{-1}	E_H, kcal mole^{-1}
Isopropylphenyl hydroperoxide	33 28	0.9±0.1[31]
Tetralyl hydroperoxide	28	0.9±0.1
Diphenylethyl hydroperoxide	30	0.96±0.11
	107	7.0±0.5
	172	11.2±0.8
	112	7.3±0.5

The occurrence of a strong intramolecular hydrogen bond in α-keto hydroperoxides was pointed out earlier[18].

Di-(1-hydroperoxycyclohexyl) peroxide was investigated by NMR[35]:



The chemical shift of the hydroperoxy-proton does not change in the concentration range 0.2 — 0.01 p.p.m. in carbon tetrachloride solution at 15 — 80°C (9.3 p.p.m.). This value agrees satisfactorily with the δ_a obtained for other hydroperoxides[21,22]. The constancy of the chemical shift of the proton signal of the OOH group in the concentration and temperature range investigated suggests a strong intramolecular hydrogen bond in this compound.

4. INTERMOLECULAR HYDROGEN BONDS IN "HYDROCARBON HYDROPEROXIDE — PROTON ACCEPTOR" COMPLEXES

Like other substances with hydroxy-groups (phenols, alcohols, and acids), hydrocarbon hydroperoxides react with proton acceptors to form hydrogen-bonded association complexes[26]. The formation of the latter may influence the kinetics and mechanisms of reactions involving hydroperoxides which occur in the liquid phase[36]. In this connection the study and experimental determinations of the energy of the hydrogen bonds between hydroperoxides and various proton acceptors is of both theoretical and practical interest.

Systematic studies on the formation of complexes by hydroperoxides with various proton acceptors by spectroscopic methods were begun in 1968. The only earlier study[37] on this problem dealt with the formation of complexes by t-butyl hydroperoxide with different acceptors: styrene, benzene, *o*-dichlorobenzene, and chlorobenzene.

Table 4. The frequencies, integral intensities, and association constants of the hydrogen-bonded complexes of isopropylphenyl hydroperoxide[38].

Acceptor	ν_{OH}, cm^{-1}	$\Delta\nu_{OH}$, cm^{-1}	$\Delta\nu_{1/2}$, cm^{-1}	$10^{-3}A$, litre mole^{-1}cm^{-2}	K, litre mole^{-1}
Carbon tetrachloride	3551	—	30	7.7	—
Chloroform	3530	21	58	9.7	—
o-Dichlorobenzene	3522	29	58	11.7	—
Methylene chloride	3521	30	55	11.8	—
Chlorobenzene	3510	41	54	11.9	—
Iodobenzene	3504	47	72	14.5	—
Benzene and its homologues	3503—3476	48—75	43—55	13.2—14.9	0.17—0.35
Nitrobenzene	3490	61	92	21.9	—
Nitromethane	3485	66	98	22.3	—
Anisole	3435	116	90	25.9	0.46
Acetophenone	3432	119	—	—	2.28
Benzoquinone	3430	121	—	—	1.25
Benzophenone	3425	126	—	—	1.67
Acetonitrile	3417	134	113	30.5	—
t-Butyl peroxide	3400	151	120	35.3	0.65
Acetone	3375	176	—	—	1.92
Cyclohexanone	3365	186	—	—	2.50
Dioxan	3357	194	133	53.2	2.20
Ethyl ether	3335	216	135	60.0	—
Isopropyl ether	3326	225	122	51.2	1.78

Shabalin and Kiva[38] examined the proton-donating capacity of isopropyl hydroperoxide and established that it is intermediate between those of alcohols and phenols. They investigated by infrared spectroscopy the complexes of isopropylphenyl hydroperoxide formed via hydrogen bonding with different proton acceptors. Table 4 lists the frequencies and integral intensities for the infrared spectra of the isopropylphenyl hydroperoxide complexes. Assuming that in all cases the interaction of isopropylphenyl hydroperoxide with a proton acceptor yields a 1 : 1 complex, the authors calculated the association constants K for certain systems (Table 4) using the equation

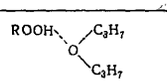
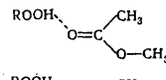
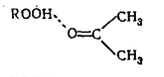
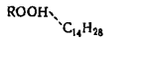
$$K=\frac{1-\frac{D}{D_0}}{\frac{D}{D_0}\left[C_a-C_{hp}\left(1-\frac{D}{D_0}\right)\right]}, \qquad (3)$$

where D_0 and D are the optical densities of the bands due to the free OH groups before and after the addition of the acceptor, C_{hp} is the initial molar concentration of the hydroperoxide, and C_a the molar concentration of the acceptor.

The same workers[39] used infrared spectra to calculate the energies of the hydrogen bonds between isopropylphenyl hydroperoxide and different acceptors. Shabalin et al.[32] also showed that an intermolecular hydrogen bond is formed between the isopropylphenyl hydroperoxide proton and the π electrons in the rings of aromatic solvents. The shift of the band due to bound OH groups is linearly related to the ionisation potential of the aromatic solvent.

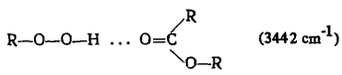
The intermolecular hydrogen bonds have been investigated and the bond energies for the t-butyl hydroperoxide — isopropyl ether and t-butyl hydroperoxide — pentyl acetate systems in carbon tetrachloride have been calculated in the range 20 — 50°C (Table 5)[34].

Table 5. The shifts $\Delta\nu$ of the band due to the C — O — O — H group on formation of the hydrogen bond and the hydrogen bond energy E_H (ROOH = t-butyl hydroperoxide)[34].

Complex	$\Delta\nu$, cm^{-1}	E_H, kcal mole^{-1}
	220	3.7±0.4
	120	3.3±0.3
	172	*
	60	—

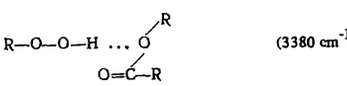
*E_H could not be determined experimentally, since in this system there is a chemical reaction between the donor and the acceptor[40].

On the basis of the infrared spectra, the authors suggest that in the system with the ester, apart from complexes of the type



(3442 cm^{-1})

the complexes



(3380 cm^{-1}),

are formed to a very small extent.

The energy of the hydrogen bond was calculated from the van't Hoff equation:

$$\ln\frac{D_1^H D_2^{bound}}{D_2^H D_1^{bound}}=\frac{E_H(T_2-T_1)}{R\ T_2\ T_1}, \qquad (4)$$

where D^H and D^{bound} are the optical densities of the absorption bands due to the "free" and bound (by hydrogen bonding) C — O — O — H groups at two temperatures.

The possibility of association via hydrogen bonding with aromatic amines was pointed out by Ivanov[41], who established by infrared spectroscopy that in the interaction between aniline and hydroperoxides, which are intermediates in the autoxidation of hydrocarbons, in particular with isopropylphenyl hydroperoxide, these substances undergo association at low temperatures with formation of the following molecular compound:

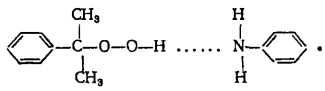


Table 6. Frequencies and half-widths of the infrared absorption band of the OH group and the energies of the intermolecular hydrogen bonds between hydrocarbon hydroperoxides and aromatic solvents.

Solvent	Isopropylphenyl hydroperoxide			t-Butyl hydroperoxide			t-Pentyl hydroperoxide		
	ν, cm^{-1}	$\Delta\nu_{1/2}$, cm^{-1}	ΔE, kcal $mole^{-1}$	ν, cm^{-1}	$\Delta\nu_{1/2}$, cm^{-1}	ΔE, kcal $mole^{-1}$	ν, cm^{-1}	$\Delta\nu_{1/2}$, cm^{-1}	ΔE, kcal $mole^{-1}$
o-Dichlorobenzene	3552	58	0.86	3530	46	0.80	3531	30	0.80
Chlorobenzene	3510	54	1.22	3523	53	1.03	3529	40	0.98
Benzene	3508	40	1.46	3511	46	1.47	3513	45	1.41
Toluene	3500	46	1.50	3508	48	1.53	3510	42	1.51
m-Xylene	3491	48	1.82	3502	49	1.75	3500	46	1.84
Pseudocumene	3484	52	1.98	3496	50	1.95	3497	48	1.95
Durene	3481	55	2.28	—	—	—	—	—	—
Pentamethyl benzene	3476	—	2.26	—	—	—	—	—	—

Recently the authors of the review used NMR and infrared spectroscopy to study the formation of hydrogen bonds in complexes of hydroperoxides with various proton acceptors. Thus more detailed studies were made of the complexes of hydrocarbon hydroperoxides with aromatic solvents[42]. The data in Table 6 shows that the stability of the complexes of hydroperoxides with aromatic solvents increases with the degree of substitution of the protons in the benzene ring by alkyl groups (CH_3). The chemical shifts of the proton involved in hydrogen bonding in the complexes of hydroperoxides with aromatic solvents are satisfactorily correlated with the ionisation potentials of the latter and also with the frequency shifts of the OOH group in the complexes. The higher thermal stability of hydrocarbon hydroperoxides in aromatic solvents (in the presence of an excess of the solvent) compared with aliphatic solvents can be accounted for by the formation of weak intermolecular complexes via hydrogen bonds between the hydroperoxide and the aromatic solvent.

Since the energy of the hydrogen bond in these complexes is lower (Table 6) than in the self-association of hydroperoxides (Table 2), the O — O bond in the hydroperoxide molecule in the complex is weakened less than in the linear hydroperoxide dimer, in consequence of which the hydroperoxide molecule in the complex is more stable than in the linear dimer.

The hypothesis that "aromatic hydrocarbon–hydroperoxide" complexes exist also explains the higher thermal stability of aliphatic-aromatic hydroperoxides compared with aliphatic hydroperoxides dissolved in an inert solvent, for example a saturated aliphatic hydrocarbon.

The formation of complexes of hydrocarbon hydroperoxides with amines has been discussed[43]. The interest in systems comprising hydroperoxides and amines is due to a number of factors. In most cases such systems are used as initiators of polymerisation processes. They are studied in order to find ways of preventing the oxidative degradation of polymers; in many cases amines are employed as inhibitors of the thermal polymerisation of monomers.

NMR data have led to a mechanism of the association of hydrocarbon hydroperoxides with amines using triethylamine as an example. At low triethylamine concentrations, association of the type OH...O (hydroperoxide — hydroperoxide) predominates, at high triethylamine concentrations the N...HO association is dominant, and in the intermediate region the dominant form is

$$R_3NH^+ \ldots {}^-OOR_1$$
$$\vdots$$
$$HOOR_1 .$$

The existence of dimers formed via a polar interaction may be expected in solution, the screening decreasing in the sequence

$$\sigma(OH \ldots O) \simeq \sigma(N \ldots HO) > \sigma(NH^+ \ldots {}^-O).$$

The low thermal stability of hydrocarbon hydroperoxides in the presence of amines and the lower activation energy for their decomposition can be explained by the formation of a strong hydrogen bond between the hydroperoxide and the amine or its salt, which facilitates the cleavage of the hydroperoxide molecule at the weak O — O bond.

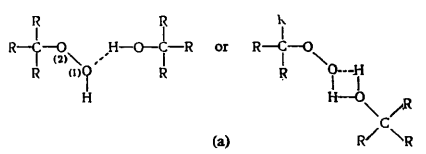
One of the final products of the decomposition of hydrocarbon hydroperoxides is an alcohol. Their interaction with hydroperoxides via hydrogen bonding may influence the rate of decomposition of the hydroperoxide. The formation of complexes by tertiary hydrocarbon hydroperoxides with a number of alcohols has been studied[35] by ^1H NMR. In all the complexes investigated, the energy of the "alcohol — hydroperoxide" hydrogen bond

$$R{-}O{-}O{-}H$$
$$\vdots$$
$$H{-}O{-}R$$

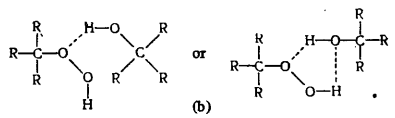
(calculated from the signal of the proton in the alcoholic OH group) is 3.5 — 4.5 kcal $mole^{-1}$ and the energy of the "hydroperoxide — alcohol" bond (ROOH...$\overset{H}{\underset{|}{O}}$ — R) (calculated from the signal of the proton in the hydroperoxide OOH group) is about 2.5 kcal $mole^{-1}$. Using the thermodynamic data obtained for the association of hydrocarbon hydroperoxides, alcohols, and their complexes, the following sequence may be established in terms of the strength of the hydrogen bond:

$$\left[\begin{matrix}\text{Hydroperoxide}\\ \text{Alcohol}\end{matrix}\right] \simeq \left[\begin{matrix}\text{Hydroperoxide}\\ \text{Hydroperoxide}\end{matrix}\right] < \left[\begin{matrix}\text{Alcohol}\\ \text{Hydroperoxide}\end{matrix}\right] < \left[\begin{matrix}\text{Alcohol}\\ \text{Alcohol}\end{matrix}\right]$$

The dependence of the chemical shifts of the OOH and OH protons in the hydroperoxide — alcohol mixture on the alcohol concentration leads to the possibility of identifying the oxygen atom of the hydroperoxide involved in the association with the alcohol. Generally speaking, one can suppose that the hydrogen bond between the alcohol and the hydroperoxide involves both the first oxygen atom of the hydroperoxide:



and its second oxygen atom:



(b)

The "alcohol — hydroperoxide" hydrogen bond is approximately equally strong for all alcohols. This conclusion is consistent with the finding that

$$\delta^{OH}_{[alcohol]\to 0} \simeq const.$$

It is extremely likely that the hydrogen bond between the alcohol and the hydrogen peroxide involves the first oxygen atom of the latter, since in this case the steric factor is less important. This is confirmed indirectly by the finding that at low hydroperoxide concentrations the "alcohol — hydroperoxide" hydrogen bonds (ROOH...$\overset{H}{O}$—R) depend on the structure of the alcohol (Table 7).

Table 7.

Alcohol	$\Delta\delta_{OOH}$, p.p.m.
C_2H_5OH	2.02
$(CH_3)_2CHOH$	2.00
$(CH_3)_3COH$	1.90
$CH_3(CH_2)_4OH$	1.80
$C_6H_5(CH_3)_2COH$	1.50

$\Delta\delta_{OOH}$ decreases with increasing importance of the steric factor in the alcohol. If the "alcohol — hydroperoxide ("σ") bond involves the second oxygen atom (the position of which is analogous to that of the oxygen atom in the alcohol), a similar relation between $\delta^{OH}_{[alcohol]\to 0}$ and the steric factor of the hydroperoxide would be expected.

The formation of complexes via hydrogen bonds between tertiary hydroperoxides and a ketone and an ether was investigated[43] and the composition of the complexes and their influence on the decomposition of the hydroperoxides were discussed. A study was also made of the complexes of t-butyl hydroperoxide with a number of olefins and dienes formed by hydrogen bonding between the hydroperoxy-proton and the π electrons of the double bond[35]. It has been shown by infrared spectroscopy that the stability of the complexes formed increases with the basicity of the olefins, i.e. with the number of alkyl substituents at the double bond.

The decomposition and dissociation of the complex ROONa.ROOH via the mechanisms[44]

$$\text{(decomposition)} \qquad ROONa \cdot ROOH \to ROONa + ROH + {}^1/_3O_2, \qquad (5)$$

$$\text{(dissociation)} \qquad \left[\begin{matrix} ROONa \\ \vdots \\ HOOR \end{matrix}\right] \rightleftarrows ROONa + ROH, \qquad (6)$$

where R = $(CH_3)_2CC_6H_5$, were investigated by ^1H NMR. In the decomposition of the complex via reaction (5), the ^1H NMR spectrum shows a combined signal due to the hydroperoxide OOH and alcoholic OH groups. The rate constants for the decomposition of the hydroperoxide in the complex and the activation energy for the decomposition process (E = 16.5 ± 1.0 kcal mole^{-1}) were calculated from the variation of the overall chemical shift due to the hydroxyl protons with reaction time and temperature. The reaction was found to be of first order with respect to the hydroperoxide in dilute solutions of the complex.

In dilute solutions the monomer of the complex may dissociate via mechanism (6). The dissociation constant of the complex $K_{30°} = 4.93 \times 10^{-2}$) and its enthalpy of dissociation (ΔH = −12.7 ± 1 kcal mole^{-1}) were calculated from the temperature variation of the chemical shift of the OOH proton in the complex at its different concentrations. The hydrogen bond in the complex of isopropylphenyl hydroperoxide and its sodium salt is much stronger than that formed in the self dissociation of isopropylphenyl hydroperoxide. The low thermal stability of the hydroperoxide in the ROONa.ROOH complex compared with the "pure" hydroperoxide can be accounted for by the effect of the stronger hydrogen bond and hence by the greater weakening of the O — O bond. "Pure" isopropylphenyl hydroperoxide is stable in solution in saturated hydrocarbons up to 130°C, while the hydroperoxide in the ROONa.ROOH complex decomposes at an appreciable rate already at 30°C.

5. THE ROLE OF THE INTERMOLECULAR HYDROGEN BOND IN THE DECOMPOSITION OF HYDROCARBON HYDROPEROXIDES

The study of the kinetics of the liquid-phase oxidation of hydrocarbons showed[45,46] that hydroperoxides, which are formed as intermediates, are cleaved by a unimolecular mechanism under certain conditions and by a bimolecular mechanism under others. The decomposition of the hydroperoxide via two mechanisms has been explained by the formation of a hydrogen bond in hydroperoxide solutions[23]. The addition to the hydrocarbon undergoing oxidation of substances capable of associating with hydroperoxides and thereby rupturing the hydrogen bonds between hydroperoxide molecules leads to a change from bimolecular to unimolecular decomposition[47].

Since hydroperoxides form hydrogen bonds with other oxygen-containing compounds, one may expect that certain oxidation products will influence the decomposition of hydroperoxides and the rate of formation of radicals (by forming various complexes with the hydroperoxide). This hypothesis is confirmed by the finding that the decomposition of hydroperoxides is facilitated in the presence of alcohols[29], organic acids[48], and other compounds capable of forming association complexes with hydroperoxides via intermolecular hydrogen bonds.

A study of the oxidation of decane showed[48] that the linear relation between the rate of branching of the radical chains and the hydroperoxide concentration obtains only in the early stages of the reaction, where the decomposition products still have almost no influence on the reaction. The further non-proportional increase of the concentration of radicals is related to the formation of oxidation products, for example acids. This phenomenon has been studied[49] in the decomposition of n-decyl hydroperoxide in the presence of caproic acid. The authors suggest that the decomposition of the hydroperoxide into radicals takes place via the intermediate formation of the complex

$$ROOH + n\,R'COOH \overset{k}{\rightleftarrows} ROOH \ldots R'COOH \overset{k'}{\to} RO^{\cdot} + \dot{O}H + R'COOH. \qquad (7)$$

Owing to the formation of hydrogen bonds in this complex, the dissociation of the O — O bond in the hydroperoxide molecule is facilitated, which leads to the formation of radicals. The activation energy for the decomposition of

the hydroperoxide in the ROOH...RCOOH complex is 16.1 kcal mole^{-1}, which is much less than the activation energy for the decomposition of the hydroperoxide in the absence of an acid (23.8 kcal mole^{-1}).

It has also been noted in the literature that the kinetics of the oxidation of hydrocarbons are influenced by solvents in which the oxidation is carried out[50]. The presence in the reaction mass of solvents capable of forming hydrogen bonds with the hydroperoxide leads to a rearrangement of the structure of the association complexes formed with participation of the hydroperoxide which in turn alters the rate of initiation of the oxidation of hydrocarbons. Similar views were also put forward before. For example, it was suggested[51] that pyridine be employed as a kind of catalyst for the oxidation of hydrocarbons, since it forms a hydroperoxide — pyridine complex the decomposition of which at the O — O bond is fairly rapid. The rate constant for the decomposition of t-butyl hydroperoxide into radicals is a factor of 200 higher in the presence of pyridine compared with the pure hydroperoxide. A study of the decomposition of t-butyl hydroperoxide in cyclohexanone showed that the presence of cyclohexanone in the reaction mass greatly accelerates (by a factor of 7 — 10) the decomposition of the hydroperoxide into radicals. The infrared spectra indicate the formation of a complex[52].

The thermodynamic data obtained for complexes of hydrocarbon hydroperoxides with various compounds and the literature data on the activation energies for the decomposition of hydroperoxides have led to a general correlation between the strength of the hydrogen bond in the complex and the activation energy for the hydroperoxide decomposition reaction[53]. With increase of the enthalpy of the hydrogen bond in the hydrocarbon hydroperoxide complexes with various compounds, the activation energy for the decomposition of the hydroperoxide falls. Thus the activation energy for the decomposition of hydroperoxides in aromatic hydrocarbons amounts to 25 — 40 kcal mole^{-1}, while in the presence of amines or in the alkali-catalysed decomposition of hydroperoxides it is 14 — 18 kcal mole^{-1}. A correlation between the chemical shift and the displacement of the stretching vibration frequency of the hydrogen-bonded complexes of hydrocarbon hydroperoxides on the one hand and the activation energy for the decomposition of the hydroperoxides on the other has also been observed.

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Reactivities of Alloxazines and Isoalloxazines

V.M.Berezovskii, L.S.Tul'chinskaya, and N.A.Polyakova

The advances in the chemistry of alloxazines and isoalloxazines in the last 10-12 years have been reflected particularly in the study of their reactivities. The review deals with the reduction, oxidation, and nucleophilic and electrophilic substitution reactions, the reactions of exocyclic amino-groups, the methyl group in the 8-position of the flavine nucleus, and others. The reactivities of alloxazines and isoalloxazines are discussed with reference to quantum-chemical parameters. The bibliography includes 245 references.

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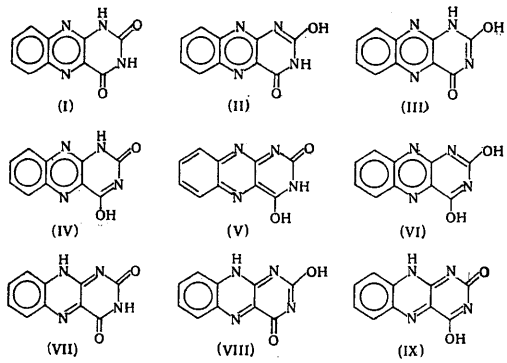
1. INTRODUCTION

Alloxazines and isoalloxazines—2,4-dioxo-1,2,3,4-tetrahydrobenzo[*g*]pteridines—constitute a heterocyclic series of compounds the natural representatives of which [riboflavin (vitamin B_2) and its coenzymes—riboflavin 5′-phosphate or flavin mononucleotide (FMN) and P^1-(riboflavin-5′)-P^2-(adenosine-5′)diphosphate or flavin-adenine dinucleotide (FAD)] combine with a specific protein and fulfil key electron transfer functions in metabolic processes.

However, for a long time after the discovery of riboflavin (1932), which proved to be the basic structural unit of the cofactors of flavin oxidation-reduction enzymatic systems, mainly the synthetic pathways of alloxazines and isoalloxazines and their analogues were investigated[1,2] using the complete flavin system as a basis for the discovery of its essential biological properties. The entire wide variety of the chemical characteristics of compounds of the alloxazine and isoalloxazine series has been demonstrated only in the last 10–12 years. Thus the electronic structures and steric configurations of the riboflavin molecule and of related compounds, the reactivities of ring nitrogen atoms, the capacity of the carbon atoms in the benzene ring for electrophilic substitution, the oxidation of alloxazines to *N*-oxides, the reactions of exocyclic amino-groups and of the methyl group in the 8-position of the flavin nucleus, photochemical reactions, spectroscopic properties of alloxazines and isoalloxazine molecules, etc. have been investigated; the results of the studies of the chemical properties have been interpreted in relation to the principal biochemical function of flavins. The combined studies on the reactivity and its dependence on the π-electronic parameters of the molecule led logically to the determination of the structure of a new flavin cofactor of succinate dehydrogenase—an enzyme which catalyses the dehydrogenation of succinic acid to fumaric acid in the key tricarboxylic acid metabolic energy cycle (the Krebs cycle)—and a new flavin cofactor of another enzyme—monoamine oxidase.

2. TAUTOMERIC FORMS OF ALLOXAZINE AND ISOALLOXAZINE

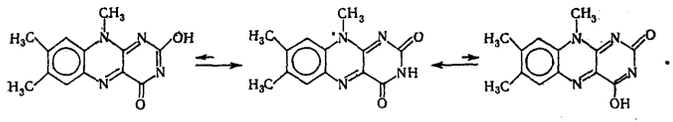
Alloxazine can have 6 possible lactam-lactim tautomeric forms (I)–(VI), while isoalloxazine has only 3 tautomeric forms (VII)–(IX) as a result of the fixation of the electronic configuration by the substitution of the hydrogen atom in the 10-position by an alkyl group:



The problem of the tautomeric forms of heterocyclic compounds is frequently solved by comparing their electronic spectra with those of model compounds having a known structure[3]. However, experimental studies of *N*- and *O*-alkyl derivatives of flavins[4-6] have shown that, owing to the insignificant differences between the absorption spectra, the study of the lactam–lactim tautomerism of such flavins by ultraviolet spectroscopy is impossible[7]. Calculation of the transition energies and oscillator strengths for the tautomeric forms (I)–(IX) by the Pariser–Parr–Pople self-consistent field (PPP SCF)

method also led to the conclusion that the transition from the lactam to the lactim form has little influence on the absorption spectra[8,9].

O-Alkyl, *S*-methyl, and deoxy-derivatives of lumiflavin differ markedly from lumiflavin itself in their basicity: they are fully protonated even in dilute acetic acid[5]. These compounds are relatively unstable and are readily hydrolysed, being easily converted into lumiflavin in the presence of weak oxidants. On this basis, it has been concluded that flavins exist in the lactam form[7] and have virtually no admixture of the hydroxyimino-forms[7,10]; the prototropic equilibrium is apparently fully displaced towards the lactam form[7]:



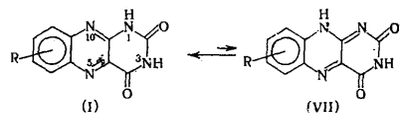
The infrared spectra of a large number of substituted alloxazines and isoalloxazines and their comparison with the spectra of compounds with fixed structures established that both alloxazines and isoalloxazines have the lactam structure in the solid state[11].

By comparing the calculated energies of the upper bonding and lower antibonding orbitals for all possible tautomeric forms of alloxazines and isoalloxazines, Nishimoto[9] showed that the electron affinity of the dioxo-forms is fairly high and that such compounds are effective oxidants. It has been suggested that in biological systems isoalloxazines are capable of tautomeric conversion into the enolic forms as a result of the formation of hydrogen bonds with proteins and thus behave as both electron donors and acceptors in biochemical reactions[9].

It is noteworthy that the π-electron energy of the 4-*C*-enolic form (IX) is higher by 4–5 eV than for the tautomeric 2-*C*-enolic form (VIII), i.e. form (IX) is energetically more favourable[12].

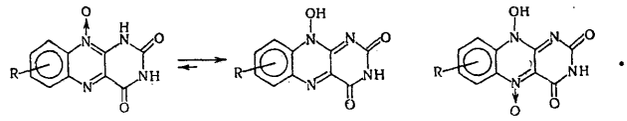
Berezovskii and Aksel'rod studied the possibility of the alloxazine and isoalloxazine tautomerism in many alloxazines[13,14], their 5-*N*-oxides[15], 10-*N*-oxides[13,14], and 5,10-di-*N*-oxides[15]. It was shown[13,14] that the difference between the structure of alloxazines and isoalloxazines, which depends on the $-N_{(5)}=C-C=N_{(10)}-$ (I) and $-N_{(5)}=C-C=N_{(1)}-$ (VII) chromophoric groups, can be established with reasonable certainty by ultraviolet and fluorescence spectroscopic methods.

Comparison of the ultraviolet, infrared, and fluorescence emission spectra of a number of substituted alloxazines with thoes of substances having fixed structures showed[11,13,16] that alloxazines as well as their 5-*N*-oxides (with the N→O bond)[15] have the alloxazine tautomeric structure of type (I). These data are consistent with the results of quantum-chemical calculations by the LCAO-MO method for a number of 7- and 8-substituted alloxazines and isoalloxazines, which indicate that the alloxazine structure (I) is energetically somewhate more favourable than the isoalloxazine structure (VII):[17]

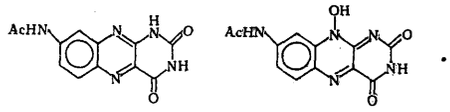


(I) (VII)

On the other hand, the *N*-hydroxy(isoalloxazine)-structure of type (VII) should be assigned to alloxazine 10-*N*-oxides and 5,10-di-*N*-oxides which lack substitutents at the 1-*N* atoms[13,15], in view of the similarity of the fluorescence and absorption spectra of such *N*-oxides with those of isoalloxazines (riboflavin and others):



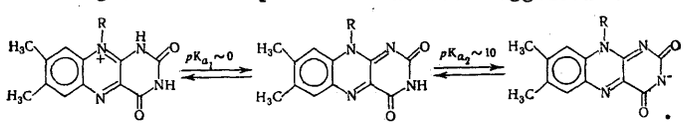
Comparison of the infrared spectra of 8-amino- and 8-dimethylaminoalloxazines established that amino-alloxazines exist in the amino- and not in the imino-form[11]. On the basis of a comparison of the absorption and fluorescence spectra with those of the 8-amino-1,3-dimethyl-alloxazine, which has a fixed structure, one may postulate that in alcoholic solutions 8-aminoalloxazines and their *N*-oxides have the alloxazine structure[14]. 8-Acylamino-alloxazines have the alloxazine structure of type (I) in alcoholic solutions and 8-acylaminoalloxazines *N*-oxides have the isoalloxazine structure of type (VII) with an N–OH group[14]:



Despite the existing extensive experimental results, hitherto no data are available on the interconversion of the tautomers and on the simultaneous presence of different tautomeric forms in solutions .

3. ACID–BASE PROPERTIES

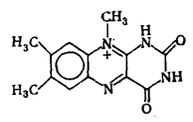
In the oxidised state flavin is weakly amphoteric; the following acid–base equilibrium has been suggested[18]:



The ionisation constants of riboflavin, 2′,3′,4′,5′-tetra-acetylriboflavin, riboflavin 5′-phosphate, and FAD have been determined from measurements of oxidation–reduction potentials[19], fluorescence[20,21] and absorption[19,22] intensities, and also by acid–base titration[23–25]. The following values have been obtained for riboflavin: pK_{a1} = 0,[26] −0.2,[19] and 0.1;[22] pK_{a2} = 9.5,[19] 10.2,[20] 9.95,[24] and 10.[23] The acid dissociation constants of alloxazine and its derivatives with substitutents in the benzene ring have been determined spectrophotometrically (by the method of Geissman and Davis); it was found that the pK_a for these compounds are satisfactorily consistent with the inductive effects of the substituents, the pK_a increasing in the following sequence[22]:

$$8\text{-Cl} < \text{H} < 7.8\text{-di-CH}_3 < 8\text{-NH}_2 .$$

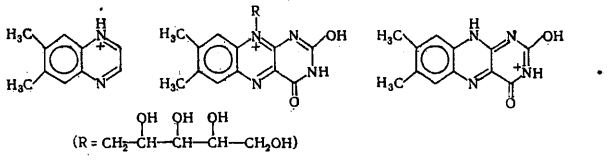
X-Ray diffraction analysis of the structures of riboflavin hydrobromide[27,28] and 10-methylisoalloxazine[29–32] established that in the crystalline state the flavin is protonated at 1-N and the cation has the following structure:



Protonation of the flavin in sulphuric acid results in a considerable hypsochromic shift of the long-wavelength

absorption band and a bathochromic shift of the band in the near ultraviolet, so that they merge into a single band at 390 nm.[7] Comparison of the ultraviolet spectrum of the unsubstituted flavinium cation with those of model alkylflavinium derivatives led Dudley et al.[7] to the conclusion that in aqueous solutions flavins are protonated at 1-N. This agrees with calculations[8,33] according to which the maximum π-electron density is localised at 1-N.

However, later calculations by the self-consistent field (SCF) method[12,34-37], the extended Hückel method[36,38], and also by the simple LCAO-MO method[17] of the distribution of electron density in substituted alloxazines and isoalloxazines established that the highest electron density is concentrated at the oxygen atoms of the carbonyl groups. It is noteworthy that the basicity of atoms of different chemical types is determined not only by electron density but also by the energy of formation of the X—H bond[38]. The similarity of the magnetic circular dichroism spectra of flavinium and 6,7-dimethylquinoxalinium cations has also been used as an argument in support of the proposed structure of the cation[39]; this structure does not conflict with the protonation of riboflavin at the oxygen of the $C_{(2)}$—O carbonyl group:

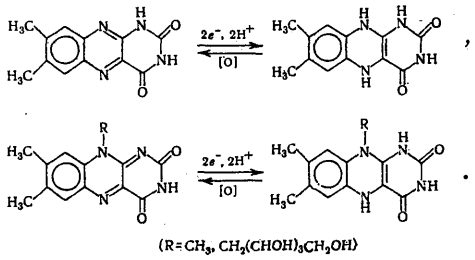


The structure of the monocations of alloxazines and isoalloxazines protonated at the oxygen atom in the 2-position has been proposed on the basis of the disappearance of one of the carbonyl absorption bands (1650 cm^{-1}) in 50% sulphuric acid[40]. The conclusion that alloxazines and isoalloxazines are *O*-protonated agrees with the available data on the protonation of lumazines—substances which are very similar to flavins[41].

Infrared spectroscopy established that, regardless of the nature of the cations, metal salts of flavins have the lactim structure in the solid state[11].

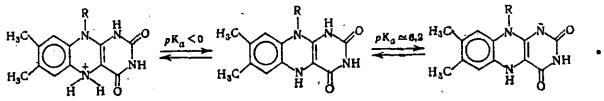
4. REDUCTION

Under aerobic conditions, both alloxazines and isoalloxazines exist in the fully oxidised form, since their oxidation-reduction potentials (for example, −0.21 V for riboflavin) are much lower than the potential of atmospheric oxygen (+0.82 V).[42] Certain reducing agents (sodium hydrosulphite, zinc in acetic or hydrochloric acid, hydrogen in the presence of the palladium or platinum catalyst, etc.) are capable of reducing these compounds under anaerobic conditions to the non-fluourscent 5,10- and 1,5-dihydro-forms[43-47]. In the presence of oxygen, the fully or partly reduced alloxazines and isoalloxazines are reoxidised:



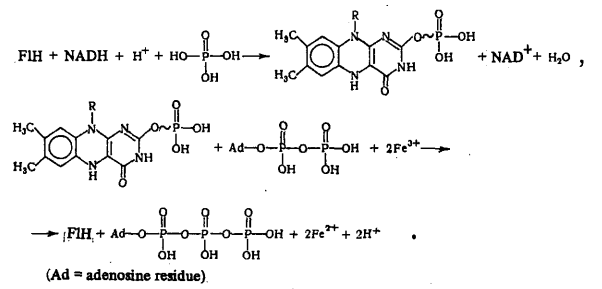
(R = CH_3, $CH_2(CHOH)_3CH_2OH$)

In dilute aqueous solutions the reduced flavins are colourless and in concentrated solutions they are orange-brown[48]. An equation has been formulated for the acid–base equilibria of flavins in the reduced form[18]:



Comparison of the ultraviolet spectra of 1,5-dihydrolumiflavin and its *NN*- and *OO*-dialkyl derivatives established that 1,5-dihydroflavins have the lactam structure, which has also been confirmed by the infrared spectra of a 5-acyl-1,5-dihydrolumiflavin and 1,5-dihydroriboflavin in chloroform[4,7]. However, in contrast to flavins, the conversion of 1,5-dihydroflavins into the lactim form does not involve a considerable energy increase, in agreement with the ease of alkylation at the oxygen atom[7].

It has been suggested that oxidative phosphorylation processes involving flavins (FlH) yield phosphate esters of the lactim form of 1,5-dihydroflavin, which transfer the phosphate group to ADP with formation of ATP:[49,50]

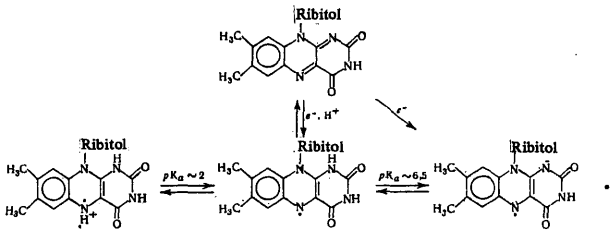


(Ad = adenosine residue)

Since alkylation at 3-N does not affect the acidity of 1,5-dihydroflavin (pK_a = 6,[18] 7.2 [51]), it is believed that the dissociable proton is at 1-N.

On the basis of the analysis of the absorption spectra at different pH, a non-polar molecular structure folded along the $N_{(5)}$—$N_{(10)}$ axis and having the "butterfly wings" conformation has been proposed for 1,5-dihydroflavin[7,10,18]. This non-planar structure of 1,5-dihydroflavins agrees satisfactorily with calculations by the Hückel[52] and self-consistent field[34] methods and has been reliably established by the X-ray diffraction analysis of 5-acetyl-3,7,8,10-tetramethyl-5,10-dihydroisoalloxazine[53] and also 5-acetyl-9-bromo-1,3,7,8,10-pentamethyl-1,5-dihydroisoalloxazine[54,55]; the planes of the benzene and pyrimidine rings are inclined at an angle of 140–160°.[53,56]

In contrast to the two-electron reduction of alloxazines and isoalloxazines discussed above, one-electron reduction of flavins, for example riboflavin, leads to the formation of free radicals—flavosemiquinones[19]:



However, one cannot be certain whether the flavosemiquinones are intermediates[57] in the two-electron reduction or whether they are formed in the interaction between the oxidised and reduced forms of flavins[58]:

$FlH + FlH_3 \rightleftharpoons FlH_2$ (green chloroflavin),

which is more likely, since flavosemiquinones exist in solution in equilibrium with other forms [7,59,60]; at pH 8–9 the concentration of radicals is minimal and the equilibrium is displaced towards the oxidised and reduced forms [61,62]. Fairly stable dimeric complexes are formed from products corresponding to different degrees of reduction [63,64]:

$FlH + Fl\dot{H}_2$ (green verdoflavin),

$Fl\dot{H}_2 + FlH_3$ (carmine red rhodoflavin hydrochloride).

Numerous studies have been made on the one- and two-electron reduction reactions of flavins and on the determination of the structure of flavin radicals [51,65–70].

The reduction of flavins in the dark takes place with only a few electron-donating substrates: NADH, NADPH, and their analogues [71–73], dihydrolipoic acid [74,75]; *cis*- and *trans*-dihydrophthalic acids and their esters [76], and mercaptans [77]. The reaction of flavins (FlH) with NADH and NADPH and with their analogues is of second order and that with dihydrolipoic acid is of first order; the reduction proceeds via a two-electron mechanism [73], rapid dissociation of one of the thiol groups preceding the reduction process. The reduction by dihydrophthalic acids and their esters is a second order reaction of pH > 9. [76] Flavins react with mercaptans according to the mechanism [73,77]

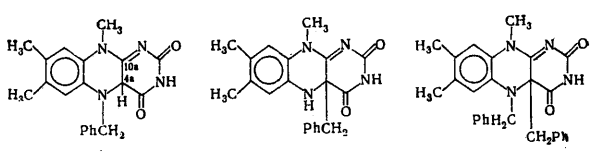
$$2RSH + FlH \rightarrow RSSR + FlH_3 .$$

Under anaerobic conditions, flavins are readily reduced photochemically by many substances which behave as electron donors: ethylenediaminetetra-acetic acid (EDTA) and aminoacids—cysteine, methionine, proline, histidine, etc. [78–83]

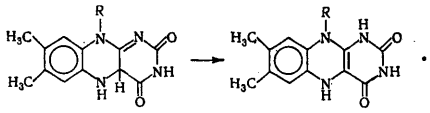
The hypothesis that water may function as the electron donor in the electrochemical reduction of flavins [84–87] appeared to be controversial [88,89], but certain experimental data obtained in recent years by manometric and mass-spectrometric methods indicate that water is decomposed in photochemical reactions involving riboflavin or lumiflavin [90–92]. Probably photoexcited flavin reacts with an external electron donor in the triplet state [93–95]. The ribityl side chain promotes the transition from the first excited singlet state of flavin to the triplet state [96,97]. In the absence of an external electron donor, its role is assumed by the ribityl side chain (in riboflavin), which is cleaved in this process [95].

It has been suggested that the direct cleavage of riboflavin to lumichrome can also proceed via the singlet excited state [98]. Different aspects of the nature of the first excited triplet and singlet states have been investigated [99–106].

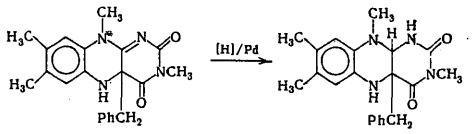
Apart from the reduction of alloxazines and isoalloxazines involving the nitrogen atom in the 1- and 5-positions, other types of reduction have been studied. Hemmerich and coworkers carried out the photochemical reduction of lumiflavin by phenylacetate ions and isolated mono- and di-benzyl derivatives of 4a,5-dihydrolumiflavin [82,107]:



It is possible that 4a,5-dihydroflavins of this kind are formed in biochemical reactions under the influence of hydride ions, for example, in the dehydrogenation of succinic acid to fumaric acid in the presence of succinate dehydrogenase [108]. It is also possible that in biochemical reactions the 4a,5-dihydroflavin is subsequently converted into the 1,5-dihydroflavin as a result of an intramolecular proton shift [108]:

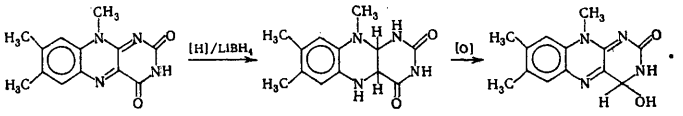


Catalytic hydrogenation of 4a-benzyl-3-methyl-4a,5-dihydrolumiflavin leads to further reduction and the formation of 4a-benzyl-3-methyl-1,4a,5,10a-tetrahydrolumiflavin [82]:



On reduction with sodium borohydride, flavinium salts are also converted into 1,4a,5,10a-tetrahydro-derivatives [109].

The reduction of isoalloxazines, for example, lumiflavins with lithium borohydride takes place via two pathways: under anaerobic conditions, 1,5-dihydrolumiflavin is formed (see above), i.e. the usual reduction product, while in the presence of atmospheric oxygen the reaction leads to the formation of 3,4-dihydrolumiflavin, which is resistant to reoxidation in the crystalline state and in solution in organic solvents, but undergoes photochemical oxidation to lumiflavin [110]. Possibly the initial product of this reaction is 1,4a,5,10a-tetrahydrolumiflavin, which is then partly oxidised and rearranges to 3,4-dihydrolumiflavin [110]:



The reduction by lithium borohydride involving the carbonyl group in the 4-position has also been observed for alloxazines, for example 1,3,7,8-tetramethylalloxazine, which is converted into the 3,4-dihydro-derivative [111].

It is remarkable that D- and L-aminoacid oxidases reduced with lithium borohydride do not lose their biocatalytic activity, which suggests that the dehydrogenation of the substrate does not involve the 4-position of the flavin prosthetic group [112].

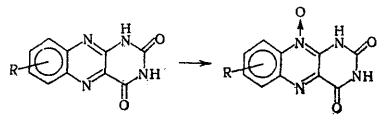
Under severe catalytic hydrogenation conditions, the benzene ring in the isoalloxazine molecule is reduced with formation of an octahydroisoalloxazine [113].

5. OXIDATION

Isoalloxazines, including riboflavin, are resistant to oxidising agents, even when these are as strong as nitric acid, hydrogen peroxide, and bromine, but are oxidised by chromic acid and potassium permanganate [1,2]. When riboflavin is oxidised with lead tetra-acetate or periodic acid, the side chain between adjacent hydroxy-groups is cleaved and 7,8-dimethyl-10-formylmethylisoalloxazine is formed [114,115]; the same compound is obtained on photolysis.

Petering and Giessen [116,117] oxidised 8-chloroalloxazine with 30% hydrogen peroxide in 88% formic acid and ascribed the structure of 8-chloroalloxazine 5,10-di-*N*-oxide to the product [116]. Later Berezovskii and Aksel'rod

showed[118,119] that in the oxidation of the 8-chloroalloxazine, alloxazine, 7-methylalloxazine, 7,8-dimethylalloxazine (lumichrome), 1,3-dimethylalloxazine, and others with 30% hydrogen peroxide in 88% formic acid, peracetic acid, and monopersulphuric acid, only the corresponding alloxazine mono-*N*-oxides can be identified unambiguously at the instant of formation:



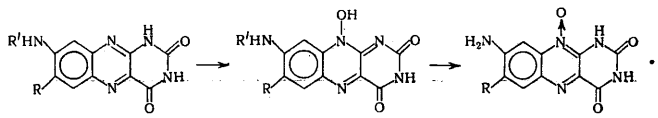
Alloxazine *N*-oxides have the 10-*N*-oxide structure[118], since the oxidation of the nitrogen atoms in the 1- and 3-positions of the pyrimidine ring and in the 5-position of the pyrazine ring in the molecule is hindered by the oxo-groups in the 2- and 4-positions.

It is noteworthy that the unambiguous course of the oxidation of the pyrazine ring of 8-chloroalloxazine agrees with the fact that the pyrazine ring of 6-chloroquinoxaline also yields mainly the mono-*N*-oxide on oxidation[120]. Alkaline cleavage of 8-chloroalloxazine *N*-oxide followed by decarboxylation yielded the corresponding 7-chloro-2-hydroquinoline 1-*N*-oxide[118].

The formation of 10-mono-*N*-oxides is consistent with calculations according to which the excess electronic charge at the nitrogen atom in the 5-position of the alloxazine rings is much lower than at the nitrogen atom in the 10-position[17,121].

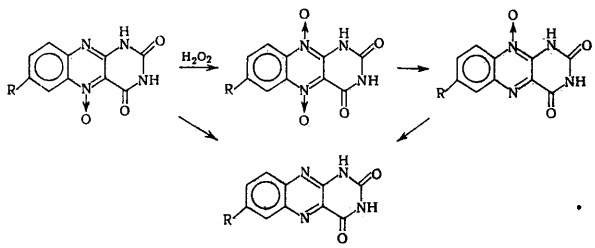
It is striking that derivatives with a nitro-group in the 9-position (for example 7,9-dinitroalloxazine and 6,9-dinitrolumichrome) are not oxidised with hydrogen peroxide and do not give rise to *N*-oxides[122]. On the other hand, 7-methyl-6-nitroalloxazine is oxidised with formation of the 10-*N*-oxide[122].

Aminoalloxazines could not be oxidised unambiguously with hydrogen peroxide to give the corresponding 10-*N*-oxides. This was achieved via the acyl derivatives of 8-aminoalloxazines. The corresponding *N*-oxides of amino- and acylamino-alloxazines were synthesised in this way[14]:



(R = H, CH_3; R' = CH_3CO, C_6H_5CO, $CH_3C_6H_4SO_2$)

The 5-*N*-oxides of alloxazine, 7-chloro-, 7-methyl-, and 1,3-dimethylalloxazine, obtained by Goldner's method[123-125] in which the corresponding nitrosouracils are cyclised, were oxidised with hydrogen peroxide in formic acid at 40°C to the corresponding alloxazine 5,10-di-*N*-oxides[15]:

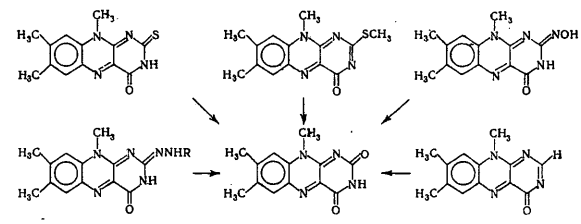


A characteristic feature of alloxazine 5,10-di-*N*-oxides is the non-equivalent stabilities of the *N*-oxide groups, which corresponds to the different basicities of the nitrogen atoms in the 5- and 10-positions of the alloxazine rings.

Thus, on heating 7-methylalloxazine 5,10-di-*N*-oxide in formic acid, the oxygen atom and the hydrogen atom in the 5-position are split off and 7-methylalloxazine 10-*N*-oxide is formed[15]. Under the same conditions, alloxazine 5-*N*-oxides are deoxygenated with formation of non-oxidised alloxazines.

The $N_{(10)} \rightarrow O$ bond is much stronger than $N_{(5)} \rightarrow O$, but prolonged boiling of alloxazine 10-mono-*N*-oxides in formic acid leads to complete deoxygenation with formation of alloxazines[15].

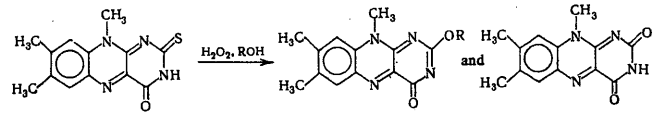
Whereas isoalloxazines, for example lumiflavin, are resistant to the action of hydrogen peroxide and other oxidants, the 2- and 4-derivatives (2- and 4-thiolumiflavins, thio- and imino-ethers, oximes, hydrazones, semicarbazones, and also 2- and 4-deoxy-derivatives) can be readily oxidised with atmospheric oxygen or dilute hydrogen peroxide to the flavin oxo-form[5,6,126-130]:



(R = H, COC_5H_4N, $CSNH_2$, $C_6H_4NO_2$)

2-Iminolumiflavin, which is not oxidsed by weak oxidising agents, is an exception[126].

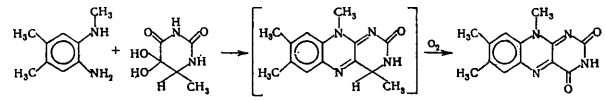
It is noteworthy that, when hydrogen peroxide is allowed to react with 2-thiolumiflavin in alcohol, the product is not 2-deoxylumiflavin, postulated previously[128], but a mixture of 2-*O*-alkyllumiflavin and lumiflavin, which can be readily separated[6]:



2- and 4-Deoxylumiflavins are unstable and are oxidised to lumiflavin at the instant of formation[127]. However, when nitrous acid, which behaves as a "radical-scavenger",[131] is employed, it is possible to obtain a stable 2-deoxylumiflavin in the form of the perchlorate[6]. It can be converted into lumiflavin by photochemical oxidation[6].

4-Deoxyalloxazine and 4-deoxylumiflavin, obtained by the condensation of the corresponding diamines with isodialuric acid, are even less stable than the 2-deoxy-isomers; they exist in the form of hydrates and at the instant of formation are oxidised by atmospheric oxygen to alloxazine and lumiflavin respectively[132].

In exactly the same way the condensation of *o*-diamines with 6-methylisodialuric acid yields lumiflavin as the sole reaction product. It is interesting to note that in this case the C–C bond is readily cleaved (at room temperature)[132]:



The introduction of nucleophilic substitutents into the benzene ring of the isoalloxazine molecule enhances the resistance of 2-deoxyisoalloxazines and 2-thioisoalloxazines to oxidation. Thus 8-acetamide-2-deoxynorlumiflavin is not oxidised by atmospheric oxygen or even weak oxidising agents[133].

In contrast to 2-thiolumiflavin, 8-amino-2-thionorlumiflavin is not appreciably susceptible to the action of atmospheric oxygen. Only the reaction with hydrogen peroxide results in a slow formation of the 2-oxo-group and the liberation of sulphur [133].

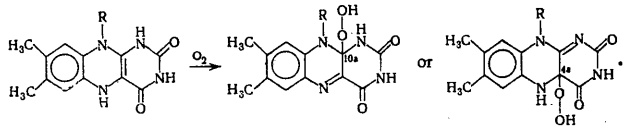
In contrast to flavins (FlH), 1,5-dihydroflavin (FlH_3) are readily oxidised even by atmospheric oxygen with the possible involvement in the reaction with oxygen of the free radicals $F\dot{I}H_2$ which are always present in a small amount in the reduced flavin [134]:

$$FlH + FlH_3 \rightleftharpoons 2F\dot{l}H_2,$$
$$2F\dot{l}H_2 + O_2 \rightleftharpoons 2FlH + H_2O_2.$$

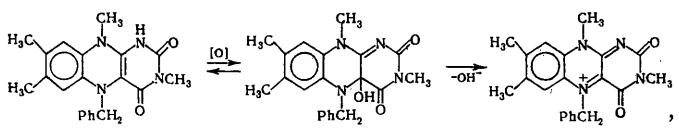
However, it is more likely that 1,5-dihydroflavins rather than the free radicals (flavosemiquinones) react with oxygen [56,135]. A spectrophotometric study of the kinetics of their oxidation established that the rate of reaction increases with the formation of the oxidised flavin and therefore the reaction may be regarded as autocatalytic [134]. Since 1,5-dihydroflavin is usually present in a non-coplanar conformation [7], it probably reacts with oxygen after transition to a planar vibrationally excited state as a result of the formation of a π-complex between the oxidised and reduced flavins [56]. Alkylation of 1,5-dihydroflavin at the nitrogen atom in the 1-position stabilises the 1-coplanar state, hinders the conformational transition of the molecule to the planar state, and sharply increases its resistance to oxidation by atmospheric oxygen [7,136].

In flavoproteins the coplanar structure of the dihydroflavin may arise as a result of the formation of a complex with adenine or tryptophan [56].

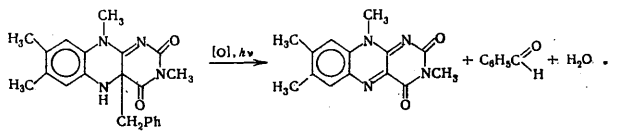
In the oxidation of 1,5-dihydroflavins and 5,10-dihydroalloxazines, the intermediates are hydroperoxides with the hydroperoxy-group in the 10a- [137-140] or 4a-position [140], the 4a-position being apparently more reactive [82,107,141]:



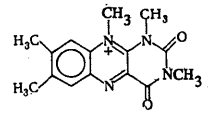
5,10-Dihydroalloxazines react with their hydroperoxides to form 10a-hydroxy-1,10a-dihydroalloxazines [142]. Whereas 5-benzyl-3-methyl-1,5-dihydrolumiflavin is reversibly oxidised in the dark via the intermediate formation of a free radical to a carbinol base, which at pH < 4 splits off a hydroxide ion and is converted into a quaternary 5-benzyl-3-methyl-lumiflavinium salt:



its isomer, 4a-benzyl-3-methyl-4a-5-dihydrolumiflavin, undergoes an irreversible photochemical oxidation with simultaneous cleavage of the C–C bond and the formation of 3-methyl-lumiflavin [82,107]:

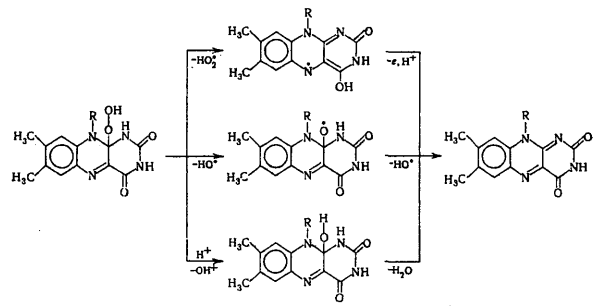


Quaternary flavinium salts are formed by the oxidation of 1,3-dialkyl-1,5-dihydrolumiflavins and their 5-acetyl derivatives with nitrous acid [136]:



O-Alkyl derivatives of 5-acetyl-1,5-dihydrolumiflavin react in the same way. The planarity of the dihydroflavin molecule in the oxidation reaction may be achieved by the intermediate formation of a free radical [136].

The prosthetic group of flavoproteins of various types has a specific protein environment and this probably determines the nature of electron transfer from the reduced form of the flavin either directly to oxygen (oxidases) or to an intermediate one-electron acceptor (dehydrogenases) and is reflected in their behaviour in the reaction with sulphite [140]. Thus oxidases form with sulphite an adduct via the nitrogen atom in the 5-position in the flavin, while dehydrogenases do not react with sulphite [140,143]. The differences between the reactions of flavoproteins of different types (dehydrogenases and oxidases) may be related also to the subsequent behaviour of dihydroflavin hydroperoxides, which can be cleaved in different ways [140]:



A similar series of reactions may be expected for the adduct inolving the 4a-position [140].

In accordance with the mode of cleavage of dihydroflavin hydroperoxides, dehydrogenases react predominantly with formation of HO_2 and an intermediate flavin radical [140]; it has been established that the majority of enzymes of this type form free Flavin radicals on reaction with oxygen, which then rapidly interact with one-electron acceptors [144,145]. A characteristic feature of the dihydro-forms of oxidases is reaction involving the formation of flavins and hydrogen peroxide [146].

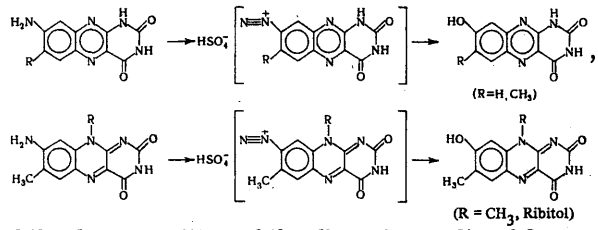
6. NUCLEOPHILIC SUBSTITUTION

8-Chloroalloxazine does not react with aliphatic and aromatic amines, pyridine, and morpholine on heating [147]. 8-Halogeno-substituted isoalloxazines behave differently—they readily react with nucleophilic agents such as monoethanolamine, diethanolamine, piperidine, and morpholine on heating in the presence of their excess or on carrying out the reaction in dimethylformamide (DMF) solution [147,148]. 8-Hydroxyethylaminonorlumiflavin was obtained in this way from 8-chloronorlumiflavin [148].

The lesser reactivity of 8-chloro-7,10-dimethylisoalloxazine compared with 8-chloro-10-phenylisoalloxazine can be accounted for by the influence of the electron-donating CH_3 group in the 7-position [147]. The chlorine atom in the 8-position of the isoalloxazine ring is also substituted

by a methoxy-group. Thus 8-chloronorlumiflavin reacts with sodium methoxide to form 8-methoxynorlumiflavin[148].

8-Hydroxyalloxazines and hydroxy-analogues of natural flavins—8-hydroxynorlumiflavin and 8-hydroxynor-riboflavin[149,150]—have been synthesised by the diazotisation of sulphuric acid solutions of 8-aminoalloxazines, their 9-azo-derivatives, and also 8-aminoisoalloxazines with subsequent hydrolytic decomposition of the diazonium salts[149,150]:



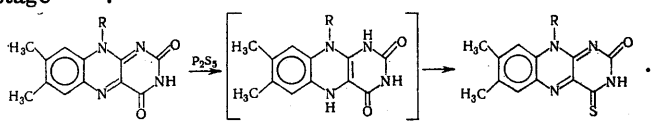
(R=H, CH_3)

(R = CH_3, Ribitol)

If the decomposition of the diazonium salts of 8-aminoisoalloxazines is carried out under the conditions of the Sandmeyer reaction, the corresponding 8-halogenoisoalloxazines are formed. 8-Chloronorlumiflavin[133], 8-chloronor-riboflavin, and 8-bromonorlumiflavin were obtained in this way[151]. It was shown that dimethyl sulphoxide promotes the nucleophilic substitution of the diazo-group in the 8-position of isoalloxazine by a halogen[151].

The reaction of alloxazines and isoalloxazines with nucleophilic agents usually does not entail substitution at the 2-C and 4-C carbon atoms of the pryimidine ring.

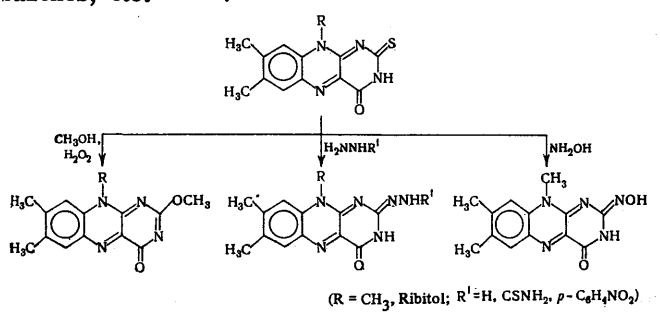
The introduction of sulphur into the 4-position of the isoalloxazine rings in the reaction of lumiflavin and 2′, 3′, 4′, 5′-tetra-acetylriboflavin with phosphorus pentasulphide in pyridine with formation of 4-thiolumiflavin[127] and 2′, 3′, 4′, 5′-tetra-acetyl-4-thioriboflavin[152] constitutes an exception. In this case there is probably initial reduction by sulphide and then substitution in the 1,5-dihydroflavin stage[10,127]:



(R = CH_3, $CH_2(CHOAc)_3CH_2OAc$)

A similar selective substitution for sulphur takes place also in the purine series[153]. The 2-oxogroup is resistant to the action of phosphorus pentasulphide.

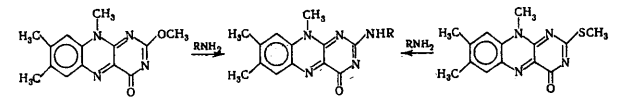
Nucleophilic substitution in the 2- and 4-positions of flavins occurs only with their derivatives: 2- and 4-thioflavins and *O*- and *S*-alkyl derivatives. 2-Thiolumiflavin and 2-thioriboflavin readily react with nucleophilic agents (the alkoxy-group, hydrazine hydrate, *p*-nitrophenylhydrazine, semicarbazide, thiosemicarbazide, and hydroxylamine) with formation of *O*-alkyl derivatives of oximes, hydrazones, semicarbazones, thiosemicarbazones, etc.[5,10,128]:



(R = CH_3, Ribitol; R′=H, $CSNH_2$, *p*-$C_6H_4NO_2$)

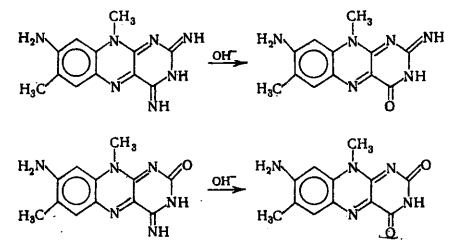
Similar reactions have also been described for 4-thiolumiflavin[5].

2-*O*-Alkyl derivatives and also 2- and 4-thioethers react with ammonia and amines (aniline, monoethanolamine, morpholine, and others) with formation of imines and iminoethers[5,10]:

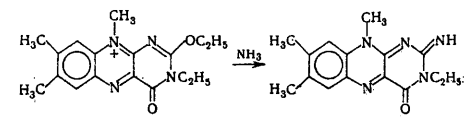


(R=H, C_6H_5, CH_2CH_2OH, $(CH_2)_5N(CH_3)_2$)

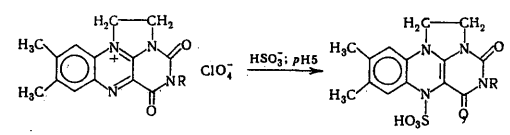
The imino-group in the 4-position is hydrolysed selectively under mild conditions. Thus 8-aminonorlumiflavin-2,4-di-imine is converted after only a brief treatment with warm alkali into the 3-monoimine, which is much more resistant to alkali; the 4-monoimine readily gives rise to the dioxo-compound under similar conditions[133]:



When nitrogen-containing heterocycles are converted into quaternary salts, the attack by nucleophilic agents is facilitated, as happens for nucleophilic substitution of pyridinium, pyrylium, thiapyrylium, and other cations[154]. Dudley and Hemmerich showed that 2-*O*,3-*N*-dialkyllumiflavinium salts react with ammonia via a simple addition–elimination mechanism with formation of lumiflavinimine[136]:



When sodium bisulphite is allowed to react with flavinium salts having substituted nitrogen atoms in the 1- and 3-positions, the nucleophilic bisulphite ion adds to the 5-position with formation of a dihydroflavin-sulphite adduct[155]:



The sulphite adduct of the 1,3,7,8,10-pentamethylisoalloxazinium salt is less stable and was not obtained in a pure form, but in this case too the sulphite anion probably adds to the 5-position[155].

It has been established that sulphite ions form adducts with the flavin prosthetic groups of many flavoproteins: glucose oxidase[143], D- and L-aminoacid oxidases, hydroxynitrile lyase, lactate oxidase, and glycolate oxidase[140], i.e. with enzymes of the oxidase type which transfer hydrogen directly to molecular oxygen. Flavin dehydrogenases, which transfer hydrogen to a specific acceptor, do not react with the sulphite anion[140]. This is an interesting case of correlation between the chemical reactivity of the flavin prosthetic group of flavoproteins of different types and their biochemical functions.

7. ELECTROPHILIC SUBSTITUTION IN THE BENZENE RING

Electrophilic substitution of the benzene ring in compounds of the alloxazine and isoalloxazine series was unknown until recently. Direct introduction of various substitutents gives rise to many possibilities for the structural modification of the molecules of riboflavin and related compounds, since the possibility of obtaining benzene ring-substituted alloxazines and isoalloxazines is greatly restricted by the limitations of the direct syntheses[1,2].

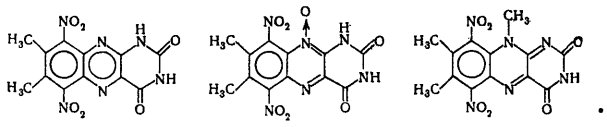
It has been established by LCAO-MO calculations[17] that the introduction of electron-donating substituents (CH_3, Cl, OH, NH_2, etc.) into the 7- and 8-positions of the alloxazine and isoalloxazine rings give rise to changes in the distribution of electron density (q_π) and peripheral electron density (f_π) mainly in the benzene component of the molecule, the type of distribution of q_π and f_π being largely similar for alloxazines and isoalloxazines.

Quantum-chemical calculations show that when either the static "isolated molecule" approximation (active centre characterised by the maximum value of q_π) or the dynamic approximation assuming localisation (the localisation energy LE is a minimum at the active centre) is employed[156] for alloxazine, lumichrome, riboflavin, and 8-amino- and 8-hydroxy-alloxazines, the electrophilic attack may be directed primarily to the carbon atom in the 9-position or to the 6-position in 7-methylalloxazine. Apart from the 9-position, the 7-position is reactive in alloxazine, 8-aminoalloxazine, and 8-hydroxyalloxazine and the 6-position is reactive in lumichrome and riboflavin[17] (see Table). These conclusions are fully consistent with the experimental data.

Berezovskii and Aksel'rod studied the nitration of alloxazines[122,157], their 10-*N*-oxides[122], and isoalloxazines[122] under conditions such that the reaction was known to have an electrophilic mechanism[158].

In the nitration of alloxazine with fuming nitric acid in the presence of concentrated sulphuric acid at 20°C, the product is a mixture of 7- and 9-mononitro-derivatives in proportions of 2:3. Nitration of alloxazine under severe conditions—with fuming nitric acid in 25% oleum at 70°C—leads to 7,9-dinitroalloxazine, which is formed also when the 7- and 9-mononitro-compounds are nitrated under the same conditions. In accordance with the directing effect of the first nitro-group, the second nitro-group substitutes the hydrogen atom in the benzene ring in the meta-position[157]. Nitration of 7-methylalloxazine and its 10-*N*-oxide with nitrating mixture at 20°C yields only the 6-nitro-derivatives[122]. Selective nitration in the 6-position is consistent with the lower localisation energy for 7-methylalloxazine (see Table) compared with the 8-position.

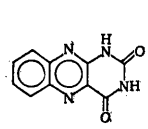
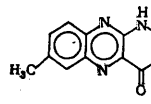
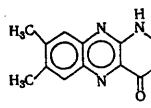
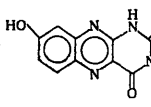
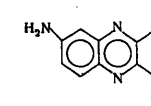
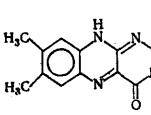
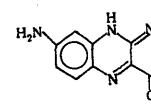
Nitration of 7,8-dimethylalloxazine, its *N*-oxide, and lumiflavin with fuming nitric acid in the presence of concentrated sulphuric acid leads unambiguously to the formation of the 6,9-dinitro-compounds[122]:



Under these conditions, mononitro-derivatives could not be obtained. Possibly the methyl groups in the 7- and 8-positions greatly enhance the nucleophilic properties of the 6- and 9-positions, which become equivalent and the nitration involves them both at the same rate. Otherwise the reaction would have terminated at the stage corresponding to the formation of the mononitro-compound (the 6- or 9-nitro-derivative) which is incapable of undergoing further nitration. Indeed it was found that 7,8,10-trimethyl-9-nitroisoalloxazine (obtained by direct synthesis) remains unchanged under the conditions of the nitration reaction[122].

McCormick[159] achieved the bromination and chlorination of lumiflavin and 2′,3′,4′,5′-tetra-acetylriboflavin in the 9-position by treatment with *N*-halogenosuccinimide in trichloroacetic acid in the presence of catalytic amounts

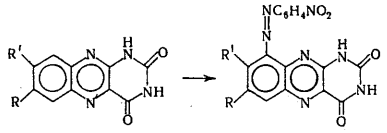
The activity indices of the 7- and 8-substituted alloxazines and isoalloxazines.

Compound	Site of substitution	q_π	f_π	LE
	6	+0.012	0.163	2.347
	7	−0.002	0.223	2.449
	8	+0.021	0.012	2.548
	9	−0.013	0.293	2.277
	6	−0.019	0.212	2.247
	8	+0.007	0.002	2.494
	9	−0.011	0.263	2.282
	6	−0.017	0.216	2.384
	9	−0.042	0.276	2.271
	6	+0.014	0.181	2.358
	7	−0.013	0.191	2.383
	9	−0.045	0.353	2.164
	6	+0.017	0.118	2.372
	7	−0.033	0.013	2.278
	9	−0.106	0.594	1.980
	6	−0.002	0.014	2.417
	9	−0.051	0.071	2.321
	6	+0.029	0.032	2.413
	7	−0.048	0.210	2.234
	9	−0.110	0.011	2.042

q_π = excess π-electron density; f_π = peripheral π-electron density; LE = localisation energy.

of benzoyl peroxide. Possibly the flavin reacts with the halogen in a protonated form via an electrophilic mechanism [159], but, since benzoyl peroxide is used as a catalyst, the possibility of a radical mechanism cannot be ruled out.

Berezovskii and Tul'chinskaya and coworkers studied the azo-coupling of 8-amino- and 8-hydroxy-alloxazines with diazotised aromatic amines [150]. When 8-amino-alloxazines were coupled with phenyl- and *p*-nitrophenyl-diazonium chlorides in aqueous DMF at pH 2–3, 8-amino-9-arylazoalloxazines were obtained and in the azo-coupling of 8-hydroxyalloxazines in a weakly alkaline medium the products were 9-arylazo-8-hydroxyalloxazines:



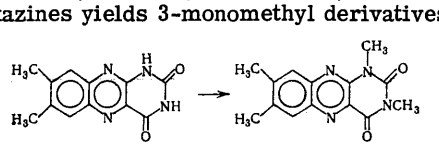
(R = H, CH_3; R' = OH, NH_2)

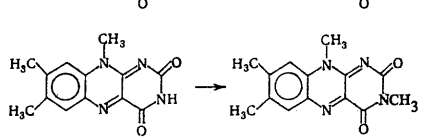
The finding that the azo-coupling of 8-amino and 8-hydroxy-alloxazines involves the 9-position of the alloxazine ring and not the 7-position is consistent with the calculated reactivity indices (q_π, f_π, LE; Table).

The attempt to carry out the azo-coupling of 8-amino-norlumiflavin and 8-aminonor-riboflavin with *p*-nitrophenyldiazonium chloride was unsuccessful, which, apart from steric factors, may be accounted for also by a reduced reactivity of the 9-position compared with 8-aminoalloxazine (a decrease of the peripheral electron density and a higher localisation energy; Table).

8. ALKYLATION

Alloxazines and isoalloxazines are alkylated in both oxidised and reduced forms. Alkylation of alloxazines with methyl iodide [44,160], diazomethane [161], or dimethyl sulphate [162] in DMF in the presence of potassium carbonate [4] involves the ring nitrogen atoms of the pyrimidine ring and leads to 1,3-dimethyl derivatives, while methylation of isoalloxazines yields 3-monomethyl derivatives [4,160,161]:



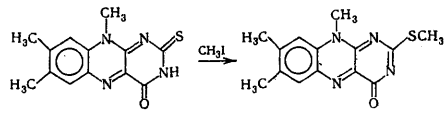


2′,3′,4′,5′-Tetra-acetylriboflavin is alkylated similarly with formation of, for example, the 3-methyl, 3-ethyl, and 3-benzyl tetra-*O*-acetylriboflavins [44]. 8-Aminonor-lumiflavin is methylated by methyl iodide in an alkaline medium in the 3-position with 8-amino-3-methylnorlumi-flavin as the product [133].

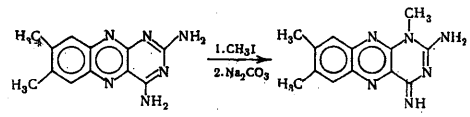
Like isoalloxazines, alloxazine *N*-oxides are not alkylated at the nitrogen atom in the 1-position. When alloxazine 10-*N*-oxide was methylated with methyl iodide or dimethyl sulphate in an alkaline medium, only 3-methyl-alloxazine 10-*N*-oxide was obtained [13].

Compounds with various substituents at 1-N and 3-N can be obtained by further alkylation of monoalkyl-substituted alloxazines [111,160].

When 2- and 4-thiolumiflavins are treated with alkylating agents (methyl iodide in chloroform), they are alkylated to the corresponding thioethers and the reaction with the 2-thio-derivative takes place also without a basic catalyst [5], for example:



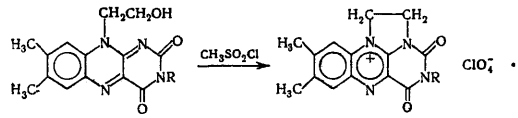
On the other hand, 2,4-diamino-7,8-dimethylbenzo[*g*]-pteridine is methylated by methyl iodide in boiling cellosolve with formation of a quaternary salt, which on treatment with aqueous sodium carbonate solution is converted into the 1-*N*-methyl derivative [163]:



Berezovskii and coworkers studied the alkylation of 8-aminoalloxazine and 8-aminoisoalloxazine with ethylene oxide [164]. Hydroxyethylation of an aqueous suspension of sodium derivatives of 8-aminoalloxazine, 8-aminonorlumi-chrome, and 8-dimethylaminoalloxazine yielded on heating 3-(2′-hydroxyethyl)-8-(2′-hydroxyethylamino)alloxazine, 3-(2′-hydroxyethyl)-8-(2′-hydroxyethylamino)norlumi-chrome, and 3-(2′-hydroxyethyl)-8-dimethylaminoallox-azine respectively, the product obtained from 8-aminonor-lumiflavin being 3-(2′-hydroxyethyl)-8-aminonorlumiflavin.

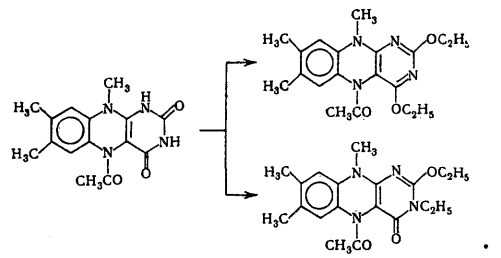
3-(2′-Hydroxyethyl)-8-(2′-hydroxyethylamino)alloxazine is readily dealkylated by 70% sulphuric acid with formation of 8-aminoalloxazine [164].

It has been established for 10-(2′-hydroxyethyl)-7,8-dimethylalloxazine [155] that isoalloxazines can undergo intramolecular alkylation in the 1-position in the presence of methanesulphonyl chloride, DMF, and potassium carbonate with formation of quaternary flavinium salts:



A similar intramolecular alkylation at the 1-N-position has been observed also for 10-formylmethyl-7,8-dimethyl-isoalloxazine [7,26].

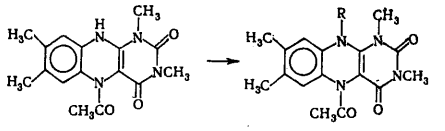
In contrast to flavins, 1,5-dihydroflavin reacts with electrophilic agents at 2-O, 4-O, 3-N, and 5-N. Owing to the high sensitivity of the dihydro-form to oxygen, stabilised 5-acetyl-1,5-dihydro-compounds were employed [4]; they are readily alkylated with formation of a mixture of 2-O, 4-O, and 2-O, 3-N-dialkyl derivatives; the nitrogen atom in the 1-position of dihydroalloxazines is not alkylated [4]:



The finding that 5-acetyl-1,5-dihydrolumiflavin is not alkylated at the 1-nitrogen atom can be accounted for by the enhanced electron density at the carbonyl oxygen in the $C_{(2)}$—O^{136} group and not by the steric hindrance due to the substituent in the 10-position [4].

5,10-Dihydroalloxazines behave differently. Thus alkylation of 5-acetyl-5,10-dihydroalloxazine in DMF in the presence of potassium carbonate yields a complex mixture of products of alkylation at 1-N, 3-N, or 10-N which contains, after acid hydrolysis and oxidation, 1- and 3-monomethylalloxazines, 1,3-dimethylalloxazine, and a small amount of 3,10-dimethylisoalloxazine [4].

If one begins with 5-acetyl-1,3-dimethyl-5,10-dihydroalloxazine, 10-alkylation takes place with formation of 5-acetyl-10-alkyl-1,3-dimethyl-1,5-dihydroisoalloxazines [136]:

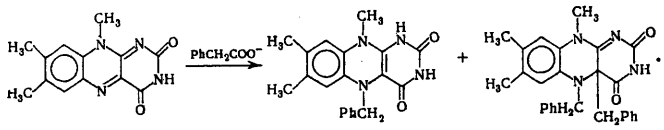


(R = CH_3, C_2H_5, $CH(CH_3)_2$, $CH_2COOC_2H_5$, $CH_2C_6H_5$)

The course of the further conversion of this compound into an oxidised form of isoalloxazine is unknown.

1,3,10-Trialkyl-1,5-dihydroflavins are alkylated in the 5-position by alkyl halides in DMF in the presence of potassium carbonate [136].

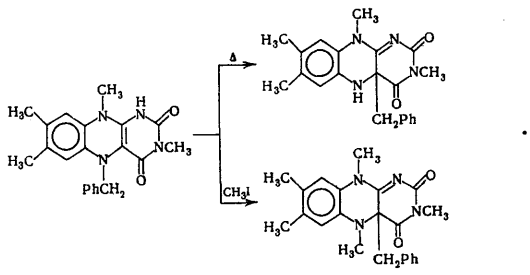
Hemmerich and coworkers studied the reductive photochemical alkylation of flavins on treatment with phenylacetate ions which are decarboxylated in this process [141], the residue formed entering into the 5- or 4a-position with formation of mono- and di-benzyldihydro-derivatives [82,107,141]:



Isolumiflavin (6,7,10-trimethylisoalloxazine) gives only the 4a-benzyldihydro-derivatives, evidently owing to steric hindrance [82].

The reductive photochemical alkylation of 5-benzyl-lumiflavin on treatment with cyclopentadiene, thiolane, and dialkyl sulphides also involves the 4a- or 5-position [165,166].

On fusion (without access of air), 5-benzyl-1,5-dihydrolumiflavin rearranges to 4a-benzyl-4a,5-dihydro-lumiflavin [82]. A similar rearrangement occurs also in the methylation of 5-benzyl-1,5-dihydrolumiflavin with methyl iodide, the rearrangement being accompanied by methylation in the 5-position [82]. Under the same conditions, the isomeric 4a-benzyl-4a,5-dihydrolumiflavin is not alkylated in the 5-position:

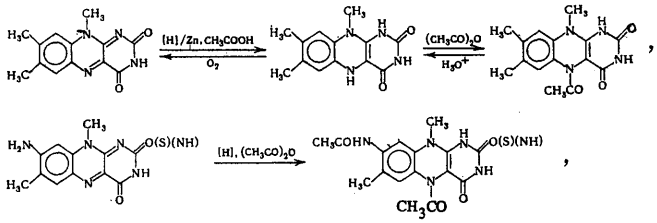


Flavin radicals alkylated in the 5-position were obtained by alkylating a mixture of oxidised and reduced flavin with alkyl halides in the presence of triethylamine [70].

9. ACYLATION

In contrast to alkylation, acylation of alloxazines and isoalloxazines takes place selectively only with their dihydro-derivatives at the 5-nitrogen atom and leads to the formation of 5-acyl-5,10-dihydroalloxazines and 5-acyl-1,5-dihydroisoalloxazines and their derivatives [127]. 5,10-Dihydroalloxazines and 1,5-dihydroisoalloxazines, which are unstable and sensitive to atmospheric oxygen, are thereby stabilised [4].

The acylation reaction is carried out simultaneously with reduction by adding zinc dust to a suspension of the alloxazine or isoalloxazine in a 1:1 mixture of acetic acid and an organic acid anhydride. Hemmerich and coworkers obtained in this way 5-acetyl-1,5-dihydrolumiflavin [127,133], 8-acetamido-5-acetyl-1,5-dihydronorlumiflavin, and its 2-thio- and 2-imino-analogues:



as well as 5-acetyl-5,10-dihydroalloxazine, its 1,3-dimethyl derivative [4], 5-acetyl-1,5-dihydro-2-thiolumiflavin [127], 2′,3′,4′,5′,5-penta-acetyl-1,5-dihydroriboflavin [4,167], etc.

On reductive acetylation, quaternary flavinium salts can be converted into the corresponding 5-acetyl-1,5-dihydro-derivatives [155].

The acetyl group in the 5-position inhibits reoxidation but at 50°C and in the presence of atmospheric oxygen it is readily hydrolysed by hydrochloric acid [4,127,133]. Simultaneous reduction and formylation with zinc dust and formic acid are achieved similarly and result in the formation of 5-formyl-5,10-dihydroalloxazine, 5-formyl-1,5-dihydrolumiflavin [4], and 4a-benzyl-5-formyl-4a,5-dihydrolumiflavin [82].

When riboflavin is treated with chlorocarbonic ester in an alkaline solution and is simultaneously reduced with sodium hydrosulphite, only the 5-position is acylated, the primary and secondary hydroxyls in the ribityl chain not being involved; the reaction leads to the formation of 5-ethoxycarbonyl-1,5-dihydroriboflavin [167]. However, when riboflavin is treated with benzoyl chloride in alkaline solution with simultaneous reduction, the product is 2′,3′,4′,5′,5-pentabenzoyl-1,5-dihydroriboflavin [167].

Brustein and Hemmerich showed that, when 3-methyl-lumiflavin reacts with pyruvic acid under aerobic conditions under illumination, reductive acetylation takes place with formation of 5-acetyl-3-methyl-1,5-dihydrolumiflavin [168]. Under anaerobic conditions, photochemical reduction predominates, leading to the formation of 3-methyl-1,5-dihydrolumiflavin [168].

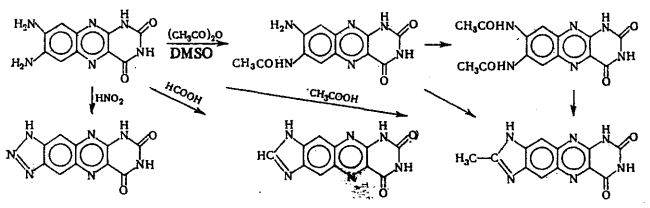
A similar reductive acylation reaction is observed in biological catalysis by flavoproteins, which are reduced by pyruvate with formation of the corresponding adduct [169]. Possibly the first stage of the flavin-dependent dehydrogenation is such "group transfer", in contrast to "species transfer" (hydride ion transfer) known previously [168]. This hypothesis is confirmed by the finding that certain flavoproteins do not exhibit oxidation-reduction properties [170], for example hydroxynitrile lyase.

10. REACTION OF AMINO-SUBSTITUENTS

The amino-groups in the benzene component of the alloxazine and isoalloxazine systems are nucleophilic centres and can react with electrophilic agents. Beresovskii and coworkers studied the acylation of 8-amino-alloxazines [14]. This showed that the weakly basic amino-group of 8-aminoalloxazines does not react with an excess of acetyl chloride under mild conditions. However, after these compounds had been heated for 20 h with acetic anhydride in pyridine at 60°C, their acetyl derivatives were obtained. 8-Benzoyl- and 8-tosyl-aminoalloxazines were synthesised by acylating 8-aminoalloxazine and 8-amino-7-methylalloxazine with benzoyl chloride and toluene-*p*-sulphonyl chloride [14].

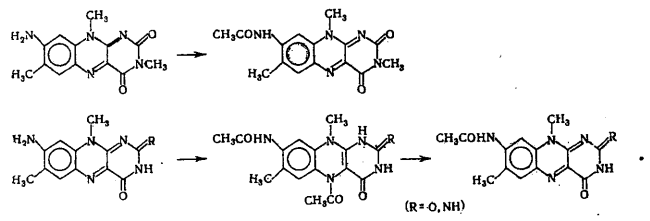
In a study of the acetylation of 7,8-diaminoalloxazine, it was shown that the reaction proceeds in steps owing to the different reactivities of the exocyclic amino-groups [171].

It proved possible to select conditions ensuring the monoacylation of 7,8-diaminoalloxazine with acetic anhydride in dimethyl sulphoxide (DMSO) at 20°C; the structure of 7-acetamido-8-aminoalloxazine was attributed to the monoacyl derivative [171]. Further acetylation yields 7,8-diacetamidoalloxazine:

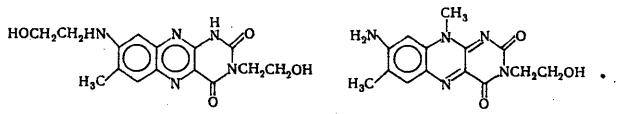


On heating, the acetyl derivatives of 7,8-diamino-alloxazine show a marked tendency to undergo the imidazole cyclisation. The corresponding imidazo-alloxazines are also obtained on refluxing 7,8-diamino-alloxazine with acetic and formic acids: interaction with nitrous acid gives rise to the triazolo[4,5-i]-alloxazine system [171].

On refluxing with a mixture of acetic anhydride and acetic acid, 8-aminoisoalloxazines are acetylated to the 8-acetamido-derivatives [133], which can also be obtained under the conditions of reductive acetylation with subsequent selective hydrolysis of the acetyl group at the 5-N nitrogen atom of the 1,5-dihydro-compound. Hemmerich and coworkers obtained in this way 8-acetamidonorlumiflavin and its 2-imino- and 2-deoxy-analogues [133]:



It has been shown that there is a difference between the reactivities of the amino-groups in the 8-positions of alloxazines and isoalloxazines with respect to hydroxyethylation [164]. Whereas on treatment with ethylene oxide and heating, the 8-amino-group in the sodio-derivatives of alloxazine and 8-norlumichrome is hydroxyethylated together with the cyclic 3-imino-group, in isoalloxazines the amino-group remains inert.



The higher reactivity of the 8-amino-group in the alloxazines ring system compared with isoalloxazine has been confirmed by calculations [17], which established that the electron density (1.830) and the peripheral electron density (0.618) at the amino-group of 8-aminoalloxazine are higher than for 8-iminoisoalloxazine (1.817 and 0.254 respectively).

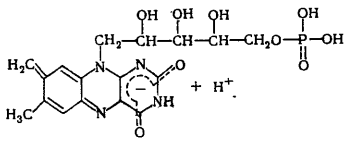
The 9-amino-group in the isoalloxazine ring system is readily diazotised by nitrous acid; the diazonium salt enters into the azo-coupling reaction and is deaminated. Lumiflavin is obtained in this way from 9-aminolumiflavin as a result of diazotisation and decomposition of the diazonium salt [172]. However, the diazo-group in this compound could not be replaced by bromine in the Sandmeyer reaction, possibly owing to steric hindrance [172].

8-Aminoalloxazines and 8-aminoisoalloxazines [133,173] are also diazotised by nitrous acid [133,149-151,174]; the diazonium salts formed are coupled in an alkaline medium to β-naphthol [164,174] and in dilute formic acid to certain aromatic amines (diethylaniline, *NN*-bis-β-chloroethyl-aniline) [175] with formation of azo-compounds.

11. REACTIONS OF THE METHYL GROUP IN THE 8-POSITION

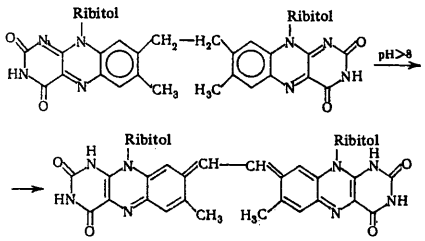
Until recently the biological importance of the two *ortho*-methyl groups in the benzene part of the molecule of riboflavin and its coenzymes (FMN and FAD) was not clear. Although the removal of the methyl groups from the flavin involves relatively small steric and electronic changes in the molecule, it nevertheless entails a sharp decrease or total loss of biocatalytic activity [176]. The replacement of these groups by other substituents (NH_2, NHRibitol, OH, Cl, etc.) yields inhibitors of certain metabolic reactions [177-179].

The 8-methyl group in the isoalloxazine ring system exhibits acidic properties, resembling those of nitrotoluene or methylbenzoquinone [18]. At pH 6.8–6.9 and 90–95°C in D_2O the protons of the 8-methyl group of FMN are exchanged for deuterium [180], which has been explained by the possible formation of an anion with a strongly delocalised charge; the formation of such an anion, which would compensate the loss of aromaticity in the benzene ring, is impossible in the deprotonation of the 7-methyl group, for example:

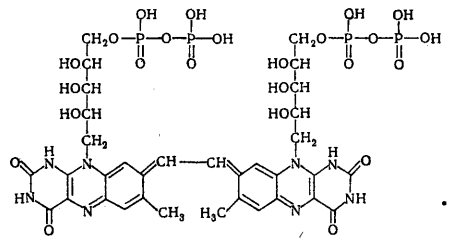


The mobility of the hydrogen atom of the 8-methyl group is shown in flavin dimerisation reactions. Hemmerich et al. established that, under non-aqueous alkaline conditions (BaO in methanol, K_2CO_3 in DMF), flavins are irreversibly dimerised [148] in a manner analogous to the oxidation of nitrotoluenes to stilbenes [18]. The 8-methyl groups in the two molecules are then oxidised and dimerised with the formation of the CH_2-CH_2 group and flavin compounds are

reduced—a diflavin biradical is formed[18] and reacts with a further flavin molecule to form the flavosemiquinone anion and the "diflavin radical"[69]. In the presence of atmospheric oxygen, this radical is oxidised to the stable benzoquinonoid bisriboflavin[148]:

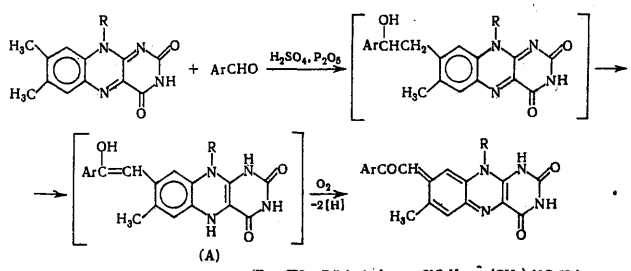


It is noteworthy that, in the phosphorylation of riboflavin under extremely dehydrating conditions (orthophosphoric acid and phosphorus pentoxide), the formation of phosphate esters of flavins with the usual structure is also accompanied to some extent by an analogous oxidative dimerisation involving the 8-methyl group with formation of the benzoquinonoid bisriboflavin 5′-diphosphate[181]:



The ^{1}H NMR spectra of the benzoquinonoid bisriboflavin 5′-diphosphate and the benzoquinonoid bisriboflavin lack the resonance signal due to the protons of the 8-methyl groups, while the signal of the 7-methyl protons is retained[181], which is evidence of a change in molecular structure involving the 8-methyl groups. The benzoquinonoid bisriboflavin 5′-diphosphate and the benzoquinonoid bisriboflavin were found to inhibit oxidative phosphorylation processes in rat liver mitochondria.

The 8-methyl group in the flavin molecule may be regarded as a nucleophilic centre. The enhanced reactivity of the 8-methyl group of flavins compared with the 7-methyl group is reflected in its capacity to interact with electrophilic agents (active carbonyl, nitrosyl, etc. groups). Thus under anhydrous conditions (concentrated sulphuric acid and phosphorus pentoxide) flavins enter into the Knoevenagel reaction with *p*-chlorobenzaldehyde and *p*-dimethylbenzaldehyde, forming the corresponding 8-α-derivatives[148,182]:

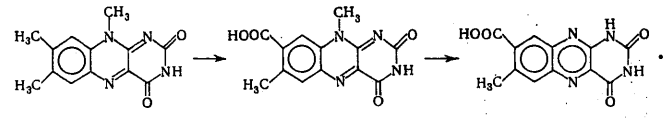


(A)

(R = CH_3, Ribitol; Ar = *p*-ClC_6H_4; *p*-$(CH_3)_2NC_6H_4$)

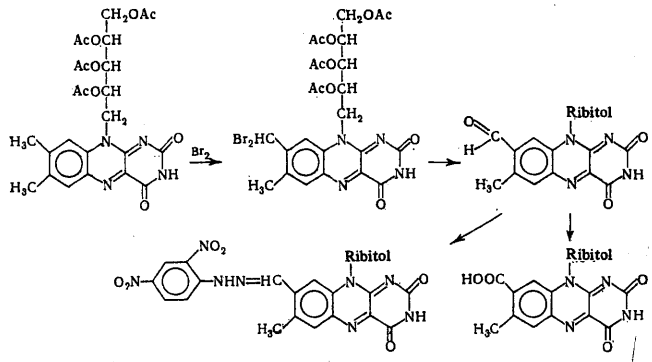
Possibly this reaction proceeds via the intermediate formation of an aldol, which is converted as a result of an intramolecular oxidation-reduction reaction into a compound of type (A) which on oxidation in air gives rise to the corresponding 8-α-derivative of the flavin[182].

The reactivity of the 8-methyl group of flavins is also shown in the reaction of lumiflavin with nitrous acid in boiling acetic acid with formation of 8-carboxynorlumiflavin[148]:



This acid is unstable and is readily converted into 8-carboxy-7-methylalloxazine in a warm alkaline solution.

McCormick achieved the bromination of the 8-methyl group of 2′,3′,4′,5′-tetra-acetylriboflavin with an excess of bromine in pyridine and dioxan; the reaction led to the formation of 2′,3′,4′,5′-tetra-acetyl-8-α-dibromoriboflavin, which was hydrolysed to 8-formylnor-riboflavin on refluxing in 6 *N* hydrochloric acid. This compound is oxidised by dilute aqueous potassium permanganate or periodic acid solution to 8-carboxynor-riboflavin. The condensation of 8-formyl nor-riboflavin with 2,4-dinitrophenylhydrazine led to the formation of the corresponding hydrazone[183]:



Hemmerich and coworkers achieved the monobromination of 2′,3′,4′,5′-tetra-acetylriboflavin at the 8-methyl group by brief treatment with molecular bromine in dioxan in the presence of catalytic amounts of dibenzoyl peroxide and obtained 2′,3′,4′,5′-tetra-acetyl-8-α-monobromoriboflavin[184].

The study of the reactivity of the substituents in the benzene ring of isoalloxazines, in particular the 8-methyl group in riboflavin[148,183], played a decisive role in the determination in 1970 of the structure of a new flavin coenzyme of succinate dehydrogenase (SD) by two groups of investigators: Ghisla et al.[184] in West Germany and Walker and Singer[185] in the USA.

Earlier Kearney, Singer, and Wang established that the flavin present as the prosthetic group in succinate dehyrogenase from ox heart[186] and pig heart[187] is not identical with FMN or FAD[188,189] and, in contrast to these coenzynes, is linked by a covalent bond to one of the protein aminoacids[190].

The flavin of succinate dehydrogenase could not be separated by the usual methods (treatment with strong acids in the cold, boiling in water and 50% ethanol) and only treatment with proteolytic enzymes (trypsin, chymotrypsin) led to the isolation of a flavin peptide derivative, called SD-FAD and containing one mole of 5-adenylic acid, one mole of D-ribose, and two phosphorus atoms joined by the pyrophosphate linkage[190]. The dinucleotide differed from FAD by a hypsochromic shift of the ultraviolet absorption band (from 375 to 350 nm) and certain other properties[190].

SD-FAD was converted into AMP and SD-FMN by brief hydrolysis in 1 *N* hydrochloric acid at 100°C or by treatment with nucleotide pyrophosphatase.

Hydrolysis of SD-FAD (6 *N* HCl, 95°C, 18 h) leads to a riboflavin derivative (SD-riboflavin) and 6–7 aminoacids: alanine, serine, glutamic acid, valine, and threonine with a second serine molecule as the terminal aminoacid residue[190]. The ribityl structure of the substituent in the 10-position was established by periodate oxidation[190].

It was shown that the covalent linkage between the flavin and the aminoacid cannot involve the 1-, 2-, 3-, 4-, and 5-, and 10-positions in the isoalloxazine ring for the following reasons. On alkaline hydrolysis of SD-FAD, urea is formed, which rules out substitution in the 1- and 3-positions[18]. Since the removal of the ribityl side chain by alkaline photolysis[191] does not rupture the bond with the aminoacid in the residual substance, the 10-position was also eliminated[18]. All possible substitutions by alkyl, aryl, acyl, alkoxy-, amino-, and mercapto-groups in the 2-, 4-, and 5-positions are reversible under the conditions of hydrolysis or weak oxidation[5,128].

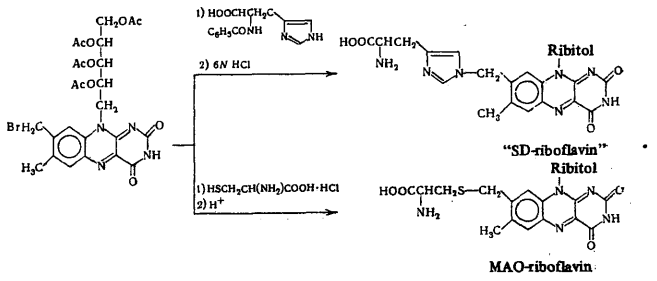
It was also shown that the hyperfine structure of the ESR spectrum of the "SD-flavin" radical differs from that of the riboflavin radical, which made it possible to eliminate the 7- and 9-positions characterised by low spin densities[189]. It was suggested that the addition to aminoacids takes place via the 8-methyl group[191], which is also consistent with the results from double resonance electron spin spectra[192].

On acid hydrolysis of "SD-riboflavin" under severe conditions in an atmosphere of helium, histidine was isolated in 80% yield. The same aminoacid is isolated on neutral photolysis and reductive cleavage of SD-FAD by hydrogen over palladium, i.e. under conditions where 3-benzylhistidine is cleaved[185].

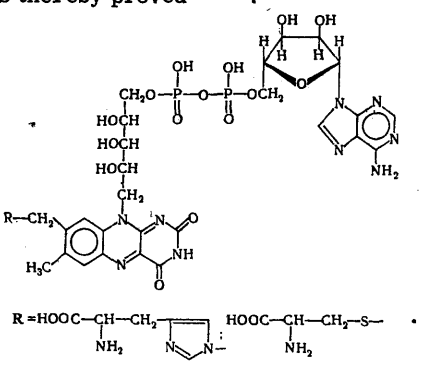
By analogy with the benzylation of histidine at 3-N and also on the basis of steric considerations, it was suggested that the flavin is linked to histidine via the 3-N atom[185].

The results led to the conclusion that "SD-riboflavin" has the structure of 8-α-(1- or 3-L-histidyl)riboflavin[183]. 8-α-(*N*-L-Histidyl)riboflavin, obtained by direct synthesis (heating of 2′,3′,4′,5′-tetra-acetyl-8-α-bromoriboflavin with benzoylhistidine in anhydrous dimethylformamide with subsequent hydrolysis by 6 *N* hydrochloric acid) prove to be spectroscopically and chromatographically identical with "SD-riboflavin"[184].

Next it was shown that the non-dissociating cofactor of monoamine oxidase (MAO) is not FAD but its derivative[193,194]. Stepwise hydrolysis of monoamino-oxidase yielded a mononucleotide and "MAO-flavin"—a riboflavin oligopeptide containing cysteine, serine, tyrosine, and two molecules of glycine. Further hydrolysis of the compound led to the isolation of 8-α-(*S*-cysteinyl)riboflavin[195,196], which Ghisla and Hemmerich also obtained synthetically by the reaction of tetra-acetyl-8-α-bromoriboflavin with cysteine hydrochloride and subsequent deacylation[197]:



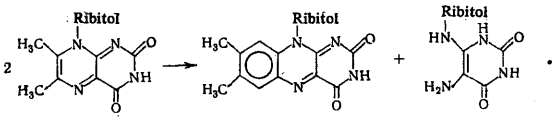
Thus detailed and far-reaching studies of the chemical behaviour of alloxazine and isoalloxazine compounds led to the determination of the unusual structures of new non-dissociating flavin coenzymes of succinate dehydrogenase [8-α-(*N*-L-histidyl)FAD][184,185] and monoamino-oxidase [8-α-(*S*-cysteinyl)FAD],[196,197] the flavin moiety of which is linked covalently to the aminoacid via the 8-methyl group; the earlier suggestion of the possibility of such a linkage was thereby proved[198,199]:



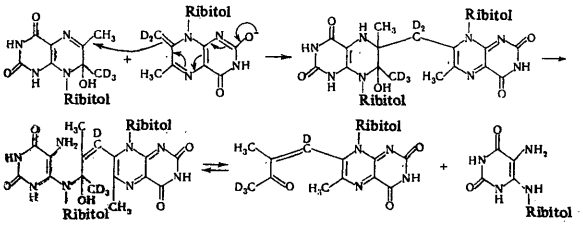
Thus the non-equivalent reactivities of the 7- and 8-methyl groups in the flavin molecule are used in nature as a fine-control factor for the construction with participation of a specific enzyme of the flavin prosthetic groups of succinate dehydrogenase and monoamino-oxidase.

It is interesting to note that the methyl groups of riboflavin are genetically related to the methyl groups of 6,7-dimethyl-8-(1′-D-ribityl)lumazine in the biosynthetic process.

The mobility of the hydrogen atoms of the methyl groups of lumazine, two molecules of which have been shown by Plaut[201,202] to be converted into one riboflavin molecule, is employed in the biosynthesis of riboflavin by the microorganisms *Eremothecium ashbyii* and *Ashbya gossypii*[200]. The same reaction was achieved *in vitro* by Cresswell et al., who showed that in a buffer solution at pH 7.3 6,7-dimethyl-8-(1′-D-ribityl)lumazine condenses into riboflavin in 55% yield on heating under nitrogen in the absence of an enzyme or an external carbon source[203]:



The study of the condensation of deuterated lumazine into riboflavin led to a possible mechanism of this reaction in which there is an initial attack by the carbanion on the 6-position of hydrated pteridine with formation of a carbinolamine in equilibrium with the ketone and finally the formation of the corresponding deuteroriboflavin[204,205]:



Plaut and coworkers propose a different mechanism for the non-enzymatic and enzymatic syntheses of riboflavin from lumazine[206–208].

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12. OTHER REACTIONS

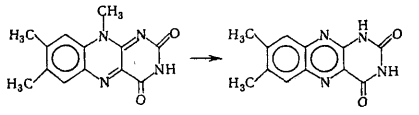
It was shown recently that, on photoexcitation with visible light under anaerobic conditions in an acid medium (pH < 5), lumichrome is hydroxylated in the aromatic ring, possibly in the 9-position, with formation of 9(6)-hydroxylumichrome [142].

An important reaction—the photolysis of riboflavin and other flavins—takes place with partial or complete removal of the side chain in the 10-position depending on the conditions; complete dealkylation leads to the conversion of isoalloxazines into alloxazines.

The studies on the photolysis of riboflavin have been reviewed [1,2,88,209].

Investigations in recent years have been devoted mainly to the identification of the intermediates in the photolysis of flavins and the study of its mechanism [210-217].

It is noteworthy that light is not a specific catalyst of the cleavage of isoalloxazines to alloxazines [4]. This reaction is catalysed also by metal ions such as Fe^{2+}, Sn^{2+}, Co^{2+}, [218,219] and in certain cases by bases [220] and reagents for the carbonyl group [4], quaternary amines, thioethers [87], etc. Thus, when lumiflavin was heated in acetic acid containing hydroxylamine for 120 h, lumichrome was obtained [4]:



The reverse transition, from alloxazines to isoalloxazines, is unknown.

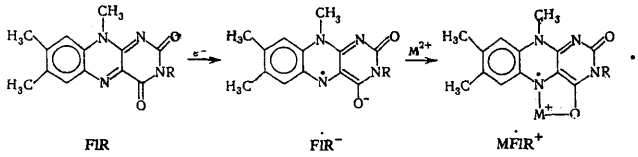
Alkaline or acid degradative cleavage of alloxazines and isoalloxazines with their conversion into quinoxalines has been investigated in fair detail and discussed in earlier papers [1,2,209]. This reaction is widely used to establish the structures of various derivatives of alloxazine and isoalloxazine [118,119,221-223].

Flavins are capable of forming complexes with different organic compounds, as a rule in 1:1 proportions [224]. Such compounds include phenols [225], indoles [226,227], purines [228,229], benzoic acid [230], aminoacids [231,232], etc. There are data showing that the tyrosine aminoacid residue in certain flavoproteins is involved in complex formation with the flavin [233]. Possibly this complex formation between flavin and aromatic aminoacids is in fact the main link between the prosthetic group and the apoenzyme in many flavoproteins [230].

In order to investigate the nature of the bond between flavins and aromatic aminoacids, McCormick and coworkers [234-237] employed as model compounds flavinylpeptides obtained by the interaction of methyl esters of aromatic aminoacids (L-tryptophan, L-tyrosine, and others), with 3- and 10-carboxyalkyl derivatives of flavins.

Riboflavin forms with certain metal salts insoluble intensely coloured chelate complexes, probably via the 5-nitrogen atom and the oxygen of the 4-carbonyl group. The metal ions involved in such complexes are Ag^+, Hg^+, Cu^+, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, and Mn^{2+}. [238,239] The chelate complexes with univalent metals are more stable than those with bivalent metals. It is noteworthy that the biocatalytic activity of many flavin enzymes is associated with the metal cations they contain, such as those of iron, molybdenum, copper, or manganese [240].

Flavins do not show an appreciable affinity for transition metal cations with a constant valence [238,241], probably owing to the low basicity of the 5-nitrogen atom and the high energy of the enolisation of the 4-carbonyl group [23]. However, in the form of flavosemiquinones, in particular radical-anions, they acquire a specific affinity for metal cations [242]. Under physiological conditions, the half-reduced flavin contains a small amount of radical-anions in consequence of disproportionation. However, in the presence of transition metal cations the equilibrium is displaced towards the formation of radicals owing to complex formation [243]. Under the experimental conditions (in dry DMF) in the presence of a stoichiometric amount of a strong base, for example potassium t-butoxide) 100% of the flavin radical-anions is formed [244]. The formation of the chelate complex can be represented by the following scheme [245]:



FlR FlR⁻ MFlR⁺

Further study of the reactions of alloxazines and isoalloxazines and of their reactivities, the elucidation of the relation between the parameters of the electronic structures in difference positions of the flavin molecule and its interaction with the apoenzyme, the study of the biochemical role of flavin radicals and flavin complexes with aminoacids and metals, as well as investigations of other types will undoubtedly promote a far reaching development of the chemistry of alloxazine and isoalloxazine derivatives and the discovery of the essential features of flavoprotein catalysis.

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Resolution of Racemic Alcohols into Optical Isomers

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The review analyses two classes of methods for the resolution of racemic alcohols into optical isomers: resolution by the synthesis and separation of diastereoisomeric derivatives and resolution without the formation or isolation of diastereoisomers. The fundamental classical studies on the resolution of racemic alcohols are noted. Attention has been concentrated on modern trends and modifications based on the latest advances in organic chemistry. It has been shown that the application of physicochemical methods leads to fundamentally new possibilities for the resolution of racemic alcohols. The bibliography includes 128 references.

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I. INTRODUCTION

The problem of the resolution of racemic alcohols arose in the past century in connection with the development of stereochemical hypotheses and a series of fundamental studies by Pasteur[1]. Pasteur's work determined the trend in studies in this field of organic chemistry for many decades. The list of racemic alcohols resolved hitherto is extremely impressive. The advances achieved in this field have been described in detail in a series of reviews[2,3] and monographs[4,5]. Modern studies on the resolution of racemic compounds differ qualitatively from earlier investigations as regards the aims of the investigators and the methods employed.

In connection with the vigorous development of biochemistry, it has become evident that the optical activity of natural compounds has a deep significance. The stereochemical characteristics of structure have a great influence on the biological activity of organic compounds. It is not fortuitous that all substances entering into the composition of cells and involved in fundamental vital processes (proteins, nucleic acids, lipids, polysaccharides, etc.) are optically active. Therefore the aim of the resolution of a racemate is frequently to obtain the optical isomer with the natural configuration. The principal task of the chemist is the creation and the preservation in the substances which he synthesises of the structures and configurations of the natural compounds.

A second feature of modern investigations is the improvement and modification of classical methods for resolution and, what is most important, the introduction into this field of modern physicochemical methods: gas–liquid chromatography (GLC), paper chromatography (PC), adsorption and ion-exchange chromatography, etc., which would make it possible to develop fundamentally new procedures for the resolution of racemates. The attempts at theoretical generalisations concerning resolution processes are important, since the available data for these processes still have more empirical features than any others in organic chemistry. The creation of a theory of resolution will make it possible both to predict the possibility of the resolution of a racemate by a particular process and to select the optimum method.

Together with the fundamental classical studies, this review describes the modern trends in the field of resolution of racemic alcohols based on the latest advances in organic chemistry. The methods of resolution have been divided into two main groups: (1) resolution by the synthesis and separation of diastereoisomeric compounds and (2) resolution without the synthesis or isolation of diastereoisomers.

II. RESOLUTION OF RACEMIC ALCOHOLS BY THE SYNTHESIS AND SEPARATION OF DIASTEREOISOMERS

The entire resolution process may be reduced to three consecutive operations (the so called "Pasteur's second method"): (1) the formation of a pair of diastereoisomers; (2) the separation of this pair using the differences between the properties of the diastereoisomers; (3) decomposition of the individual diastereoisomers with isolation of the optically pure enantiomorphs. For the first operation, it is necessary that the reaction of the racemic alcohol with the asymmetric agent should have a fairly high yield. The possibility of the second operation has been greatly improved recently when effective physicochemical methods have become available together with the crystallisation procedure. The third stage should be quantitative and should occur under mild conditions excluding the possibility of racemisation.

The two principal versions of resolution via diastereoisomeric compounds are discussed below.

1. INTRODUCTION INTO THE RACEMIC ALCOHOL MOLECULE OF A FUNCTIONAL GROUP CAPABLE OF FORMING DIASTEREOISOMERIC SALTS WITH OPTICALLY ACTIVE BASES

Historically this is one of the first and widely used methods. Salt formation is convenient because the resulting diastereoisomeric crystalline salt can be separated by fractional crystallisation. The first mention of the theoretical possibility of a large-scale employment of this type of resolution occurs in an early communication by Erlenmeyer and Arnold[6]. The fundamental idea of this method consists in the introduction into the alcohol molecule of the so called "connecting link" containing a functional group (carboxy-group) capable of forming a salt with an optically active base, for example:

$$R{-}OH + HOOCR_1COOH \rightarrow ROOCR_1COOH \xrightarrow{R^*} ROOCR_1COOH \cdot R^*,$$

where R–OH is the racemic alcohol, $HOOCR_1COOH$ the "connecting link", and R* the optically active base.

Evidently in this case the "connecting link" is a dibasic acid. Phthalic acid has been most frequently employed. The work of Pickard and Kenyon [7] was one of the earliest. Subsequently this acid was employed in many cases for the resolution of various racemic alcohols [8-10]. There is no necessity to enumerate all the resolutions achieved via acid phthalates—only a few need be considered. The classical method of Pickard and Kenyon (acid phthalate → brucine salt) has been used to resolve a number of diols, for example 3-(2-methylphenoxy)propane-1,2-diol [11] and butane-2,3-diol [12], and acetylenic alcohols, for example 3-methylpent-1-yn-3-ol [13] and 3,5-dimethylhex-1-yn-3-ol [14], difficulties arising in the last case in the fractional crystallisation of the brucine salts owing to a possible adsorption of the more soluble salt on the crystals of the less soluble salt. Recently the same method was employed to resolve 2-octanols (crystallisation of the salts with phenylethylamine, employed for the first time instead of the usual brucine) [15] and 2-butanols (salts with brucine) [16]. It is also possible to achieve the optical resolution of steroids containing a hydroxy-group via cinchonine salts of acid phthalates [17].

An interesting modification of this method was proposed in 1969, [18] consisting in the simultaneous application of the processes of Pope and Peachey [19] and Kantor and Hauser [20]. Pope and Peachey [19] showed that the resolution, which depends on relatively small differences between the solubilities of diastereoisomeric salts, can be made more effective when it involves an optically inactive reactant (A) competing with an optically active resolving agent (B) in the reaction with the racemic substance (±C). In successful cases the inactive reactant interacts completely with one enantiomorph while the optically active reactant interacts with the other.

(1) Classical resolution:

$$2(\pm C) + 2B_{act} \rightarrow (+)\text{-C.B.} + (-)\text{-C.B.}$$

(2) Pope and Peachey process:

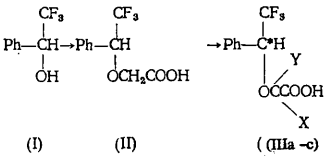
$$2(\pm C) + B_{act} + A_{inact} \rightarrow \begin{matrix}(+)\text{-C.B} + (-)\text{-C.A} \\ \text{or} \\ (-)\text{-C.B.} + (+)\text{-C.A}\end{matrix}.$$

Owing to the slight differences between the solubilities of the diastereoisomers, in process (1) their separation requires repeated recrystallisations. In process (2), where the products are not diastereoisomers, with a successful choice of A the separation could be achieved more readily and with a smaller number of recrystallisations. The process of Pope and Peachey was applied in the classical procedure [7] for the resolution of various secondary alcohols using triethylamine as A, brucine as B and acid phthalates derived from secondary alcohols as ±C. The optical purity of the alcohols isolated was high even without additional recrystallisation. The resolutions of 2-butanols, 2-octanols, and 1-phenylethanols were achieved. An additional advantage of this modification consists in a decrease of the consumption of the asymmetric reactants (B) which are usually expensive. In 1953 Kantor and Hauser [20] modified process (1) in the resolution of acid phthalates derived from 2-butanol by using a deficiency of the solvent for the reactants. After prolonged refluxing, the salts formed are effectively recrystallised before their isolation, which leads to higher optical yields in a single stage than in the usual procedure (82% optical purity in the case of 2-butanol). The simultaneous use of the process of Pope and Peachey and the modification of Kantor and Hauser leads to secondary alcohols with a higher optical purity than can be obtained by processes (1) and (2), [18] albeit at the expense of the yield.

In 1951 Zeiss showed [21] that tertiary alcohols, for example ethylmethylphenylmethanols, can be resolved by the method of Pickard and Kenyon (via the acid phthalate with subsequent formation of a brucine salt). Later Kenyon and coworkers carried out a similar resolution of 2-(1-naphthyl)butan-2-ol [22], 2-phenylbutan-2-ol [23], and 2-methyl-3-phenylpropane-1,2-diol [24]. Admittedly in the last case the resolution via the acid phthalate was unsuccessful since neither the phthalate nor its salts with various alkaloids were crystalline. The resolution was achieved by the reaction of 3-nitrophthalic acid followed by the formation of its strychnine salt. The diastereoisomeric salts were separated by crystallisation and decomposed with ammonia. Subsequent treatment of the 3-nitrophthalate with alkali yielded the optically active 2-methyl-3-phenylpropane-1,2-diol [24]. 3-Nitrophthalic acid was used in a number of other cases, for example by Holding et al. [25]

Succinic acid has also been used as a "connecting link" in the resolution of alcohols [26]. The optical isomers of cyclopent-2-en-1-ol were separated via the formation of salts of the acid esters of succinic acid and (+)-α-(1-naphthyl)ethylamine [27]. A number of resolutions have been carried out using phthalamic [28] and sulphuric [29] acids. Sulphates may be suitable for the resolution of certain glycols although as a rule acid alkyl sulphates are unstable and difficult to prepare.

It should be noted that the method under consideration does not always lead to the desired results. For example, the attempt to resolve the acid phthalates derived from 2,2,2-trifluoro-1-phenylethanols (I) via diastereoisomeric salts with optically active bases [30] was unsuccessful, since the ester of this alcohol proved to be readily hydrolysable even on treatment with brucine. This is because of the acidity of the alcoholic hydroxyl group. In 1968 the separation of the optical isomers of compound (I) was achieved [31] with a low yield by the fractional crystallisation of its esters with acetoxyandrost-5-ene-17β-carboxylic acid by a method which is discussed in detail in the next section. The high interest in 2,2,2-trifluoro-1-phenylethanol is due to the fact that in many cases the optically pure enantiomorph of this alcohol is a suitable solvent for NMR spectroscopic studies. Recently Pirkle et al. [32] achieved a new and novel resolution of compound (I) using a monobasic acid (substituted acetic acid) as the "connecting link":

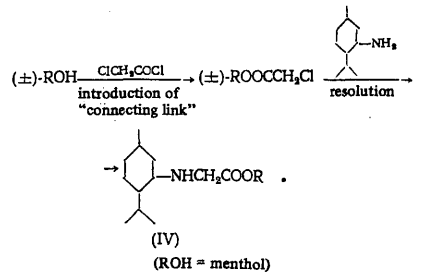


(I) (II) (IIIa-c)

(a, X=H, Y=Br; b, X=Br, Y=H; c, X=Y=Br)

The interaction of the alcohol (I) with ethyl bromoacetate led to 2-trifluoro(phenyl)ethoxyacetic acid (II), the optical isomers of which were then separated via salts with amphetamine [$PhCH_2CH(CH_3)NH_2$]. The α-bromoesters (III, a – c), readily hydrolysable to the optical isomers of the alcohol (I), were obtained by regenerating the optical isomers of the acid (II) from the diastereoisomeric salts and by treating them with bromosuccinimide. The introduction of bromine is necessary to facilitate the subsequent hydrolysis. 2,2,2-Trifluoro(1-naphthyl)ethanol optical isomers were separated similarly [32]. This method can be used for the resolution of other acids and similar alcohols when the classical process does not lead to the desired result.

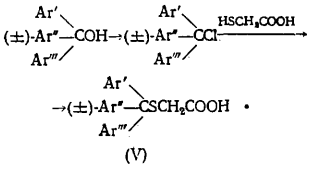
The formation of an ester with chloroacetic acid has been used to separate menthol isomers[33]. Here the asymmetric agent is (−)-menthylglycine formed by the reaction:



(IV)
(ROH = menthol)

The diastereoisomeric esters (IV) obtained were separated by crystallisation. The addition of acrylic acid has been used[34] to introduce a carboxy-group into the molecule. The reaction of (±)-1-trifluoromethylethanol with acrylic acid led to the adduct (±)-β-(1-trifluoromethylethoxy)-propionic acid the optical isomers of which were separated via diastereoisomeric salts with strychnine. The alcohol isolated from the separated adduct racemate was optically active.

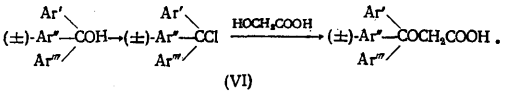
The separation of the isomers of trityl alcohols presents considerable difficulties. The separation of the isomers of biphenylyl-α-napthylphenylmethanol and 12-phenyl-12-benzoxanthenol, a trityl alcohol in which two aryl groups are linked together to form a heterocyclic ring, via the diastereoisomeric salts of substituted thioglycolic acid and alkaloids was reported by Wallis and Adams as late as 1933:[35]



(V)

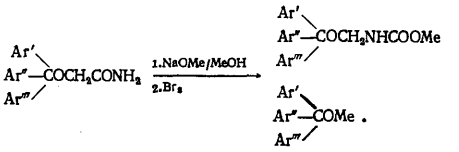
The isomers of the acid (V) were separated via their brucine salts. Treatment of the separated acids with silver nitrate in aqueous acetone yielded the optically active alcohols. Later this method was recognised as unsatisfactory[2] but Murr[36] showed that the optical yield amounts to 60% and may be increased.

The difficulty of separating the optical isomers of trityl alcohols is due to the lability of the trityl ester bond formed on introduction of a carboxy-group via the esters of dibasic acids. Although the separation of the isomers of α-naphthylphenyl-*p*-tolylmethanol by the classical method of Pickard and Kenyon[7] has been reported[37], it was not reproducible[38,39]. It was therefore suggested that the carboxy-group be introduced into the trityl alcohol molecule via an ether linkage[36,38]. The formation of an ether with glycolic acid was employed:

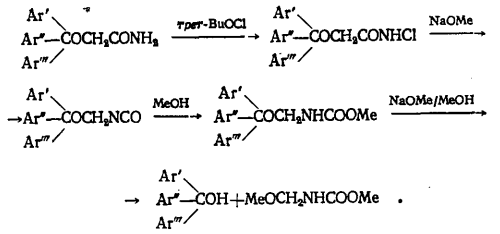


(VI)

The isomers of the acid (VI) were separated via salts with brucine [for the (−)-form] and cinchonidine [for the (+)-form]. The attempt to regenerate the optically active alcohol from the acid (VI) via the formation of an amide with subsequent Hofmann degradation did not yield the desired result owing to the dissociation of the ether linkage:

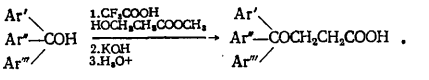


The yield of the ethyl ether of the tritylmethanol was 85%. The regeneration was achieved via the chloramide according to the following scheme:



The isomers of biphenylyl-α-naphthylphenylmethanol were separated in this way[38] but the attempt to separate those of biphenylyl-*p*-chlorophenylphenylmethanol were unsuccessful.

Derivatives of hydracrylic acids were used in 1969 to separate the isomers of α-naphthylphenyl-*p*-tolylmethanol[39]:



(±)-β-(α-Naphthylphenyl-*p*-tolylmethoxy)propionic acid was resolved via the diastereoisomeric salts with brucine. The alcohols were regenerated from the methyl esters of the separated acids by the reverse Michael reaction.

In conclusion mention should be made of a study[40] which proved to be useful in the isolation of the acid ester of an alcohol with a dibasic acid from the separated diastereoisomeric salts. The authors suggest that ion-exchange chromatography be used for this purpose, which makes it possible to isolate the acid ester in almost quantitative yield.

Summarising this method for the resolution of alcohols (using a "connecting link"), we should note that it made it possible to obtain a large number of optically active alcohols. The numerous dibasic acids and optically active bases (among which alkaloids are frequently employed) permit an extensive variation of their combinations in cases of failure. Nevertheless the investigator cannot be absolutely certain that the differences between the solubilities of the diastereoisomeric salts and their chemical stabilities will be sufficient for a successful resolution. A serious disadvantage of the method is associated with the isolation in a pure form and a sufficiently large amount of only one of the enantiomorphs (from the less soluble salt), while the other is isolated in only a small amount and with an inadequate optical yield. In view of the salt-like nature of the diastereoisomers, crystallisation is perhaps the only process suitable for their separation. The next modification of the resolution procedure via diastereoisomeric compounds does not suffer from this disadvantage.

2. DIRECT INTERACTION OF THE RACEMIC ALCOHOL WITH THE OPTICALLY ACTIVE RESOLVING AGENT AND THE FORMATION OF DIASTEREOISOMERIC DERIVATIVES

This method has the advantage that the stage involving the introduction of the "connecting link" is eliminated and the diastereoisomeric products are obtained by the direct interaction with a particular asymmetric agent. However, until recently this method had not been used quite so widely as the preceding one, since the diastereoisomeric compounds obtained (usually esters of an optically active acid) are normally difficult to crystallise. Nevertheless the use of modern physicochemical methods and of new asymmetric agents for the resolution (such as carbohydrate derivatives) has greatly extended the scope of this method.

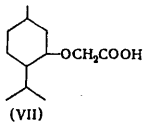
a. The Formation of Diastereoisomeric Esters of Optically Active Acids

Many optically active acids have been employed in classical resolution of this kind.

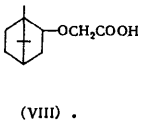
Mandelic acids [41]. This expensive reagent, which is used, in particular, for the resolution of (±)-menthol, is fully racemised in the alkaline hydrolysis of the diastereoisomers, which constitutes a serious disadvantage. The resolution of *erythro*-1-(4-hydroxyphenyl)-2-(1-methyl-2-phenoxyethylamino)propan-1-ol isomers [42] may serve as an example of resolutions with the aid of mandelic acid. The isomers of synthomycin were separated via esters with D-(−)-acetylmandelic acid, which yielded laevomycetin [43].

Camphoric acid. The majority of the diastereoisomeric esters of camphoric acid could not be separated by crystallisation, so that resolution with the aid of this agent is usually only partial [44]. Camphorsulphonic acids have also been used [45].

The employment of menthoxyacetic acid (VII) and bornylacetic acid (VIII) as asymmetric agents is promising for the resolution of phenols, glycols, and alcohols with a high molecular weight:



(VII)



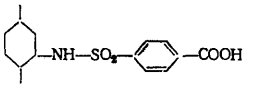
(VIII).

This version resembles the previous method, since an optically active alcohol is in fact employed for the resolution and the acetic acid residue constitutes a "connecting link". The acids (VII) and (VIII) are readily obtained from chloroacetic acid and the sodium derivatives of the corresponding alcohols. The resulting esters of the racemic alcohols have a fairly high specific optical rotation and are readily crystallised. Hydrolysis of the separated esters leads to an optically active alcohol, while the asymmetric agent is regenerated. The isomers of *trans*-cyclohexane-1,2-diol were separated in this way [46]. With the aid of the chloride of the acid (VII), Taub et al. [47] separated the isomers of the 4-*O*-methyl ester of the macrolide zearalenone and obtained the product with the natural configuration.

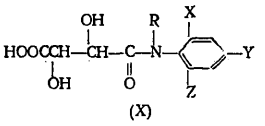
Recently the range of acids suitable for the resolution of alcohols via the diastereoisomeric esters have been greatly extended. Thus the reaction of (+)-*threo*-2-amino-1-(*p*-nitrophenyl)propane-1,3-diol hydrochloride or hydrogen sulphate with dibenzoyl-D-tartaric acid readily yields the crystalline neutral ester only with the D-isomer, which permitted a ready separation of the optical isomers [48]. (±)-2-Dimethylaminocyclohexanol was resolved with the aid of dibenzoyl-L-tartaric acid [49]. 3β-Acetoxyandrost-5-ene-17β-carboxylic acid was used in the resolution [31] of trifluoromethylphenylmethanol mentioned above. On the other hand, certain racemic steroids (the 3-methyl ether of oestradiol and 19-nortestosterone) were resolved via the formation of esters with the monomethyl ester of diacetyl-D-tartaric acid [50].

Aminoacids have been used in a number of cases for the resolution of alcohols. Halpern and Westley [51] proposed a method for the chemical resolution of racemic secondary alcohols into optical isomers, consisting in the esterification of the alcohol with an L-aminoacid in the presence of toluene-*p*-sulphonic acid with subsequent separation of the resulting ester sulphonates by fractional crystallisation and isolation of the optically pure (98 to 100%) (+)-isomer of the alcohol. Valine and alanine, with the aid of which it was possible to separate the isomers of 2-butanol, 2-methylcyclohexanol, menthol, and other alcohols, were employed as the L-aminoacids. In 1967 Germyn [52] extended the Halpern–Westley method to primary alcohols having obtained the enantiomorphs of 2-methylpentan-1-ol by the crystallisation of the tosyl derivatives of their esters with D- and L-valine; the use of alanine, tyrosine, leucine was unsuccessful. Probably a successful choice of aminoacid would make it possible to resolve also other racemic alcohols by the Halpern–Westley method, which can therefore be regarded as fairly general.

Campholic acid (1,2,2,3-tetramethylcyclopentanecarboxylic acid) has been proposed as a new convenient asymmetric agent for the resolution of menthol isomers [53], since only one of the diastereoisomeric esters [the (−)-menthyl ester of (+)-campholic acid] is crystalline, while the other is a liquid. This method is unsuitable for the resolution of the neo- and iso-forms of menthol, because neither diastereoisomeric ester is crystalline. Other agents which may serve for the resolution of alcohols are (−)-menthyl-*p*-sulphamoylbenzoic acid (IX), proposed by Everard and Mills [54], and also substituted tartranilic acids (X) suggested recently [55] for the resolution of racemic bases, since tartranilic acid itself has been used for the resolution of alcohols [56]:



(IX)



(X)

(R=H, Me; X=NO_2, Cl, Br, Me, H; Y=H, Cl, Br; Z=H, Cl, Br.).

So far we have considered studies in which diastereoisomeric esters of racemic alcohols and an optically active acid were separated by crystallisation processes. As mentioned above, the development of physicochemical methods has made it possible to achieve the separation of many diastereoisomers, including those which are not crystalline. This has occurred mainly owing to advances in adsorption, ion-exchange, gas–liquid, and paper chromatography. Small differences between the physical properties of diastereoisomeric esters proved sufficient to separate small amounts of substances both for preparative and for analytical purposes. As a rule the use of physicochemical methods yields both enantiomorphs with a high optical purity.

Thus optically active secondary alcohols can be separated with about 100% optical purity via the chromatography of their esters with optically active acids on an optically inactive ion exchanger. The enantiomorphs of (±)-2-butanol were separated via the esters with

(−)-mandelic acid by chromatography on Dowex-50W-X2.[57] The resolution by analogous chromatography of 3-methylbut-2-yl lactate was even easier, 26 millimoles of a mixture of diastereoisomeric esters yielding 1.2 millimoles of the optically pure (+)-3-methylbutan-2-ol.[58] The separation of esters formed by (±)-2-methylbutan-1-ol with mandelic acid was not achieved by ion-exchange chromatography[58] but by gas–liquid chromatography (g.l.c.)[59]; the authors suggested that, for the successful chromatographic separation of the esters, it is necessary that the hydroxy-group should be linked to the asymmetric carbon atom.

Until recently the separation of diastereoisomeric esters by g.l.c. was used mainly for analytical purposes (for tests of the optical purity of the specimen, the determination of the absolute configuration, etc.)[60]. The optical purity of asymmetric alcohols was determined by g.l.c. in 1963.[61] Subsequently the formation of R-(−)-menthyloxycarbonyl derivatives of asymmetric alcohols (in particular α-phenylalkylmethanols) was used for this purpose[62]. Gil-Av et al. showed[60] that many gas–liquid chromatographic resolutions are possible also on a preparative scale. They separated[63] the esters formed by 2-alkanols containing between 4 and 19 carbon atoms with hydroxypropionic acids with the aid of g.l.c. on columns containing squalene, poly(propylene glycol), and other phases. The DL-(or LD-) derivatives have longer retention times than the LL-(or DD-) derivatives. Carbonic acid esters of the type ROCOOR' are particularly convenient for the preparative separation by g.l.c. of the enantiomorphs of racemic alcohols[64] in view of the ease of their synthesis and subsequent hydrolysis. The structural features of diastereoisomeric esters which favour their separation by g.l.c. have been investigated[65]. Such attempts at theoretical generalisation based on the accumulated factural data are particularly valuable, since they allow a well founded choice of a particular resolving agent for the racemic mixture, the prediction of the necessary chromatographic conditions (such as temperature, solvent, etc.), and an understanding of the reasons for the differences between the physicochemical properties of diastereoisomers. The authors deduced a number of relations: (1) the higher the conformational stability of the groups linked to both asymmetric centres, the better the separation; (2) in view of the small free energy differences, slight structural changes in diastereoisomeric esters can lead to a great improvement in separation; (3) in the study of the mechanism of the separation of esters by g.l.c., both steric and electronic factors can be taken into account.

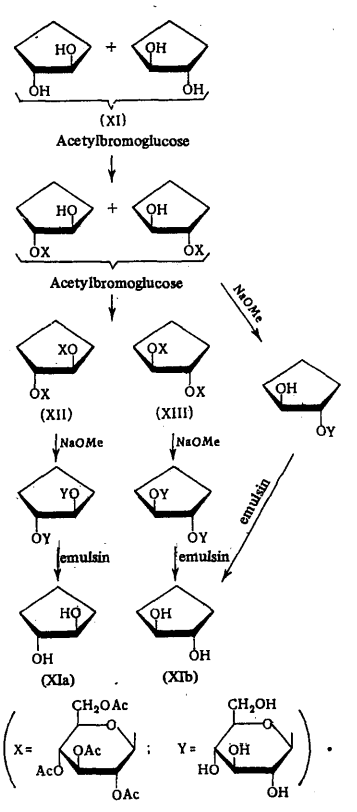
Among other modifications of this method, mention should be made of the possibility of separating the diastereoisomeric esters of lower alcohols and optically active acids by distillation through a sufficiently effective fractionating column using the slight differences between the vapour pressures of the diastereoisomers. This has been demonstrated in the separation of the optical isomers of 2-butanol via esters with L-lactic, L-2-acetoxypropionic, and D-2-propyloxypropionic acid by [fractional] distillation.

b. Formation of Diastereoisomeric Urethanes

The formation and separation of diastereoisomeric urethanes obtained by treating the racemic alcohol with L-menthyl isocyanate is one of the earliest methods of resolution[67]. However, the low availability of the asymmetric agent, the difficulty of hydrolysing the urethanes and also the conversion of L-menthyl isocyanate into an amine by hydrolysis greatly reduce its value[68]. The diastereoisomeric *N*-(1-phenylethyl)urethanes derived from certain secondary alcohols and obtained by the reaction of the aliphatic alcohol with a slight excess of (+)- or (−)-1-phenylethyl isocyanate, can be separated by thin-layer chromatography t.l.c. on silica gel G.[69] The following alcohols have been investigated: oct-1-en-3-ol, 2-octanol, 2-heptanol, 3-octanol, and 3-pentanol. It has been shown that the (++)-, and (−−)-diastereoisomers have a higher R_f than the (+−)- or (−+)-diastereoisomers, which makes it possible to establish the absolute configuration of the alcohol present in microamounts or to test its optical purity.

c. Resolution via Diastereoisomeric Carbohydrate Derivatives

Only a few cases of the use of carbohydrate derivatives as asymmetric agents for the resolution of racemic alcohols have been described in the literature. Probably this is because the glycosides employed are obtained in insufficient yields and the isolation of the optically active alcohols from the separated glycosides requires severe conditions or the use of enzymatic systems. Neuberg et al.[70] were the first to succeed in resolving pentyl alcohol, menthol, and borneol via the corresponding D-glucosides. Subsequently Helferich and Hiltmann[71] carried out a similar separation of the isomers of *trans*-cyclopentane-1,2-diol (XI):

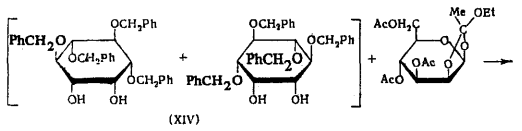


The diglucosides (XII) and (XIII) could be separated by crystallisation and enantiomorphs (XIa) $\{[\alpha]_D = -33.8°\}$ and (XIb) $\{[\alpha]_D = +33.8°\}$ were obtained after hydrolysing the

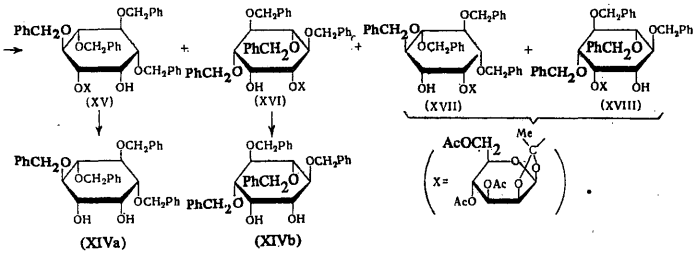
acetate groups and subsequent cleavage of the glycosidic linkage with the aid of emulsin. Hydrolysis of the monoglucoside led to a product the treatment of which with emulsin gave the dextrorotatory enantiomorph (XIb). The hydrolysis of a mixture of the diastereoisomeric menthol β-D-glucosides, as a result of which the menthol isolated after incomplete hydrolysis was optically active, shows an interesting optical selectivity [72].

The separation of the optical isomers of alcohols via diastereoisomeric glycosides has not found a wide application owing to numerous difficulties encountered in this procedure. Angyal and Shelton [73] synthesised in this way diastereoisomeric mannosylmyoinositols in a yield of about 4%. Although the diastereoisomers were readily separated by fractional crystallisation, it is impossible to employ them as the starting materials for the preparation of optically active asymmetrically substituted myoinositols owing to their small amount.

Nevertheless the use of other derivatives of monosaccharides and alcohols and different methods for the separation of diastereoisomers may greatly extend the scope of this method. This has been demonstrated for the resolution of asymmetrically disubstituted myoinositols, which have attracted attention in connection with their role in biochemical processes. The attempts at the resolution of these compounds by classical methods were unsuccessful [74]. A recently proposed method for the resolution of racemic myoinositols [75] is based on the interaction of the racemate with the orthoacetates of D-mannose and lower alcohols under the conditions of the transesterification reaction with subsequent separation of the resulting diastereoisomeric D-mannose orthoesters and myoinositol derivatives by chromatography or crystallisation and the isolation of the enantiomorph from the separated orthoesters. For example, 1,4,5,6-tetra-*O*-benzylmyoinositol (XIV) was resolved in this way [76]:

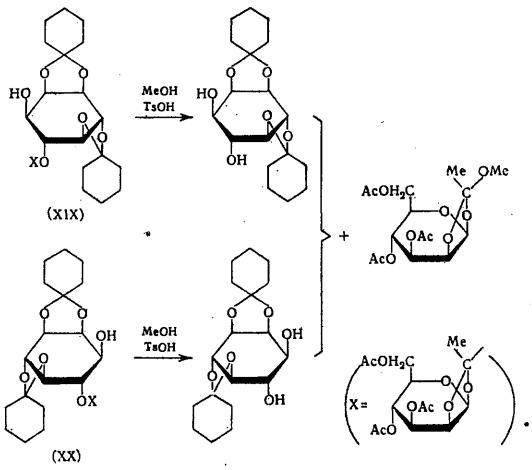


(XIV)



(XIVa) (XIVb)

The diastereoisomeric orthoesters (XV), (XVI), and the mixture of (XVII) and (XVIII) were separated by crystallisation and preparative t.l.c. The enantiomorphs (XIVa) and (XIVb) were isolated by mild acid hydrolysis of the separated orthoesters (XV) and (XVI). The isomers of 1,2,4,5,6-penta-*O*-benzylmyoinositol [77] and 1,2:5,6-di-*O*-cyclohexylidenemyoinositol [78] were separated similarly, in the latter case the enantiomorphs being isolated from the separated diastereoisomeric orthoesters (XIX) and (XX) in high yields by "reverse" transesterification with methyl alcohol, since acid hydrolysis was inapplicable owing to the lability of the *trans*-cyclohexylidene group:



(XIX)

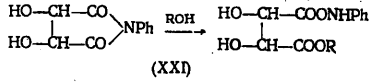
(XX)

We believe that this method may prove to be suitable for the resolution of other racemic compounds, in particular cyclic alcohols with a fixed steric configuration, with the aid of a suitably selected monosaccharide orthoester.

Mention should also be made of a study [79] where it was shown that the configuration of carbohydrates can be established by means of their diastereoisomeric derivatives with alcohols. This applies to the carbohydrates which can be readily and quantitatively oxidised to aldanic acids, the esterification of which with racemic alcohols (2-butanol, 3-methylbutan-2-ol, and 3,3-dimethylbutan-2-ol) leads to volatile diastereoisomers which can be separated by g. l. c. The peaks were identified by comparison with a specimen obtained as a result of esterification with an optically active alcohol. In all cases (lyxonic, ribonic, xylonic, arabonic, glyceric, and other acids), the separation was best with sterically hindered alcohols, in agreement with the findings of Karger and coworkers [64].

g. Other Asymmetric Agents

Of other agents proposed for the direct formation of diastereoisomeric derivatives of racemic alcohols, mention should be made of *N*-phenyl-D-tartrimide (XXI), which reacts with alcohols according to the following mechanism [56]:



(XXI)

If the alcohol molecule contains another functional group, it too can be used for the direct formation of diastereoisomeric products. Thus separation of the enantiomorphs of certain carbinols of the type RR'R"COH, where R = phenyl, R' = 2-pyridyl or 4-pyridyl, and R" = n-octyl, was achieved via salts with D-camphorsulphonic or tartaric acids [80]. Natural D-(+)-*erythro*-dihydrosphingosine was obtained by the separation of the racemic aminodiol via the salts with L-glutamic acid [81] and the enantiomorphs of 3-*O*-benzoylsphingosine were separated with the aid of D- and L-tartaric acids [82].

III. RESOLUTION OF RACEMIC ALCOHOLS WITHOUT THE SYNTHESIS OR ISOLATION OF DIASTEREOISOMERS

This large group of methods for the resolution of racemic alcohols, which includes, together with Pasteur's classical procedures, also modern methods which have been recently developed, involves a direct resolution of racemates without the formation or isolation of diastereoisomeric products. If the diastereoisomers are in fact formed, they are usually extremely unstable and cannot be isolated. An advantage of such methods is the absence of the necessity for the isolation of diastereoisomers which in many cases (for example in separation by adsorption) makes it possible to carry out the separation as a continuous process.

1. RESOLUTION OF RACEMIC ALCOHOLS BY THE CRYSTALLISATION OF ENANTIOMORPHS

The so called "Pasteur's first method" [83] is based on the mirror image differences between the enantiomorph crystals, which can therefore be separated mechanically. This method is laborious and slow and has not found a serious practical application. Very often attempts at resolution proved unsuccessful: for example, LeBel [84] could not separate the crystals of barium 2-butylsulphate; the attempt to separate mechanically the crystals of (±)-erythritol [85] was also unsuccessful. Although there is some evidence that (±)-*cis*-β-decalol can be separated by Pasteur's first method using the properties of its crystals [86], no actual resolution of this substance has been reported in the literature. The separation of the enantiomorphs of isohydrobenzoin has been quoted as a successful example [87].

The resolution of racemates by selective crystallisation is of more interest. It is usually achieved by introducing a seed of one of the enantiomorphs into a supersaturated solution of the racemate. Studies on such resolution were begun with the publication in 1866 of the report by Gernez[88], but so far few attempts have been made at a theoretical generalisation of the numerous factural data available. It is now known only that the resolution is possible if the solubility of each pure enantiomorph is higher than that of the racemic modification [89] and if the racemate consists of a mechanical mixture of the enantiomorph crystals and not a solid solution. Many substances resolved by crystallisation are known. Thus Shelomova et al. [90], who employed the method of Velluz et al. [91], elaborated the conditions for the resolution of (±)-*threo*-2-amino-1-*p*-nitrophenylpropane-1,3-diol, which involve rapid cooling of a system consisting of 86% of the racemate in the form of the hydrochloride, 14% of the free racemic aminodiol, and 10% (relative to the weight of the racemate) of the L-(+)-form. The study of the solubility curves of the racemate and the enantiomorphs of the diol showed that, if the system contains an excess of one of the enantiomorphs, its crystallisation begins. In his large review, Secor [92] quotes numerous cases of selective crystallisation, discusses the theoretical possibilities and limitations of the method, and examines the phase diagrams for systems containing optical isomers.

Powell [93] noted that the racemic substance can form crystalline molecular compounds with an optically inactive compound. This results in overcoming the van der Waals forces maintaining the enantiomorphs in the crystalline racemate and, instead of the racemate (*dl*), the *Md* and *Ml* compounds crystallise from solution, *M* being the optically inactive substance. The majority of these molecular compounds are resolved spontaneously. The advantages of such resolutions are evident: no chemical reactions are involved, there is no need to introduce additional functional groups into the racemic alcohol molecule, it is possible to resolve small amounts of substances into their enantiomorphs, etc. Powell [93] suggests that similar processes may have resulted in the appearance of the initial asymmetry in nature. A study [36] of the resolution of biphenylyl-1-(8-methylnaphthyl)phenylmethanol may be quoted as an example of the "spontaneous" resolution of racemic alcohols: the (+)-enantiomorph was isolated by crystallisation from ether and the (−)-enantiomorph was crystallised from cyclohexane.

2. CHROMATOGRAPHIC RESOLUTION

This group of methods includes the chromatographic resolutions on natural asymmetric agents (wool, polysaccharides, crystals of optically active quartz, and others [94]) and also on synthetic asymmetric agents. Examples of resolution by adsorption are discussed in detail in Klabunovskii's review [95]. The relations governing the resolution of racemic substances on starch columns have been formulated [96]. The use of brucine as an adsorbent made it possible to resolve (±)-2-octyl hydrogen phthalate [97]. Recently many resolutions have been carried out on synthetic optically active ion-exchange resins. Many such ion exchangers have been synthesised. Suda and Oda [98] prepared resins from the chloromethylated copolymer of styrene with divinylbenzene and brucine or quinone. In a recent review, Suda [99] discusses the synthesis of optically active ion-exchange resins by the polycondensation of various optically active acids or bases and the separation of racemic substances on these exchangers. Poly{[L-(1-carboxy methyl)sulphamoyl]styrene} and the D-isomer of the polymer were employed for the partial resolution of atrolactic acid [$C_6H_5(OH)C(CH_3)COOH$], mandelic acid, and other substances [100]. There is no doubt that synthetic optically active ion-exchange resins can also be employed for the resolution of various derivatives of racemic alcohols. Mixtures of racemic terpene alcohols were resolved by being brought into contact with optically active polymers under the conditions of the transesterification reaction with subsequent elution [101]. Racemic menthol in tetrahydrofuran in the presence of catalytic amounts of toluene-*p*-sulphonic acid was introduced into a column containing a granular resin obtained by the copolymerisation of a 1 : 1 mixture of (+)-s-butyl methacrylate and maleic anhydride with 2–20 wt.% of divinylbenzene and then slowly eluted with tetrahydrofuran containing alcohol and toluene-*p*-sulphonic acid, which led to the isolation of the enantiomorphs of menthol.

In 1969 resolutions with the aid of liquid ion exchangers were achieved [102]. The authors synthesised two liquid ion-exchangers: (−)-*N*-methyl-α-methylbenzyl-(1-naphthyl)amine and (−)-*N*-α-methylbenzyl(n-octadecyl)amine and determined the separation factors for the enantiomorphs of the sodium salts of (±)-mandelic acid and (±)-*N*-acetylalaline in periodic partition between aqueous solutions of the salts and the solutions of the ion exchangers in chloroform. The optical isomers of the first salt were separated by countercurrent partition; the optically pure product can be isolated even if the liquid ion exchanger is not optically pure. Although this study concerns directly only the resolution of salts of racemic

acids, the equations and principles quoted are also applicable to the resolution of other racemic substances, including alcohol derivatives, by chromatography or countercurrent partition, which yields in a single operation both enantiomorphs in equal amounts.

The development of the gas–liquid chromatographic method has led to the possibility of direct resolution of racemic alcohols and other substances by g.l.c. on an optically active stationary phase. The studies in this field were stimulated by the fact that the influence of solvents (employed in adsorption chromatography), which might have a levelling effect on the difference between the absorption properties of the enantiomorphs, is eliminated in g.l.c. Experimental conditions for the resolution of α-pipecoline, acetylmethylmethanol and other compounds have been described [103] but subsequently this study could not be reproduced [104]. Later Gil-Av et al. reported the resolution of racemates by g.l.c. on an optically active stationary phase using capillary columns equivalent to a large number of theoretical plates. Apart from its use for analytical purposes, the resolution of racemates by g.l.c. can also be of preparative value [60]. The resolution of 2-butanol, 2-pentanol, and phenylethanol by g.l.c. on an optically active quartz column has been investigated [105] and has been shown to be unsatisfactory.

The resolution of racemates by paper chromatography has been discussed by Yanovskaya [106]. The most detailed reviews of the chromatographic resolution of racemates have been published by Rogozhin and Davankov [107] and Buss and Vermeulen [108].

3. RESOLUTION WITH THE AID OF OPTICALLY ACTIVE LIQUID SUBSTANCES

A study of the resolution of racemates with liquid ion-exchangers has already been mentioned [104]. The different interfacial tensions between the enantiomorphs and an optically active liquid can also be used for the resolution of a racemic mixture [109]. If the liquid racemate is emulsified in an optically active liquid or in a solution of an optically active substance, the enantiomorphs will be deposited at different rates.

Nevertheless the most promising processes for resolution with the aid of optically active liquids are crystallisation and extraction. Although van't Hoff [110] suggested as early as the end of the last century that the solubilities of enantiomorphs in optically active substances will be different, for a long time resolution by crystallisation from optically active solvents could not be achieved. Recently examples of such resolutions have been published. 2,3-Dibromobutane-1,4-diol and di-(4-pyridyl)glycol were resolved into optical isomers by crystallisation from di-isopropyl-D-tartrate [111]; after the third recrystallisation 167 mg (!) of the optically active substance was obtained from 20 g of the racemate. The same substances were partly resolved by partitioning their racemic modifications between an aqueous medium and D-tartaric acid esters [112]. It has been suggested that there is a type of bonding between the racemate and the solvent medium and that, owing to the differences between the configurations, one enantiomorph is geometrically more suitable for the formation of such bonding than the other. If hydrogen bonds are possible, these are the most likely to be formed [113].

If each of the two enantiomorphs forms an azeotrope with a third optically active substance, the diastereoazeotropes can have boiling points differing so much that they can be separated by fractional distillation [114]. This hypothesis has not been confirmed in attempts to resolve 2-octanol with (+)-limonene as the third component under different experimental conditions. Nevertheless the study of the boiling point diagrams for systems gives rise to the hope that certain resolutions can be achieved by the distillation of diastereoazeotropes.

4. OTHER METHODS OF RESOLUTION

Sometimes the racemate is resolved by its interaction with an optically active substance which results in the formation of readily decomposed molecular complexes instead of diastereoisomers. By employing digitonin as the complex-forming agent, it proved possible to resolve the racemates of α-terpineol, tetrahydro-β-naphthol, and *i*-carvomenthol [115]. 2-Phenylbutan-1-ol was partly resolved into its optical isomers with the aid of deoxycholic acid [116]. The authors suggested that the optically selective action of lipolytic enzymes may be due to bile acids.

Numerous examples of the kinetic resolution of alcohols by selective interaction with an optically active agent have been described in the literature. Marckwald and McKenzie [117] carried out a partial esterification of (±)-2-octanol with D-tartaric acid, the unreacted part of the alcohol proving to be optically active. Here mention should also be made of stereoselective biochemical processes which consist in the selective action of various micro-organisms on one of the enantiomorphs (the so called "Pasteur's third method" [118]).

The methods enumerated in this section have been analysed in detail in special reviews and monographs [2–5].

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A good example of classical resolution carried out recently is the separation of the enantiomorphs of 2-chloro-9-fluorenol [119]. The attempts to resolve 2-chloro-9-fluorenyl phthalate with the aid of brucine, strychnine, quinidine, and cinchonidine in various solvents were unsuccessful; also unsuccessful were the attempts at resolution with the aid of ephedrine in benzene, chloroform, and acetone. A partial resolution was achieved via the diastereoisomeric salts with ephedrine in alcohol. The acid phthalate obtained was crystallised from chloroform; the racemate was less soluble (cubic crystals) and the optically active form was subsequently isolated in the form of long needles. The isolation of the enantiomorphs of 2-chloro-9-fluorenol from the acid phthalates was achieved by treatment with methylmagnesium iodide in ether, since hydrolysis leads to racemisation. Anders and Cooper [121] isolated by g.l.c. the diastereoisomeric esters formed by racemic alcohols with 3β-acetoxy-Δ^5-etienic acid, which were separated previously [120] by fractional crystallisation. Methylphenylmethanol, ethylphenylmethanol, cyclohexylphenylmethanol, n-hexylmethylmethanol, and other alcohols were resolved in this way. Preparative separation of diastereoisomeric alcohol derivatives by g.l.c. was achieved by a number of other investigators [122,123]. For example the racemic mixture of 3,3-dimethylbutan-2-ols was resolved [123] by synthesising their esters with *N*-trifluoroacetyl-L-alanine, which were then separated by g.l.c. In a continuation of studies [79] on the resolution of racemic carbohydrates, Pollock and Jermany [124] separated by g.l.c. the diastereoisomeric esters formed by galactonic and gluconic acids with 2-butanol, 3-methylbutan-2-ol, and

3,3-dimethylbutan-2-ol. A further development of the theoretical aspects of the resolution of diastereoisomers by g.l.c. is described by Feibush [125].

Recently the present authors reported [126] the separation of the optical isomers of 1,2,4,5,6-penta-*O*-acetylmyoinositol via the diastereoisomeric D-mannose orthoacetates and of 1,4,5,6-tetra-*O*-acetylmyoinositol with subsequent deacetylation of the separated orthoacetates and the isolation of the enantiomorphs of myoinositol penta-acetate by mild acid hydrolysis. Molotkovsky and Bergelson [127] carried out a new resolution of myoinositol penta-acetates by the crystallisation of the diastereoisomeric salts of the acid oxalates of myoinositol penta-acetate with quinidine or α -phenylethylamine. The physicochemical constants of the enantiomorphs, which they isolated by treating the separated acid oxalates with lead tetra-acetate in a pyridine–dioxan mixture in an atmosphere of argon, were close to those of the optically active myoinositol penta-acetates which we obtained previously [126].

Modern methods for the resolution of alcohols are described in a recent review by Boyle [128].

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Cleavage of Saturated Nitrogen-containing Heterocycles at the C-N Bond by Electrophilic Agents

E.I.Levkoeva and L.N.Yakhontov

The review deals with reactions involving the opening of saturated nitrogen-containing rings at the C-N bond under the influence of acids, their anhydrides, esters, acid halides, and a number of other electrophilic agents. The use of the reverse Ritter reaction and of the Braun reaction for the cleavage of saturated heterocycles containing a secondary nitrogen atom is discussed.
The bibliography includes 137 references.

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I. INTRODUCTION

The cleavage reactions of saturated nitrogen-containing heterocycles at the C — N bond are widely used to establish the structures of natural compounds and are of definite preparative value in organic synthesis.

Various methods for the rupture of endocyclic C — N bonds in saturated systems have been described in the literature. In the first place mention should be made of the cleavage of quaternary ammonium bases and their salts by the Hofmann and Emde methods involving heat treatment or treatment with alkalis, amalgams, and alkali metals in liquid ammonia.

These methods, which have been used successfully in the study of the structures of alkaloids and other complex heterocyclic systems, have been discussed in detail in fairly complete reviews[1-7]. Methods for the dissociation of C — N bonds in the catalytic dehydrogenation of alkaloids and on their distillation with zinc dust have been analysed in other reviews[8,9].

More specific are examples, described in various publications, of the cleavage at the C — N bonds of saturated cyclic amines in hydrogenolysis[10], the Wolff-Kishner[11-13] and Clemmensen[14-19] reduction reactions, and also as a result of oxidative[20] and electrochemical processes[21,22], in rearrangements[23-25], in transamination reactions[5,26], and in various tautomeric conversions[27-32].

In recent years attention has been increasingly drawn to a wide variety of methods for the opening of the C — N bond of saturated heterocyclic rings with a secondary or tertiary nitrogen atom by a number of electrophilic agents.

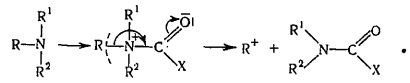
In view of the lack of reviews on reactions of this kind, it is desirable to give a general account of data from a fairly large number of publications.

The present review consists of two sections: the first deals with the cleavage reactions of saturated heterocycles containing a tertiary nitrogen atom by acids, anhydrides, acid halides, and esters and the second deals with the dissociation of C — N bonds of saturated cyclic secondary amines under the conditions of the reverse Ritter reaction and the Braun reaction.

The cleavage of tertiary cyclic amines by cyanogen bromide using the Braun method has not been included in the present paper, since the problem is dealt with in a fairly complete review[33] where the mechanism, conditions, and applications of this reaction are discussed in detail.

II. CLEAVAGE OF SATURATED HETEROCYCLES CONTAINING A TERTIARY NITROGEN ATOM

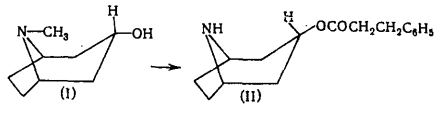
One of the methods for the dissociation of the C — N bond in tertiary amines involves their conversion into quaternary compounds by interaction with carboxylic acids or their derivatives: anhydrides, acid halides, chlorocarbonic esters, phosgene, and certain other electrophilic agents. The functional group attached to nitrogen withdraws the electron pair from the bond mainly as a result of its $-E$ effect, facilitating further dissociation:



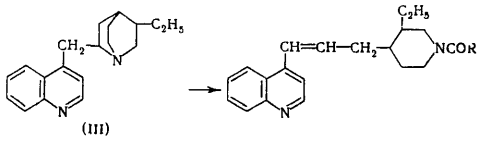
The cleavage of many tertiary cyclic amines has been achieved by this mechanism, the carbonium cation R^+ being subsequently stabilised either by the abstraction of a proton and the formation of a double bond or as a result of attack by nucleophilic agents (halide ions, water, alcohols, nitrogenous bases, etc.) with conversion into derivatives having the corresponding functional groups.

1. Dissociation of the C — N Bond by Acids

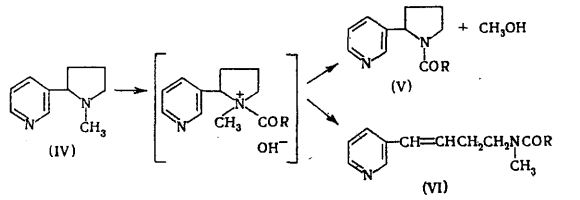
Saturated heterocyclic systems with a tertiary nitrogen atom are usually resistant to organic and inorganic acids. For example, *N*-methylpyrrolidine and *N*-methyl-1, 2, 3, 4-tetrahydroisoquinoline undergo only *N*-demethylation without ring opening on refluxing with benzoic, palmitic, acetic, or dihydrocinnamic acids[34]. When tropine(I) is heated to 200°C in the presence of dihydrocinnamic acid, the corresponding nortropine ester (II) is formed[34]:



Ring opening by acids is achieved only in compounds where the C — N bond is weakened owing to electron-accepting or bulky substituents at the carbon atom adjoining the nitrogen atom. Thus the quinuclidine ring is readily opened by acids when the α-position relative to the nitrogen atom contains a bulky substituent which is involved in addition in the formation of a conjugated bond system after ring opening. Similar cleavage takes place with dihydrodeoxycinchonine (III):[35]

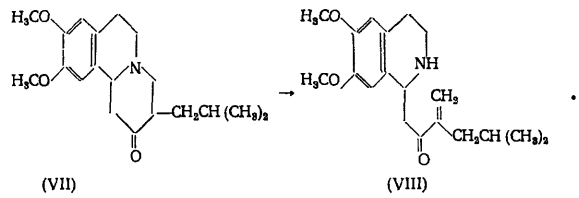


When nicotine (IV) is heated with benzoic or dihydrocinnamic acid until it starts to boil slightly, a product (VI) with an open pyrrolidine ring is formed together with *N*-acylnornicotine (V); the amount of compound (VI) increases with reaction temperature[36]:



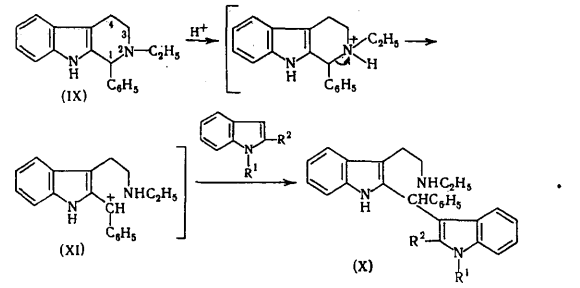
The acid cleavage of the C — N bond in saturated nitrogen-containing rings has been used to establish the structures of a number of natural compounds. Studies on the chemistry of Pereiro alkaloids containing the indoline group[37] and the *Voacanga africana* alkaloids—voacamine and voacorine, which are derivatives of 1, 2, 3, 4-tetrahydro-β-carboline[38]—may be quoted as examples.

In the course of the synthesis of emetine, Brossi et al.[39] showed that, when substituted benzoquinolizine (VII) is refluxed with acetic acid, the piperidine ring is cleaved and an unsaturated compound (VIII) is formed:



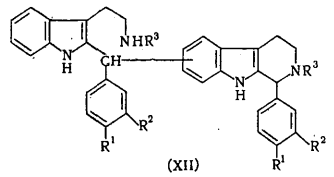
The mechanism of the opening of nitrogen-containing rings by acids has been examined in detail for the reactions of 1-aryl-1, 2, 3, 4-tetrahydro-β-carbolines[40].

When 2-ethyl-1-phenyl-1, 2, 3, 4-tetrahydro-β-carboline (IX) is heated with various indole derivatives in the presence of acetic and phosphoric acids, condensation products of type (X) are formed in high yields:



The cleavage of compound (IX) in an acid medium takes place exclusively at the $C_{(1)}$ — N bond, since only in this case is a mesomerically stabilised carbonium ion (XI) (similar to the diphenylmethyl cation) formed. The authors suggest that the $C_{(1)}$ — N bond is polarised owing to the protonation of the 2-N-nitrogen atom and attack by the nucleophilic agent (indole) at the 1-C atom, which leads ultimately to the dissociation of the ring. The carbonium cation (XI) formed interacts with the most reactive position (the 3-position) of the indole molecule. If the 3-position is occupied, the condensation involves the 2-position, which is much less reactive. In the case of 2, 3-disubstituted indoles, the reaction involves the benzene ring. Dimers of 1-aryl-1, 2, 3, 4-tetrahydro-β-carbolines (XII), which

are structural analogues of the alkaloid voacamine, were synthesised similarly[40]:

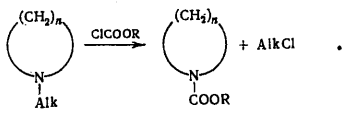


(XII)

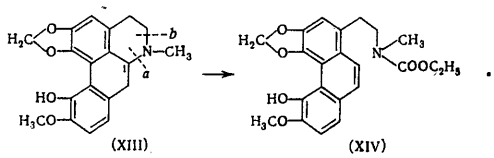
When the aryl substituent at 1-C is replaced by an alkyl substituent, the addition of indole does not take place, since the stabilisation of the carbonium cation (XI), which is essential for the reaction, cannot take place. The introduction of electron-accepting groups in the *para*-position of the phenyl substituent at 1-C enhances appreciably the reactivity of the compounds.

2. Dissociation of the C — N Bond by Chlorocarbonic Esters

Chlorocarbonic esters are regarded as "group agents" for the opening of the piperidine ring in 1,2,3,4-tetrahydroisoquinolines. The capacity of tetrahydroisoquinoline to be cleaved readily at the $C_{(1)}$ — N bond under the influence of ethyl chlorocarbonate was first observed as early as 1921 by Gadamer and Knoch[41]. Subsequently it was shown[42-44] that different quinoline, isoquinoline, pyridine, piperidine, and pyrrolidine derivatives do not undergo ring opening under these conditions. When chlorocarbonic esters are allowed to react with *N*-alkyl piperidines[43,44], tropane[44], or *N*-alkylpyrrolidines[42], only *N*-dealkylation processes take place with formation of alkyl chlorides and *N*-alkoxycarbonyl derivatives of the initial heterocycles:

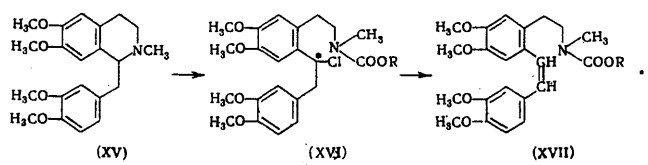


On the other hand, the majority of 1,2,3,4-tetrahydroisoquinolines readily undergoes selective dissociation at the $C_{(1)}$ — N bond on treatment with chlorocarbonic esters and are converted in quantitative yields into the corresponding open-chain urethanes. For example, the alkaloid bulbocapnine (XV), the Hofmann degradation of which is not unambiguous (it can occur via pathway *a* and *b*), gives rise only to compound (XIV) on treatment with ethyl chlorocarbonate, i.e. it is cleaved only at the $C_{(1)}$ — N bond[41]:



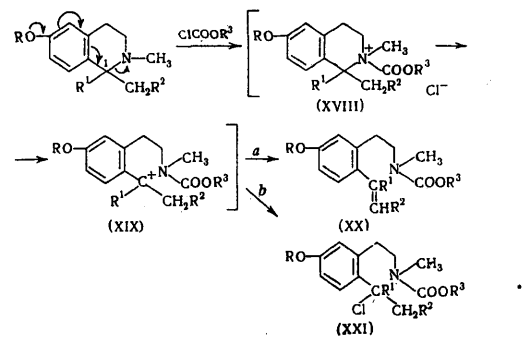
(XIII) (XIV)

When (-)-laudanosine (XV) interacts with chlorocarbonic esters, the initial product is the optically active chloroderivative (XVI), which splits off hydrogen chloride in the presence of alkali and gives rise to compound (XVII):[41,45]



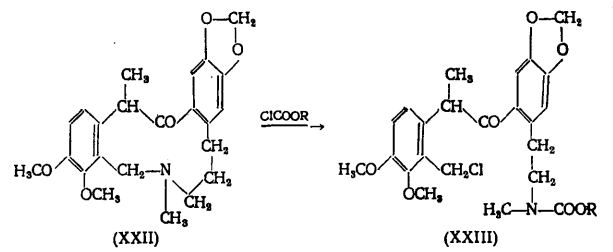
(XV) (XVI) (XVII)

Knabe and coworkers[45-49] examined the effects of substituents in the benzene ring on the ease of dissociation of the $C_{(1)}$ — N bond in 1,2,3,4-tetrahydroisoquinolines and proposed a possible reaction mechanism. They established that, on treatment with chlorocarbonic esters, the piperidine ring in *N*-methyl-1,2,3,4-tetrahydroisoquinoline cannot be cleaved, which can be accounted for by the inadequate polarity of the $C_{(1)}$ — N bond in this compound. The introduction of electron-donating groups in the *ortho*- or *para*-position of the benzene ring enhances the polarisation of the $C_{(1)}$ — N bond and facilitates the addition of the chlorocarbonic ester residue to the nitrogen atom. This results in the formation of a quaternary compound of type (XVIII) in which the $C_{(1)}$ — N bond is readily dissociated and the carbonium cation (XIX) thus obtained may be stabilised in two ways: (a) with elimination of a proton and formation of the unsaturated compound (XX); (b) via attack by a chloride ion with formation of the chloroderivative (XXI):



(XVIII) (XIX) (XX) (XXI)

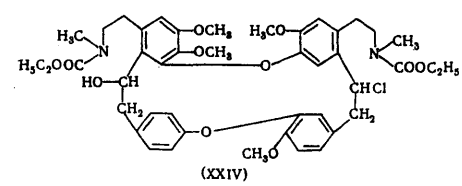
If the carbon atom adjoining 1-C does not have a proton capable of being split off, for example in the alkaloid corycavidine (XXII), a stable chlorourethane (XXIII) is formed[50]:



(XXII) (XXIII)

Otherwise, as mentioned above for (-)-laudanosine (XV), an unsaturated compound can be readily obtained.

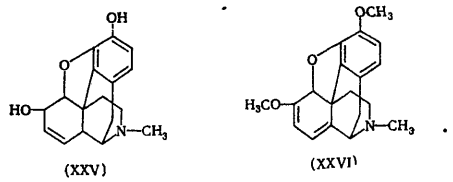
When the methyl ether of hydroxyacanthine is cleaved by chlorocarbonic ester in the presence of potassium hydroxide, the initially formed carbonium cations are stabilised by the addition of chloride and hydroxide ions with formation of compound (XXIV):[46,51]



(XXIV)

The reaction of chlorocarbonic esters with morphine (XXV) and codeine is known to result only in the acylation of the alkaloid at the hydroxy-group, while in the reaction

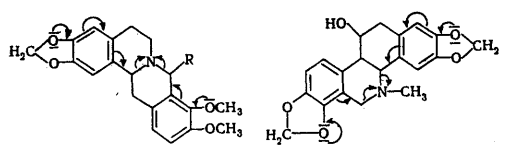
with thebaine (XXVI) the opening of the piperidine ring takes place with an almost quantitative yield[41,52]:



(XXV) (XXVI)

The example of thebaine shows that an aromatic system is not essential for ring opening. It is sufficient that the electron-donating substituent is conjugated with an allylamine residue.

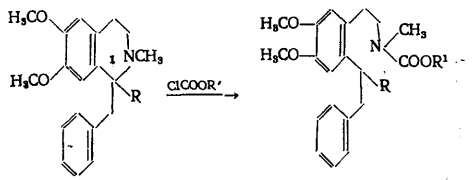
It is interesting that alkaloids of the tetrahydroberberine group (XXVII), which have, as it were, a "double benzylamine structure", do not undergo the opening of the piperidine ring when acted upon by chlorocarbonic esters[46,48]:



(R = H, $CH_2C_6H_5$) (XXVII) (XXVIII)

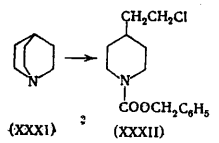
Initially it was suggested[46] that the opposed electron shifts in the two benzylamine systems in compounds of this type may reduce the polarisation of the C — N bond and prevent the reaction with chlorocarbonic ester. However, the alkaloid chelidonine (XXVIII), which also has a "double benzylamine structure", is readily cleaved at the C — N bond under these conditions[41].

Evidently not only electronic but also steric factors, primarily the degree of screening of the nitrogen atom attacked, play a major role in these processes. Indeed, whereas the yield of the urethane (XXIXa) from 1-benzyl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (XXXa) is nearly quantitative[48], the introduction of a methyl group in the 1-position reduces the yield of compound (XXIXb) to 29% and the 1-ethyl homologue (XXXc) does not form the corresponding urethane (XXIXc) at all under standard conditions[49].



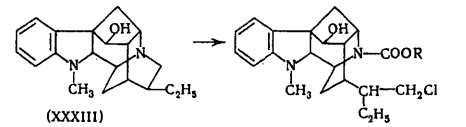
(XXX) [R = H (a), CH_3 (b), or C_2H_5 (c)] (XXIX)

Further studies showed that the cleavage of heterocycles at the $C_{(1)}$ — N bond by chlorocarbonic esters is not confined to substituted 1,2,3,4-tetrahydroisoquinolines or analogous systems in which electron-donating substituents are conjugated with the allylamine residue. It was possible to cleave the quinuclidine ring in an aprotic medium with the aid of these esters. When unsubstituted quinuclidine (XXXI) was treated with benzyl chlorocarbonate, the urethane (XXXII) was obtained in 88% yield[44]:



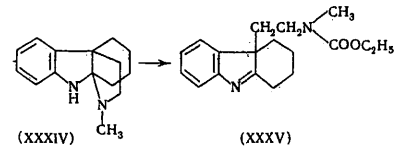
(XXXI) (XXXII)

It has been shown for 21-deoxyajmaline (XXXIII) that bicyclic systems with a nitrogen bridge are cleaved when acted upon by benzyl chlorocarbonate in a higher yield (98%) than on treatment with the corresponding ethyl ester (yield 55%)[44]:



(XXXIII)

Ethyl chlorocarbonate has been successfully used for the dissociation of the N — C bond also in *N*-methylechibolinе (XXXIV).[53] This involves the opening of the condensed pyrrolidine ring, the urethane (XXXV) being isolated in a yield of 65%:

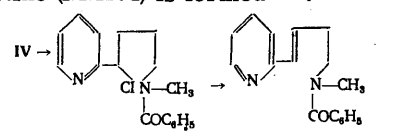


(XXXIV) (XXXV)

3. Dissociation of the C — N Bond by Acid Halides

Since acid halides are powerful electrophilic agents, they should apparently have found a wide application in reactions involving the cleavage of heterocyclic tertiary amines. However, the reaction of acid halides with tertiary amines containing even one α-hydrogen atom usually gives rise to the corresponding ketens. Therefore mainly phosgene or benzoyl halides, which are incapable of the formation of ketens, were used previously in C — N bond dissociation reactions.

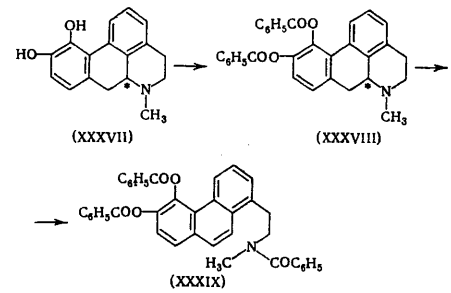
Thus, as early as 1894, a study of the reaction of benzoyl chloride with nicotine (IV) established that, when a mixture of these substances is heated to 200°C, *N*-benzoylmetanicotine (XXXVI) is formed[54,55]:



(XXXVI)

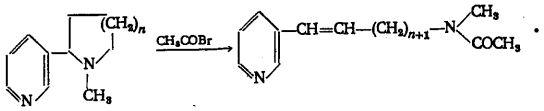
A thorough investigation of the products of this reaction led to a convincing proof of the structural formula of nicotine[54-56].

In the determination of the structure of apomorphine (XXXVII), its cleavage was also achieved with the aid of benzoyl chloride[57]. The optically active dibenzoyl derivative (XXXVIII) formed initially in this reaction reacts further with the excess benzoyl chloride, which results in the opening of the piperidine ring and the formation of an optically inactive non-basic product (XXXIX):



(XXXVII) (XXXVIII) (XXXIX)

Recently it was suggested that, with amines which are cleaved particularly readily, the amount of keten formed from the acid halide can be reduced to a minimum[58]. Indeed the reaction of acetyl bromide with nicotine (IV) yielded *N*-acetylmetanicotine (XLa) in 46 — 52% yield, while *N*-methylanabasine gave a 23% yield of the product (XLb), which is formed on opening of the piperidine ring:

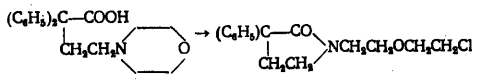


(IV) (XL) (*a*) $n=1$; (*b*) $n=2$

Appreciable amounts of keten were not detected in these reactions.

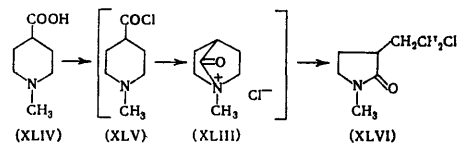
The cleavage of the piperidine ring of thebaine (XXVI) was achieved with the aid of acetyl and benzoyl chlorides in moist ethyl acetate, the corresponding codeinoacylnormethines being obtained in yields of about 90%.[52]

The intramolecular acylation of the chlorides of γ-aminoacids with a tertiary ring nitrogen atom has been the subject of a special study[59]. It was found that the reaction of γ-*N*-pyrrodinyl-, γ-*N*-piperidinyl-, and γ-*N*-morpholinyl-αα-diphenylbutyric acids (XLI) with thionyl chloride results in the opening of the heterocycle and the formation of the corresponding chloroalkyl derivatives of the *N*-substituted α-pyrrolidinone (XLII):



(XLI) (XLII)

A similar reaction occurred in the synthesis of the bicyclic lactam (XLIII) as a result of the interaction between thioonyl chloride and *N*-methylisonipecotic acid (XLIV).[59] Compound (XLIII) proved to be extremely unstable and was converted under the reaction conditions into β-chloroethyl-*N*-methyl-α-pyrrolidinone (XLVI):



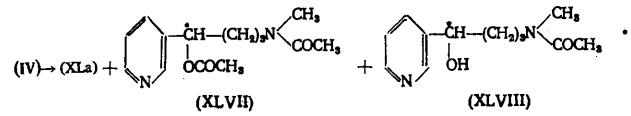
(XLIV) (XLV) (XLIII) (XLVI)

4. Dissociation of the C — N Bond by Acid Anhydrides

Acid anhydrides (mainly acetic anhydride) are fairly widely used for the cleavage of tertiary amines, including saturated nitrogen-containing heterocycles.

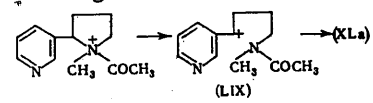
Tiffeneau's classical studies[60] showed that acid anhydrides cleave most effectively tertiary amines in which the nitrogen atom is linked to the benzyl residue and that the nature of the substituents in the benzine ring is important.

The ease of opening of the pyrrolidine ring in nicotine was also explained by its belonging to amines of the "benzyl type"[55]. In a recent study[61] of the effect of structural factors on the cleavage of tertiary amines by acetic anhydride, the interaction of the latter with nicotine (IV) was examined in detail. 1-Acetoxy-4-(*N*-methylacetamido)-1-(β-pyridyl)butane (XLVII) and 1-hydroxy-4-(*N*-methylacetamido)-1-(β-pyridyl)butane (XLVIII), which on vacuum distillation are converted into compound (XLa), were isolated from the reaction product together with *N*-acetylmetanicotine:



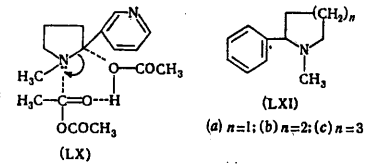
(XLVII) (XLVIII)

It is very likely that the formation of compound (XLa) from nicotine proceeds via the intermediate carbonium cation (LIX), which is stabilised subsequently by the elimination of a proton and the formation of a double bond conjugation with the pyridine ring:



(LIX)

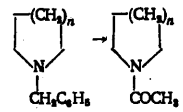
The presence of the hydroxy-derivative (XLVIII) and the acetoxy-derivative (XLVII) among the reaction products might be regarded as due to the addition of a hydroxy-group and an acetic acid residue respectively to the carbonium cation (LIX). However, the products obtained on stabilisation of the carbonium cation (LIX) should be racemates, while compounds (XLVIII) and (XLVII) proved to be optically active. Since the yield of the products of the cleavage of nicotine by acetic anhydride increases in the presence of water[62] or acetic acid[61], it was suggested[63] that the reaction proceeds simultaneously via two mechanisms: (1) via the formation of the carbonium cation (LIX), which gives rise immediately to *N*-acetylmetanicotine (XLa); (2) via a six-membered transition state of type (LX), which leads to compounds (XLVII) and (XLVIII).



(LXI) (*a*) $n=1$; (*b*) $n=2$; (*c*) $n=3$

(LX)

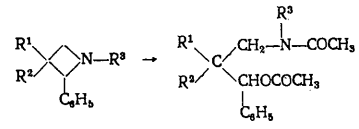
It has been shown[61] that a benzene analogue of nicotine—*N*-methyl-α-phenylpyrrolidine (LXIa)—is cleaved like nicotine on its interaction with acetic anhydride. On the other hand, the reaction of *N*-benzylpyrrolidine and *N*-benzylpiperidine, which do not contain substituents in the α-positions of the ring, with acetic anhydride in the presence of acetic acid involves the dissociation of the exocyclic C — N bond only:



It is noteworthy that the course of the above reaction is determined not only by the nature of the substituents at the nitrogen and α-carbon atoms but also by the size of the ring undergoing cleavage. Thus *N*-alkylpiperidines remain unchanged even after refluxing for 100 h with acetic anhydride and acetic acid. Under the same conditions, *N*-alkylpyrrolidines and *N*-alkylhexamethyleneimines form the corresponding acyclic amides, albeit in low yields (11 — 14%). Similarly the piperidine ring in *N*-methyl-α-phenylpiperidine (LXIb) is cleaved by acetic anhydride with much more difficulty than the five- or seven-membered ring in compounds (LXIa, c)[61].

The four-membered ring of *N*-alkylazetidines (LXII) is opened very readily on heating with acetic anhydride.

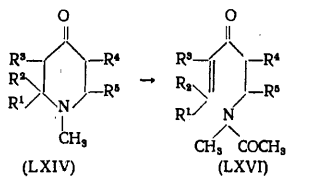
This results in the formation of quantitative yields of the corresponding γ-acetamidoacetates (LXIII):[64]



(LXII) (LXIII)

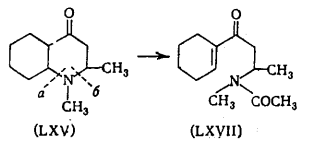
The nature of the substituents at the β-carbon atom in azetidine does not have a significant influence on the ease of ring opening and in the presence of a substituent at the α-carbon atom the C — N bond adjoining the substituent is dissociated[64,65].

A number of studies have been made[66,67] on the interaction of acetic anhydride with *N*-methylpiperidine-4-ones (LXIV) and *N*-methyldecahydro-4-quinolones (LXV) containing methyl groups in various positions in the piperidine ring. It was established that at room temperature or on heating the components to 100°C, the piperidine ring is not cleaved. The corresponding β-acylaminoketones (LXVI) are formed in maximum yields (60 — 80%) on refluxing with acetic anhydride for 2.5 — 10 h.



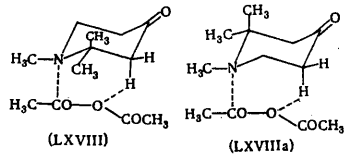
(LXIV) (LXVI)

It has been noted[66,67] that the opening of the piperidine ring always takes place with formation of "amidoketones" (LXVI) in which the vinyl group is alkylated to the maximum extent, i.e. the dissociation takes place at the most straining C — N bond. 1,2-Dimethyldecahydro-4-quinolone (LXV) is converted into a cyclohexene derivative (LXVII) on refluxing with acetic anhydride. There is no cleavage at the N — C(CH_3) bond. Consequently the effect of the cyclohexane ring, responsible for the cleavage of the piperidine fragment via pathway *a*, is much greater than that of the methyl group:



(LXV) (LXVII)

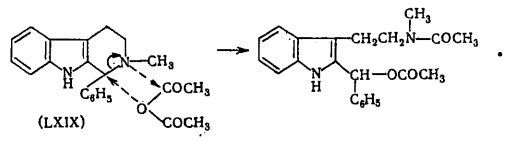
In the discussion of the possible mechanism of the opening of the γ-piperidine ring in compound (LXIV), it was suggested[67] that the reaction proceeds via a six-membered intermediate state (LXVIII):



(LXVIII) (LXVIIIa)

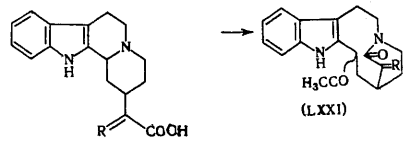
However, the formation of (LXVIII) has not been demonstrated experimentally. On the other hand, one should note that the existence of such an intermediate state does not account for the preferential dissociation of the C — N bond adjoining the most alkylated carbon atom. Indeed, it would in fact appear that the geminal substituents at the α-carbon atom should hinder the formation of the transition state (LXVIII) and should facilitate the formation of (LXVIIIa).

Therefore it appears more likely that such reactions take place via four-membered intermediate complexes of type (LXIX), proposed by Freter and coworkers[40,68] in their description of the interaction of 1-phenyl-1,2,3,4-tetrahydro-β-carboline derivatives with acetic anhydride:



(LXIX)

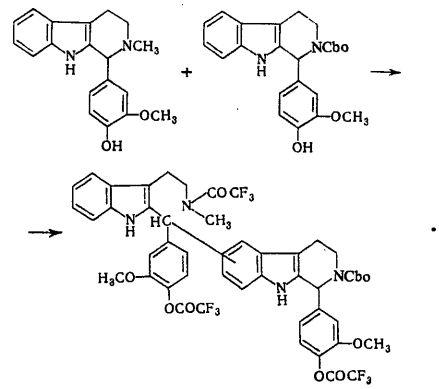
The piperidine ring of dihydrocorynantheine (LXX) was opened similarly in the presence of acetic anhydride and the cleavage products were isolated in the form of acetoxylactams (LXXI):[69]



(LXXI)

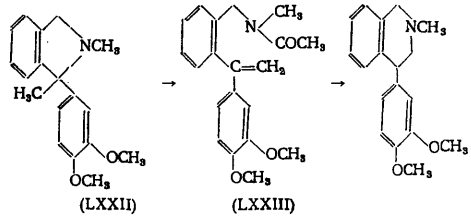
(LXX): R = H_2, CH_3OCH

Catalytic amounts of carboxylic acids may have a definite influence on the mechanism of the reactions under consideration. In order to eliminate acid catalysis, the C — N bond in 1,2,3,4-tetrahydro-β-carbolines was dissociated by trifluoroacetic anhydride in tetrahydrofuran (THF):[40]



However, the presence of phenolic hydroxyls in the initial compounds, the acylation of which involves the formation of trifluoroacetic acid, invalidates the conclusions of this investigation to some extent.

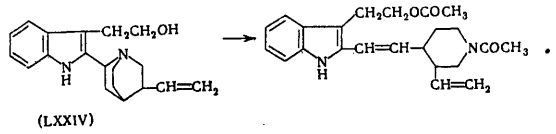
A novel method of converting the isoindoline structure into the 1,2,3,4-tetrahydroisoquinoline structure was described recently[70]. When acted upon by acetic anhydride, isoindoline (LXXII) is cleaved to the unsaturated amide (LXXIII), which then undergoes ring closure in a highly alkaline medium to a 1,2,3,4-tetrahydroisoquinoline derivative:



(LXXII) (LXXIII)

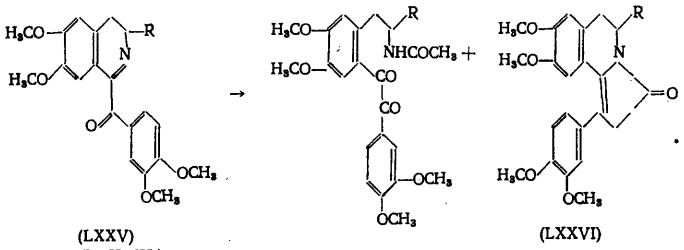
An interesting example of the use of acetic anhydride for the opening of a nitrogen-containing ring is provided by a study[71] undertaken to demonstrate the structure of

cinchonamine (LXXIV). The quinuclidine ring in this alkaloid is dissociated by acetic anhydride at the C — N bond adjoining the carbon atom linked to the indole component of the molecule:



(LXXIV)

It should be noted that unsaturated rings, such as the 3,4-dihydroisoquinoline ring in compound (LXXV), are also readily cleaved on refluxing with acetic anhydride. However, in these cases the process is complicated by the formation of side products of type (LXXVI):[72]

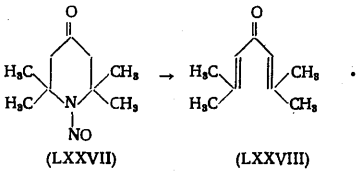


(LXXV) (R=H, CH_3) (LXXVI)

III. CLEAVAGE OF SATURATED HETEROCYCLES CONTAINING A SECONDARY NITROGEN ATOM

The C — N bond in saturated secondary amines is appreciably stable. Its thermal dissociation can be achieved only on heating to 350 — 400°C. However, the ease of dissociation of this bond may be increased by introducing certain substituents both at the nitrogen and at the α-carbon atom. For this purpose, the nitrogen atom should contain strongly electron-accepting groups, namely NO,[73] COR,[74] $SO_2C_6H_5$,[75] Br,[75,76] and others and the α-carbon atom should be linked to bulky geminal substituents which increase the strain in the C — N bond[77,78], or to allylic substituents which facilitate the stabilisation of the carbonium cation formed as a result of the dissociation of the C — N bond.

As an example one may quote 2, 2, 6, 6-tetramethyl-*N*-nitrosopiperidin-4-one (LXXVII), which on heating to 80°C yields phorone (LXXVII):[73]

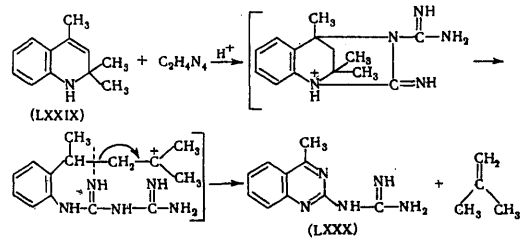


(LXXVII) (LXXVIII)

Two factors operate at once in this case: those associated with the electron-accepting nitroso-group at the nitrogen atom and the two bulky substituents at the α-carbon atom, which leads to a comparatively easy dissociation of the ring.

The introduction of electron-accepting polyfunctional groups at the nitrogen atom usually entails not only the dissociation of the C — N bond weakened thereby but also further reactions (various intramolecular condensations and rearrangements) which frequently lead to unexpected compounds.

For example, 2, 2, 4-trimethyl-1, 2-dihydroquinoline hydrochloride (LXXIX) reacts with dicyanodiamide in aqueous solution to give a 68% yield of 2-guanidino-4-methylquinazoline hydrochloride (LXXX):[79,80]

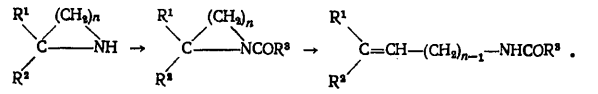


(LXXIX) (LXXX)

The most thoroughly investigated reactions involving the opening of saturated secondary cyclic amines include the reactions of their *N*-acyl derivatives with the dissociation of the endocyclic C — N bond under the conditions of acid hydrolysis on heating (the reverse Ritter reaction) and also under the influence of compounds such as phosphorus pentoxide under the conditions of the Braun reaction.

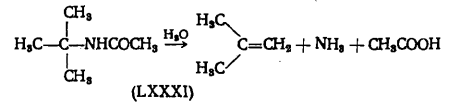
1. Dissociation of the C — N Bond under the Condition of the Reverse Ritter Reaction

In order to open the rings of saturated cyclic secondary amines containing geminal substituents at the α-carbon atom, the following method is frequently employed nowadays: the amine is converted into an *N*-acyl derivative, which is then cleaved to an unsaturated acyclic compound on heating in an acid medium:



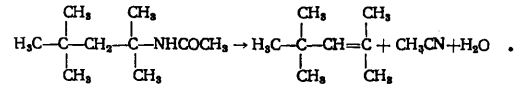
A similar cleavage of amides in which the nitrogen atom is linked to a quaternary carbon atom is known as the reverse Ritter reaction.

It has been shown[74] for t-butylacetamide (LXXXI), which is hardly hydrolysed by alkalis[81], that in an acid medium compounds of this kind readily decompose into an olefin, ammonia, and an acid via the following mechanism:



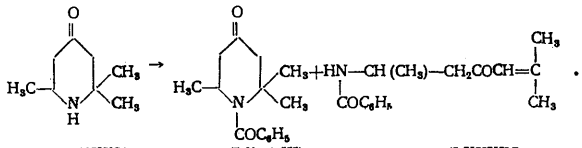
(LXXXI)

Steric hindrance at the α-carbon atom makes amides with this structure inert in relation to other substances. These compounds do not react with Grignard reagents and with acylating substances and are not reduced by hydrogen even at elevated temperatures and pressures. However, on heating to boiling, the most unstable of them decompose with formation of the corresponding nitriles and unsaturated compounds[74]:



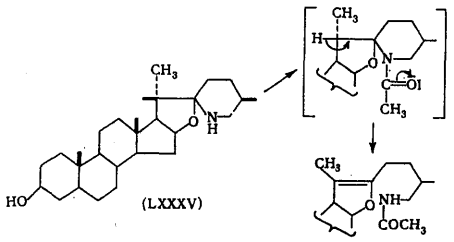
An *NN*-disubstituted amide usually yields an unsaturated monoamide. For example, the interaction of vinyl diacetoneamine [2, 2, 6-trimethyl-4-oxopyrrolidine] (LXXXII) with benzoyl chloride gives rise, together with the

expected *N*-benzoyl derivative (LXXXIII), to its cleavage product—the acyclic amide (LXXXIV):[82]



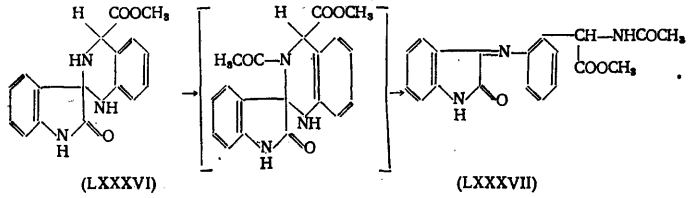
(LXXXII) (LXXXIII) (LXXXIV)

In the *N*-acetyl derivatives of the steroid alkaloids solasodine tomatidine (LXXXV), the piperidine ring is cleaved extremely readily under the conditions of the reverse Ritter reaction: after refluxing for 15 min in the presence of acetic or propionic acid and even at room temperature in the presence of hydrochloric or perchloric acid[83]:



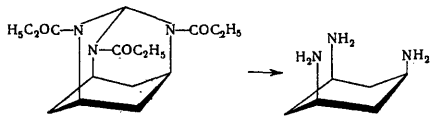
(LXXXV)

In the determination of the structures of isamic acid esters (LXXXVI), the tetrahydropyrimidine ring was opened under the influence of acetic anhydride with formation of the compound (LXXXVII), which has a highly strained system of conjugated bonds[84]:



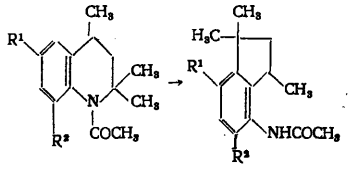
(LXXXVI) (LXXXVII)

When *NN'N"*-Tripropionyl-2,4,10-triaza-adamantane (LXXXVIII) is heated with concentrated hydrochloric acid, *cis*-1,3,5-triaminocyclohexane (LXXXIX) is formed[85]:



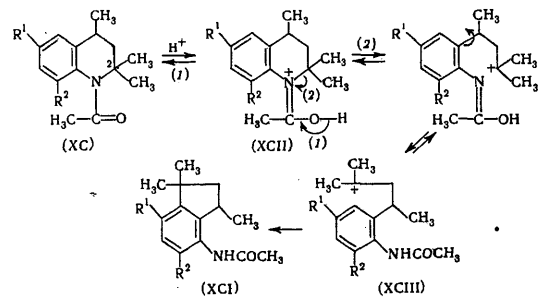
(LXXXVIII) (LXXXIX)

Electrophilic substitution reactions in an acid medium involving sterically hindered cyclic amides can be accompanied by the cleavage of the ring via the reverse Ritter reaction. Thus nitration of substituted 1-acetyl-2,2,4-trimethyl-1,2,3,4-tetrahydroquinolines (XC) (at 100°C for 1 h) in the presence of sulphuric or polyphosphoric acid led to the isolation of the corresponding indane derivatives (XCI):[86]



(XC) (XCI)
(R^1 и R^3=H, Br, NO_2)

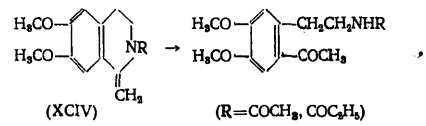
It is believed[86] that the protonation of the amide carbonyl with formation of the unstable ion (XCII) plays a decisive role in the rearrangement:



(XC) (XCII) (XCI) (XCIII)

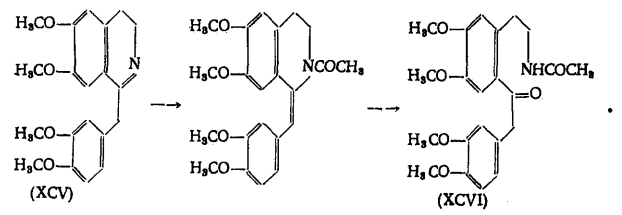
The ion (XCII) may be stabilised either by the loss of a proton (pathway *1*) or by conversion into the carbonium ion (XCIII) (pathway *2*). Then in compound (XCIII) the free *ortho*-position in the benzene ring is attacked with formation of the indane derivative (XCI). The authors[86] state that examination of atomic models demonstrates an appreciable steric interaction between the carbonyl group of the amide and the *gem*-dimethyl substituents at 2-C. After the removal of one methyl group, the strain of the $C_{(2)}-N$ bond is appreciably reduced. Thus *gem*-dimethyl groups at the α-carbon atom on the one hand facilitate the dissociation of the $C_{(2)}-N$ bond and on the other hand stabilise the intermediate ion (XCIII).

The opening of the piperidine ring in 2-acyl-1-methylene-1,2,3,4-tetrahydroisoquinolines (XCIV) in the presence of hydrochloric acid is facilitated by the electron-donating effect of the benzene ring with methoxy-groups in the 6- and 7-positions[87]:



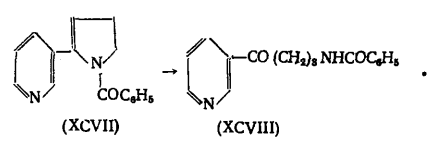
(XCIV) (R=$COCH_3$, COC_2H_5)

The dihydroisoquinoline ring of the intermediate in the synthesis of norapormorphine (XCV) is cleaved similarly to compound (XCIV); its *N*-acetyl derivative, containing the benzylidene substituent at 1-C, is converted on heating with hydrochloric acid into the corresponding deoxybenzoin (XCVI):[88]



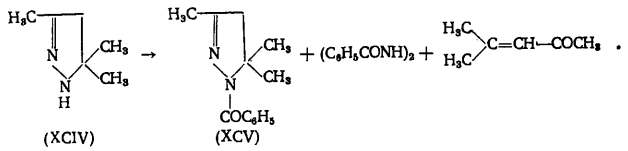
(XCV) (XCVI)

The cleavage of *N*-benzoylmyosmine (XCVII) leading to compound (XCVIII), may serve as an example of the opening of the Δ^2-pyrroline ring[89]:



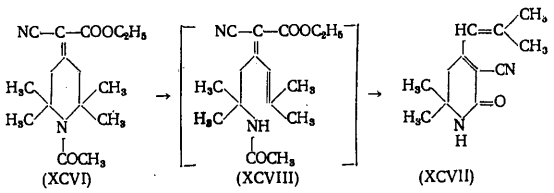
(XCVII) (XCVIII)

When pyrazolines are acylated by acid chlorides, the dissociation of C — N bonds and ring opening are also observed[90–93]. Benzoylation of 3, 5, 5-trimethylpyrazoline (XCIV) leads to the formation of dibenzoylhydrazine and mesityl oxide together with the expected amide (XCV):[93]



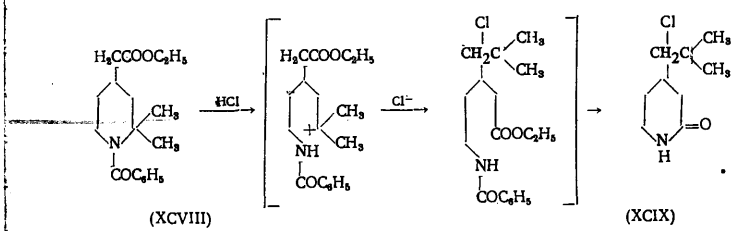
(XCIV) (XCV)

Heating of *N*-acetyl derivatives of piperidine with geminal substituents in the α-position also leads to relatively easy dissociation of the $C_{(\alpha)}$ — N bond accompanied in many cases by further reactions of the substance. For example, 1-acetyl-4-(cyanoethoxycarbonylmethylene)-2, 2, 6, 6-tetramethylpiperidine (XCVI) is converted on heating to 130°C into dehydro-2-piperidinone (XCVII)—a product of the intramolecular condensation of the unsaturated amide (XCVIII):[94]



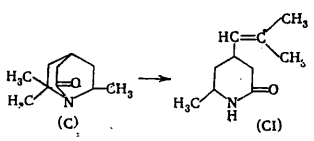
(XCVI) (XCVIII) (XCVII)

When *N*-benzoyl-4-ethoxycarbonylmethyl-2, 2-dimethylpiperidine (XCVIII) is refluxed with hydrochloric acid, a substituted 2-piperidinone (XCIX) [95] is formed, probably via the following mechanism:



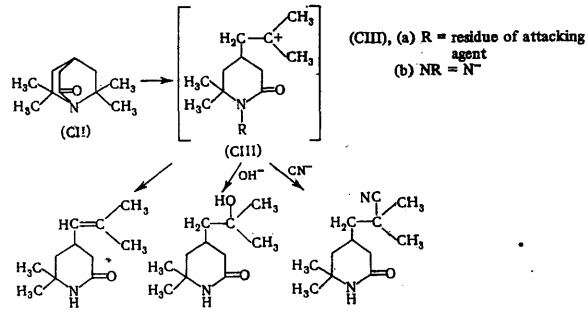
(XCVIII) (XCIX)

In many cases the products of the reverse Ritter reaction were not isolated and their formation was inferred from the change in the infrared spectrum of the reaction mass. For example, after 6, 6, 7-trimethyl-2-quinuclidone (C) ($\nu_{C=O}$ = 1750 cm^{-1}) has been allowed to stand for a long time, an absorption band appears in the infrared spectrum in the region of 1640 cm^{-1}; it was assigned to absorption by the amide carbonyl of the open-chain form (CI):[96]



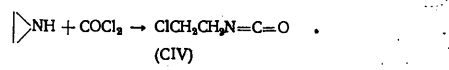
(C) (CI)

A similar cleavage of 6, 6, 7, 7-tetramethyl-2-quinuclidone (CII) takes place even more readily[97]. Here the unstable carbonium cation (CIII) is probably formed initially and then stabilised either by the addition of nucleophilic agents or as a result of the elimination of a proton with formation of an unsaturated compound:



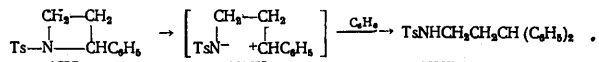
(CI!) (CIII), (a) R = residue of attacking agent (b) NR = N^-

Evidently the cleavage of cyclic secondary amines by phosgene or sulphonyl chlorides belongs to reactions of this type. Under the influence of phosgene, aziridine readily gives rise to β-chloroethyl isocyanate (CIV):[98]



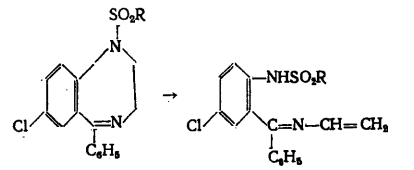
(CIV)

The introduction of the tosyl or methanesulphonyl group at the nitrogen atom also favours ring opening at the C — N bond. On refluxing in benzene, 2-phenyl-*N*-tosylazetidine (CV) is converted into the acyclic sulphonamide (CVI), which is formed as a result of the Friedel — Crafts alkylation of benzene by the cleavage product of the azetidine ring (CVII):[99]



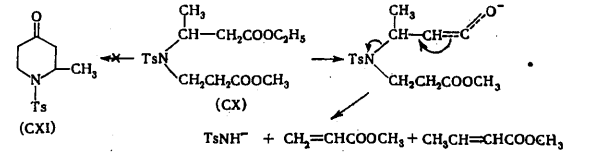
(CV) (CVII) (CVI)

When an attempt was made to remove with the aid of sodium hydride the tosyl (or methanesulphonyl) group from substituted 1, 4-benzodiazepines (CVIII), the vinylimines (CIX) were obtained, their structure being demonstrated by synthesis[100]:



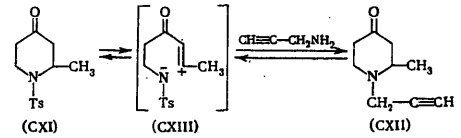
(CVIII) (CIX)

Mistryukov and Aronova[101] observed that, under the conditions of the Dieckmann reaction, the *N*-tosyl derivative (CX) does not give rise to the corresponding γ-piperidinone (CXI) but is decomposed under the influence of sodium hydride via the following mechanism:



(CXI) (CX)

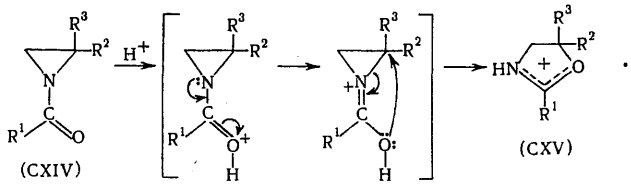
An attempt to split off in a similar way toluenesulphonamide from compound (CXI) was unsuccessful[101]. When 2-methyl-*N*-tosylpiperidin-4-one (CXI) was treated with propargylamine, only traces of the expected 2-methyl-*N*-propargylpiperidin-4-one (CXII) were detected:



(CXI) (CXIII) (CXII)

It is believed[101] that this is either due to the considerable shift of the equilibrium (CXI) ⇌ (CXIII) towards the cyclic form (CXI) or to the reduced nucleophilic properties of the open-chain form (CXIII) owing to the negative charge on the sulphonamide nitrogen.

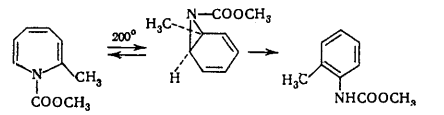
There are numerous publications on the cleavage, under the conditions reverse of the Ritter reaction, of small rings (azetidines and aziridines) with different electron-accepting residues at the nitrogen atom[102-107]. Thus, in a highly acidic medium, substituted 1-acylaziridines (CXIV) are converted quantitatively into the corresponding oxazolonium cations. The study of the ^{1}H NMR spectra at −55°C led to the hypothesis[104] that initially the amide group in compound (CXIV) is *O*-protonated with rapid opening of the aziridine ring and conversion into the *O*-protonated oxazolone, the latter being immediately converted into the oxazolonium ion (CXV):



(CXIV) (CXV)

(R^1 = CH_3, C_6H_5)

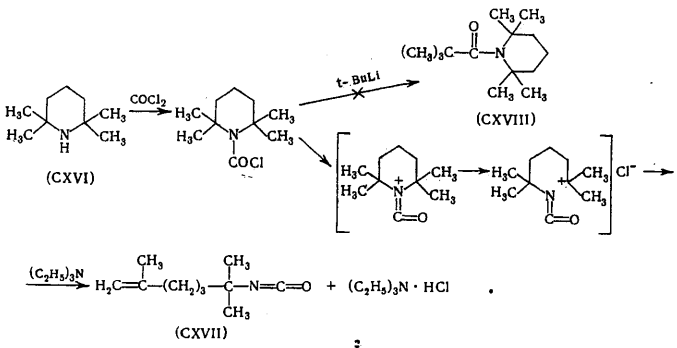
The reactions of 1-*H*-azepines accompanied by aromatisation may be regarded as of the same type. On heating to 200°C, *N*-methoxycarbonylazepines substituted in the 2-position are known to be converted[108,109] in high yields into aromatic urethanes:



In the presence of dilute acids, these processes take place much more readily, frequently at room temperature[109-111]. When the molecule contains several substituents, isomers may be formed as a result of sigmatropic migrations[109].

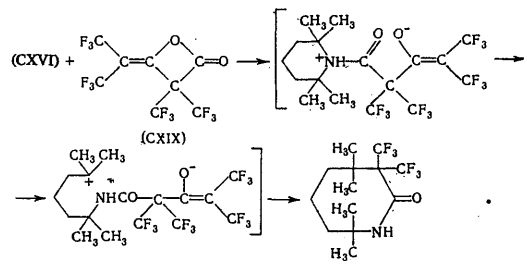
In a study dealing with amide conjugation in cyclic systems[112], it was noted that attempts at the synthesis of sterically hindered amides, where a planar disposition of the −N−C=O group is impossible, lead to molecular rearrangement already in the course of acylation. This leads to the formation of the usual conjugated amide system. An increase of steric hindrance by the branching of the alkyl substituents in the amine molecule promotes the dissociation of the C−N bond with formation of a stable t-alkyl cation.

When 2,2,6,6-tetramethylpiperidine (CXVI) reacts with phosgene in the presence of lithium t-butoxide, only the isocyanate (CXVII) is obtained and the expected cyclic amide (CXVIII) is hardly formed:



(CXVI) (CXVIII) (CXVII)

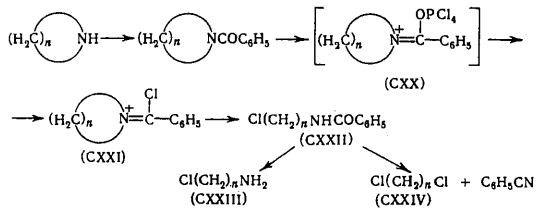
Examination of atomic models showed that the most favourable steric conditions for cleavages of this kind obtain in screen β-lactones as acylating agents. For example, on reaction with the β-lactone (CXIX), 2,2,6,6-tetramethylpiperidine (CXVI) undergoes the following transformations[112]:



(CXIX)

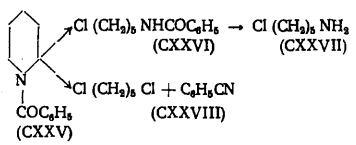
2. The Braun Reaction

The dissociation of the C−N bond in secondary cyclic amines can be achieved by a method developed by Braun[113,114]. For this purpose, the benzoyl derivative of the amine is heated with phosphorus pentachloride at 115−120°C. This results in the formation of the unstable tetrachlorophosphoranoate (CXX)† which then readily decomposes to the corresponding chloroimino-derivative (CXXI). Hydrolysis of compound (CXXI) yields a substituted benzoylamine (CXXII), the hydrolysis of which gives the monochloro-substituted amine (CXXIII). Further interaction of compound (CXXI) with phosphorus pentachloride at 180−200°C yields the dichloro-derivative (CXXIV) and benzonitrile:



(CXX) (CXXI) (CXXII) (CXXIII) (CXXIV)

For example, when *N*-benzoylpiperidine (CXXV) was allowed to react with phosphorus pentachloride at 120°C, the product was 1-(*N*-benzamido)-5-chloropentane (CXXVI), the alkaline hydrolysis of which leads to 1-amino-5-chloropentane (CXXVII). An increase of reaction temperatures to 200°C results in the formation of 1,5-dichloropentane (CXXVIII) and benzonitrile[114]:



(CXXV) (CXXVI) (CXXVII) (CXXVIII)

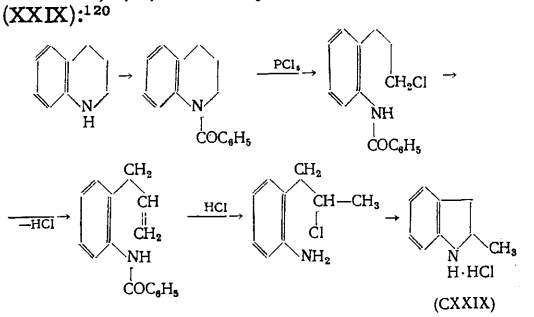
Apart from phosphorus pentachloride, phosphorus pentabromide[116], phosgene[117], and thionyl chloride[117,118] may be used in the Braun reaction. An attempt has been made to employ thionyl bromide also[117], but, on heating, the latter decomposes readily and acts as a brominating

† The lifetime of tetrachlorophosphoranoate derivatives of amides is usually very short. However, in the case of acid amides, containing powerful electron-accepting substituents, these compounds have been isolated and characterised [for example, the products of the interaction of trichloroacetamides with phosphorus pentachloride: $CCl_3C(OPCl_4)$ = NR].[115]

agent, leading to the formation of a large number of side products.

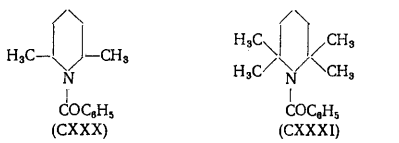
The scope of the Braun reaction is fairly wide and it has been used to open the rings of pyrrolidine[119], 1,2,3,4-tetrahydroquinoline[114,120-122] and its derivatives[123,124], indoline[125] and its derivatives[124,126,127], the alkaloids coniine[128], camphidine[129], etc.

The Braun reaction can be used also for the contraction of nitrogen-containing rings; this was demonstrated in the conversion of 1,2,3,4-tetrahydroquinoline into 2-methylindoline (XXIX):[120]



(CXXIX)

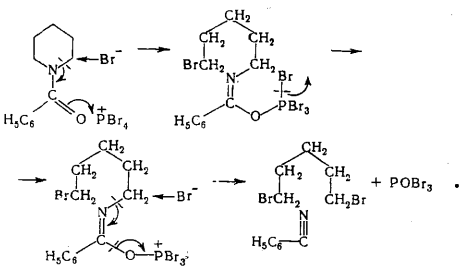
A number of studies have been made on the mechanism of the Braun reaction[130-136], in which the structure of the intermediates, the effects of substituents in the amine and acyl components of the molecule, and the kinetics of the individual stages of the process were considered. Leonard and Nommensen[134] studied several series of *N*-disubstituted benzoylamines in order to determine the effect of the screening of the α-carbon atom by alkyl substituents on the course of the Braun reaction. During this investigation, it was established that, whereas *N*-benzoylpiperidine reacts with phosphorus bromide to form 1,5-dibromopentane in 78% yield[114], the yield of the corresponding dibromide decreases with increasing steric hindrance at the α-carbon atom. With *N*-benzoyl-2,6-dimethylpiperidine (CXXX), the reaction takes place only to the extent of 19% and the tetramethyl derivative (CXXXI) does not form an aliphatic halogeno-derivative at all[134]:



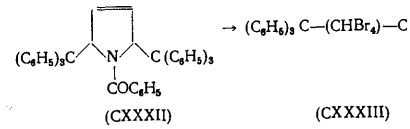
(CXXX) (CXXXI)

Similarly the yield of alkyl halides in the Braun reaction decreases with increasing screening also in the series of *N*-benzoyl derivatives of the isomeric heptyl- and butyl-amines, which supports a bimolecular reaction mechanism.

In addition, it has been shown for *N*-benzoyl-s-butylamine that, in the presence of an asymmetric carbon atom, the situation is reversed. On the basis of these findings, it has been suggested[134] that the bimolecular process in the reaction under consideration may be represented in the following way:

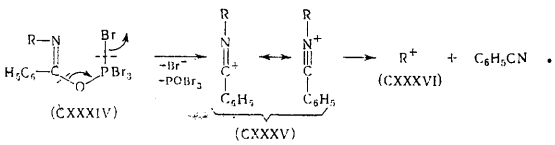


At the same time in a number of cases it has proved possible to achieve the Braun reaction with amides where the approach α-carbon atom is hindered by substituents. Thus the interaction of *N*-benzoyl-2,5-di(triphenylmethyl)-Δ^3-pyrroline (CXXXII) with phosphorus pentabromide yields 1,2,3,4-tetrabromo-1,4-di(triphenylmethyl)butane (CXXXIII) in 15% yield[137]:



(CXXXII) (CXXXIII)

Probably such sterically hindered amides react via a different mechanism involving an intermediate "carbonium-ammonium" ion. Leonard and Nommensen illustrate this mechanism by the reaction of *N*-alkylbenzoylamines with phosphorus pentabromide[134]:



(CXXXIV) (CXXXV) (CXXXVI)

The first attack by phosphorus pentabromide leads to the abstraction of a proton from the amide nitrogen and the formation of the intermediate (CXXXIV) which on decomposition can give rise to the "carbonium-ammonium" ion (CXXXV). The latter decomposes on heating into benzonitrile and the carbonium ion (CXXXVI), which, depending on its structure and the nature of the surrounding medium, can be converted into an olefin (with elimination of a proton) or can react with the available bromide ions to form an alkyl bromide.

Certain aspects of the Braun reaction have been investigated in recent years[135,136]. Various conclusions concerning the influence of the screening of the α-carbon atom in the amine part of the molecule have been confirmed and it has been shown for *N*-benzoylamine that the Braun reaction can be achieved as a rule with high yields when there are no substituents at the α-carbon atom[136].

Comparison of the yields of alkyl halides from substituted *N*-benzoylamines established that they correspond to the stability of the carbonium ion (CXXXVI). For example, the yield of benzyl chloride is 20 — 50%, while benzyl chlorides substituted in the *ortho*-position are formed in 80 — 85% yield.

New hypotheses have arisen in recent years concerning the role of the acyl residue in the Braun reaction. Earlier much importance was not attached to the nature of this part of the molecule. Braun used for acylation benzoyl chloride, which is most readily available, although he believed that any aromatic acid halide may be used for this purpose[114]. Leonard and Nommensen noted[134] that the screening of the α-carbon atom in the acyl part of the amide molecule does not affect the yield of the halogeno-derivative. However, Carlson[118,136] showed that the yields of substituted benzyl chlorides from the corresponding *N*-benzoylbenzylamines are higher than from the analogous *N*-acetylbenzylamines. This finding can also be accounted for by the fact that the phenyl group promotes the stabilisation of the intermediate ion of type (CXXXV) to a greater extent than does the methyl group.

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Effects of Steric Hindrance in Molecules on the Properties and Synthesis of Hydrocarbons

V.V.Voronenkov and Yu.G.Osokin

Data on the steric hindrance in hydrocarbon molecules have been reviewed. The effect of steric hindrance on the physical properties of hydrocarbons (specific gravity, refractive index, and refraction) and on their ultraviolet and ^{1}H NMR spectra has been demonstrated. The influence of steric hindrance on the synthesis of hydrocarbons in alkylation, oligomerisation, and polymerisation reactions has been examined. A theoretical explanation has been given for a number of reactions occurring anomalously under the influence of steric hindrance.
The bibliography includes 160 references.

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I. INTRODUCTION

Hydrocarbons are a valuable starting material for the main products of large-scale organic synthesis[1]. At the same time they are convenient for the investigation of steric hindrance in molecules. This is because in hydrocarbons interactions of other types are reduced to a minimum. Therefore, when steric hindrance arises in molecules, its effect is shown most clearly in hydrocarbons. In the literature[2-10] dealing with the study of compounds of this class, the important role of steric hindrance in chemical reactions of hydrocarbons has been frequently pointed out. However, so far there have been almost no systematic descriptions of data on this problem. This review deals with the effect of steric hindrance on the physicochemical properties and synthesis of hydrocarbons.

II. THE NATURE OF STERIC HINDRANCE

Examination of numerous literature data for hydrocarbons leads to the conclusion that steric hindrance alters their molecular geometry, which entails an increase of the internal energy of such molecules, so that among the isomers of hydrocarbons, sterically hindered structures become thermodynamically less stable.

The change in molecular geometry takes place in the following three ways: rotation about the bonds with the displacement of one part of the molecule from the plane of the other, deformation of valence angles in the plane, and extension of the bonds between atoms.

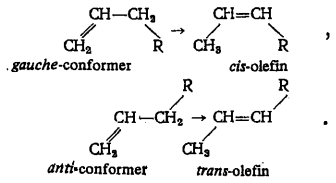
The changes undergone by the molecule under the influence of steric hindrance occur simultaneously. However, since the extension of bonds requires a much larger energy than does rotation about a single bond and the deformation of the valence angle of such a bond, it evidently follows that the first two types of geometrical changes will be mainly observed.

1. Rotational Isomerism in Hydrocarbons

When the distribution of atoms in space was considered in terms of classical stereochemistry, account was taken only of the interatomic distances and valence angles. Although this made it possible to understand many features of the structure and chemical behaviour of hydrocarbons, no less significant results in this field were achieved after the appearance of conformational concepts[9-13].

Interesting electron diffraction studies on the conformations of hydrocarbon molecules in the gas phase were carried out by Vilkov and coworkers[14]. In the determination of the energetically favourable molecular conformation, they took into account not only the repulsion between atoms not linked by valence bonds but also the interaction between the bonds in the molecule. Table 1 presents the preferred conformations of the rotational isomers of a number of hydrocarbons, taking into account the above factors.

For propene, but-1-ene, and other α-olefins, the eclipsed and *gauche*-conformations predominate. This has been demonstrated in a study of the ^{1}H NMR spectra[15] of but-1-ene, pent-1-ene, and hex-1-ene and has been confirmed by calculation[16]. In the ground state of liquid alk-1-enes the *gauche*-conformations predominate, but, on passing to olefins with a more bulky group R, the *anti*-conformations become more stable owing to a reduced steric hindrance. Such distribution of conformations accounts satisfactorily for the experimentally observed[17,18] *cis*-stereospecificity of the positional isomerism of various olefins.



Studies on a number of conjugated dienes by ultraviolet spectroscopy[19] revealed a transoid conformation of the sterically unhindered alkyl-substituted diene hydrocarbon. The *trans*-configuration of such hydrocarbons is additionally stabilised by the maximum degree of π,π conjugation.

Evidently the conjugation effect is responsible for the stable configurations of phenylcyclobutane and phenylcyclopropane, since the "banana bonds" of the latter are capable of conjugation with the aromatic ring. The rotational isomerism of alkyl derivatives of cyclic hydrocarbons is important[20-23]. Its effect on the reactions of

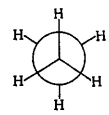
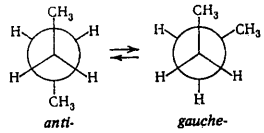
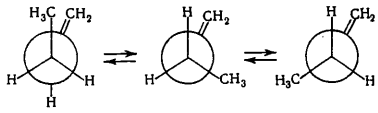
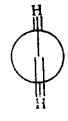
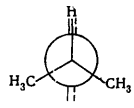
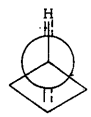
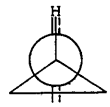
cyclic hydrocarbons has been examined in a review by Bragin and Liberman [10].

At the present time conformational analysis of hydrocarbons has developed so much that it has now become possible to make satisfactory predictive calculations of the energetically favourable conformations [16,28,29]. Thus, according to Kitaigorodskii [28], the potential energy which determines the conformational properties of molecules consists of the energy of interaction (repulsion) between atoms not linked by valence bonds and the elastic energy of the valence angles. The optimum conformation should correspond to an energy minimum and should arise from a compromise between the tendency of the non-bonded atoms to move apart to equilibrium distances and the tendency of the valence angles to retain the ideal values. In this connection it is of interest to quote a statement by A.A. Chugaev who wrote as early as 1904 "Chemical molecules represent [are a result of] a mechanism involving a certain energy store. In order to understand the operation of such mechanisms, it is necessary to know to an equal extent their internal structure and the distribution of energy in them" [30].

Kitaigorodskii calculated the most favourable conformations of certain hydrocarbons (bicyclic terpenes). Kitaigorodskii's method makes it possible to predict accurately the deviations of the C–C–C angles in alkanes from the tetrahedral value to 112.5°.

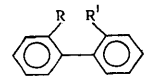
Using Kitaigorodskii's concepts, Dashevskii [29] developed a method for the calculation of the energies of formation of hydrocarbon molecules from atoms. He calculated the geometries and atomisation energies of straight-chain alkanes and their isomers.

Table 1. Stable conformations of the rotational isomers of various hydrocarbons.

Hydrocarbon	Conformation of isomer	References
Ethane		24
Butane	 *anti-* *gauche-*	12,13
Propene		14,25
α-Butene		14
Butadiene		14
Cumene		26
Phenylcyclobutane		26
Phenylcyclopropane		27

2. Atropisomerism of *oo'*-Dialkyl-substituted Biphenyls

A special case of conformational isomerism is the atropisomerism of *oo'*-disubstituted biphenyls:



As a result of the interaction of the groups R and R' in the *oo'*-positions of biphenyl, rotation of the benzene rings about the common axis becomes impossible; therefore the molecule becomes asymmetric and optical isomerism appears. Thus Meisenheimer [31] and Mills [32,33] showed by calculation that the presence of methyl groups in the *oo'*-positions is sufficient to hinder rotation. According to the Adams empirical rule, the resolution of biphenyls into optical isomers is possible when the sum of the C–R and C–R' bond lengths is greater than 2.90 Å. The steric hindrance in *oo'*-dialkylbiphenyls and their steric strain increase fairly rapidly with increasing branching of the alkyl group. Therefore the synthesis of *oo'*-di-t-butylbiphenyl is extremely difficult [34].

3. Effect of Steric Hindrance on the Physical and Chemical Properties of Hydrocarbons. The Auwers–Skita rule

The first constant widely used in organic chemistry to assess the molecular structure of hydrocarbons was molecular refraction. It was noted that the refraction of *o*-dialkylbenzenes is lower than the refractions of the corresponding *m*- and particularly *p*-isomers [35,36]. Since molecular refraction is proportional to atomic volume [37], its lower value for *o*-dialkylbenzenes is evidence of a denser packing of the atoms of the alkyl groups in their molecules compared with the *m*- and *p*-isomers. This conclusion is confirmed by the finding that *o*-dialkylbenzenes have higher densities, refractive indices, and boiling points than the *p*-substituted derivatives where there is no steric hindrance (Table 2).

Thus a kind of steric "contraction" (condensation) is observed in *o*-dialkylbenzenes, due to the interaction of adjacent alkyl groups not linked by valence bonds (the "ortho-effect"). Such "contraction" results in the appearance of repulsion forces which hinder the rotation of the alkyl groups about the single $C_{ar}-C_{alk}$ bond, leading to the deformation of the angles between these bonds and an increase of the internal energy of the molecule [38-39].

o-Dialkylbenzenes are geometrically similar to *cis*-olefins and the *p*-isomers are similar to *trans*-olefins (the Werner rule [40]). This analogy is reflected also in the

physical properties. The densities, refractive indices, and boiling points of *cis*-olefins, like those of *o*-dialkylbenzenes, are higher than for the *trans*-isomers; at the same time the molecular refractions of *cis*-olefins are lower than those of *trans*-olefins (Table 3).

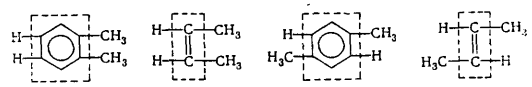


Table 2. Physical constants of *o*- and *p*-dialkylbenzenes.

Hydrocarbon	MR_D, cm^3	B.p., °C	ρ_4^{20}, g cm^{-3}	n_D^{20}
p-Xylene	36.02	138.35	0.8610	1.4958
o-Xylene	35.77	144.41	0.8802	1.5054
p-Cymene	45.34	177.25	0.8573	1.4909
o-Cymene	45.04	178.35	0.8766	1.5000
p-Diethylbenzene	48.82	183.75	0.8619	1.4948
o-Diethylbenzene	48.53	183.42	0.8799	1.5026

Thus a steric "contraction" of alkyl groups analogous to that in *o*-dialkylbenzenes is observed in *cis*-olefins. It has been shown by ^{1}H NMR [42] that in *cis*-but-2-ene there is indeed an appreciable overlapping of the van der Waals spheres of the methyl groups, which does not happen in the *trans*-isomer.

Table 3. Physical constants of *cis*- and *trans*-olefins [41].

Hydrocarbon	MR_D, cm^3	B.p., °C	ρ_4^{20}, g cm^{-3}	n_D^{20}
trans-Pent-2-ene	25.61	36.35	0.6432	1.3793
cis-Pent-2-ene	25.38	36.94	0.6555	1.3898
trans-Hex-2-ene	29.59	67.88	0.6779	1.3936
cis-Hex-2-ene	29.34	68.84	0.6872	1.3976
trans-Hex-3-ene	29.61	67.08	0.6770	1.3943
cis-Hex-3-ene	29.40	66.45	0.6799	1.3950

The overlapping of the van der Waals spheres leads to the mutual repulsion of the *cis*-alkyl groups, which in turn leads to an increase of the valence angles and of the strain in the double bond ("cisoid repulsive strain") [43]. The strain in the double bond can be estimated experimentally from thermochemical data by comparing the negative heats of hydrogenation of olefins (Table 4).

It follows from Table 4 that, with increase of the bulk of the alkyl groups in the *cis*-position of the olefin, the negative heat of hydrogenation also increases, which corresponds to a greater strain in the C=C bond and hence to a greater deviation of the C=C–C valence angle [from the ideal value], which amounts to 136° in *cis*-di-t-butylethylene. The main consequence of such strain in the double bond is an enhanced reactivity in reactions characteristic of the usual olefins. This interesting question has been discussed in detail in a review by Zefirov and Sokolov [43]. Steric hindrance is observed also in the series of monoalkylnaphthalenes [44]. α- and β-Substituted isomers are typical for these compounds, the relation between their physical properties being similar to that in *cis*- and *trans*-olefins or *o*- and *p*-dialkylbenzenes respectively. This can be inferred from the specific gravities, refractive indices, boiling points, and molecular refractions of alkylnaphthalenes (Table 5). However, one should note that, whereas the steric hindrance in *o*-dialkylbenzenes and *cis*-olefins is due to adjacent alkyl groups, in α-monoalkylnaphthalenes it arises due to "peri-hydrogen".

Table 4. Negative heats of hydrogenation of *cis*- and *trans*-olefin isomers.

Compound	ΔH_{hydr}, kcal mole^{-1}
cis-But-2-ene	28.5
trans-But-2-ene	27.5
cis-t-Butylmethylethylene	30.8
trans-t-Butylmethylethylene	26.5
cis-Di-t-butylethylene	36.2
trans-Di-t-butylethylene	26.87

In 1,2-*cis*-isomers of cyclic compounds [45], steric "contraction" is observed as in the *cis*-derivatives of ethylene. According to the Auwers–Skita rule [46], in the series of isomeric hydroaromatic compounds the *cis*-isomer has a higher density, refractive index, and boiling point and a lower molecular refraction and hence a lower molecular volume than the *trans*-isomer. However, the studies of Kazanskii and Liberman and coworkers [47–52] showed that this rule must be used with caution. They demonstrated for a large number of examples that the *cis*-isomers of dialkylcycloalkanes can also have boiling points lower than those of the *trans*-isomers.

Table 5. Physical constants of α- and β-alkylnaphthalenes.

Hydrocarbon	MR_D, cm^3	B.p., °C	ρ_4^{20}, g cm^{-3}	n_D^{20}
β-Methylnaphthalene	49.24	241	0.9904	1.6026
α-Methylnaphthalene	48.82	244.7	1.0203	1.6180
β-Ethylnaphthalene	53.88	252	0.9922	1.6028
α-Ethylnaphthalene	53.46	258.7	1.0081	1.6089
β-Isopropylnaphthalene	58.89	268	0.9780	1.5861
α-Isopropylnaphthalene	58.48	272	0.9762	1.5877
β-Butylnaphthalene	63.31	275	0.9750	1.5818
α-Butylnaphthalene	62.88	280	0.9768	1.5820

The steric hindrance in hydrocarbons has a significant influence on exaltation (EM_D). Bruhl [53,54], who introduced this concept, showed that exaltation occurs on bond conjugation, i.e. in the presence of an enhanced electron mobility in the molecule. The exaltation of *p*-dialkyl-substituted benzenes, *trans*-olefins [55], and β-monoalkyl-substituted naphthalenes [56] is much higher than the corresponding values for the *o*-, *cis*-, and α-substituted isomeric hydrocarbons—compounds with steric hindrance. Thus steric hindrance in the hydrocarbon molecule leads to a decrease of exaltation, i.e. to a decrease of the mobility of its electron system.

Another example of steric hindrance in the molecule affecting exaltation and hence also conjugation in hydrocarbons is provided by the phenomenon of "central depression" [57], the essential feature of which is that substitution of the hydrogen atom by alkyl groups in the centre

of a diene molecule leads to a decrease of exaltation compared with that of the diene hydrocarbon in which the alkyl groups are present at the edges (Table 6).

Table 6. Refractions and exaltations of certain diene hydrocarbons.

Compound	MR_D, cm^3		EM_D
	expt.	calc.	
trans-CH_3—CH=CH—CH=CH_2	25.97	24.35	1.62
cis-CH_2—CH=CH—CH=CH_2	25.40	24.35	1.10
CH_2=C(CH$_3$)—CH=CH_2	25.40	24.35	1.05
CH_3—CH=CH—CH=CH—CH_3	30.73	28.97	1.76
CH_2=CH—CH=C(CH$_3$)—CH_3	30.39	28.97	1.42
CH_3—CH=CH—C(CH$_3$)=CH—CH_3	34.59	33.59	1.00

The greatest steric hindrance in hydrocarbon molecules appears when t-alkyl groups are present as substituents. The mutual influence of a number of alkyl substituents in hydrocarbons has been observed by ^{1}H NMR spectroscopy (Table 7).

Table 7. Chemical shift of the protons in the t-butyl group [58].

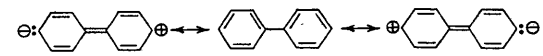
Compound	δ, p.p.m.	Compound	δ, p.p.m.
$(CH_3)_3C$—C$(CH_3)_3$	0.870	1,3-[$(CH_3)_3C]_2$—C_6H_4	1.31
$(CH_3)_3C$—H	0.905	1,4-[$(CH_3)_3C]_2$—C_6H_4	1.31
$(CH_3)_3C$—CH_3	0.927	1,2-[$(CH_3)_3C]_2$—C_6H_4	1.54
$(CH_3)_3C$—CH=CH_2	1.000	1,3,5-[$(CH_3)_3C]_3$—CH_3	1.34
$(CH_3)_3C$—C≡CH	1.20	1,2,4-[$(CH_3)_3C]_2$—C_6H_3	1.53
$(CH_3)_3$—C_6H_5	1.32	1,2,4,5-[$(CH_3)_3C]_4$—C_6H_2	1.48

4. Steric Hindrance to π,π- and σ,π Conjugation. Ultraviolet Absorption Spectra of Hydrocarbons

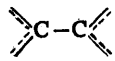
One of the main methods for the detection of steric hindrance in hydrocarbon molecules containing a π,π- or σ,π conjugated bond system consists in the investigation of their ultraviolet absorption spectra. The ultraviolet spectra of conjugated hydrocarbons depend to a considerable degree on the steric disposition of atoms in their molecules [59].

Theoretical studies by Hückel [60] and Pauling [61] and X-ray diffraction analysis established that a π,π conjugated system tends towards a distribution in one plane, since in this configuration the axes of the *p*-electronic orbitals are parallel and the orbitals overlap to the maximum extent.

The decrease of the mutual overlapping of *p* orbitals in a conjugated system when its coplanarity breaks down is shown in a change of the ultraviolet absorption spectra. These changes consist of a displacement of the *K* absorption bands towards shorter wavelengths with a simultaneous decrease of absorption intensity (ϵ_{max}). An example of this is provided by the ultraviolet absorption spectra of stilbene and dialkyl-substituted biphenyls [62]. Biphenyl, the molecule of which is coplanar owing to mesomeric forms,



absorbs much more intensely than *oo'*-dimethylbiphenyl (Fig. 1). The absorption due to the latter is very similar to that of toluene, which is evidence of a decrease of π,π conjugation via the central bond as the phenyl rings are displaced from coplanarity owing to the *oo'*-dimethyl groups. Binaphthyls [63] and 2,3-dialkyl-substituted buta-1,3-dienes [19] have similar ultraviolet spectra. The electronic spectrum of *αα'*-binaphthyl resembles that of naphthalene, while the spectrum of *ββ'*-binaphthyl reveals a strong conjugation between the naphthyl systems, that of *αβ*-binaphthyl being of an intermediate type. Thus the "peri-hydrogen atom" in naphthalene gives rise to fairly considerable steric hindrance to rotation about the



bond in *αα'*-binaphthyl.

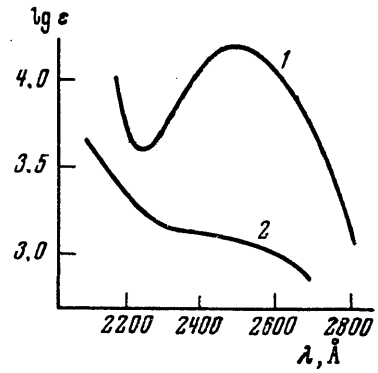
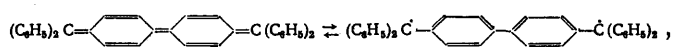


Figure 1. Ultraviolet absorption spectra (in ethanol): 1) biphenyl; 2) *oo'*-dimethylbiphenyl.

On the basis of the ultraviolet absorption spectra of methylated biphenyls, Suzuki [64] calculated the angle of φ between the planes of the benzene rings and found that the angle for the biphenyls in solution depends on the number of substituted *o*-positions. The relevant data are given in Table 8.

Koptyug et al. [65] showed that, in the ^{1}H NMR spectra of methylated biphenyls, the signals due to the protons of the methyl group in the *o*-positions are displaced to a lower field relative to the signals of the protons in the methyl groups occupying the *m*- and *p*-positions.

The steric hindrance to π,π conjugation in biphenyls promotes the stability of the corresponding free radicals [66,67]. Thus Chichibabin's hydrocarbon [68],



is a biradical only to the extent of 4%, but, when methyl groups are introduced into the *oo'*-positions of its biphenyl system, it exhibits the properties of a biradical to the extent of 100%:[69]

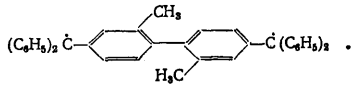
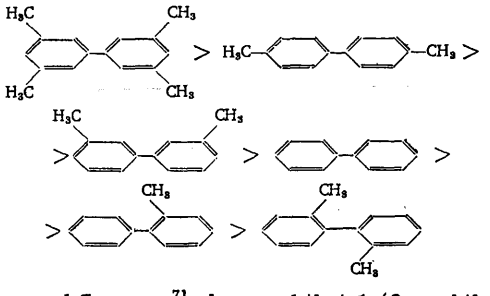


Table 8. The angle φ between the benzene rings in *o*-substituted biphenyls.

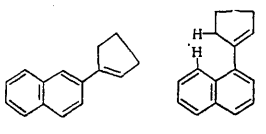
Substituents in positions				$\varphi°$
2	2'	6	6'	
H	H	H	H	20
CH_3	H	H	H	58
CH_3	CH_3	H	H	70
CH_3	CH_3	CH_3	CH_3	90

This implies that the mutually perpendicular (or nearly so) positions of the benzene rings, which arise owing to the *oo'*-dimethyl groups, are to a considerable degree responsible for the independence of the π electrons of these nuclei and of both unpaired electrons.

The steric hindrance to π,π conjugation in *oo'*-dimethyl derivatives of biphenyls has a significant influence on the stability of the molecular complexes of the methyl derivatives of biphenyl (donor) with trinitrobenzene (acceptor)[70]. It has been shown that the substitution of methyl groups in the *ortho*-positions in biphenyl, in contrast to the substitution in the *meta*- and *para*-positions, has an unfavourable effect on the stability of the complex, which diminishes in the following sequence:



Klemm and Sprague[71] observed that 1-(2-naphthyl)cycloalk-1-enes, particularly cyclopentene and cyclohexene derivatives, form with 2,4,7-trinitrofluorenone in acetic acid more stable complexes than those of 1-(1-naphthyl)-cycloalk-1-enes:



The low stability of the complexes formed by donors of the second type is due to the fact that the cycloalkene ring is displaced from the plane of the naphthalene ring system owing to steric hindrance caused by the peri-hydrogen.

Changes in the electronic absorption spectra analogous to those of alkyl-substituted biphenyls are observed for alkyl-substituted dienes and styrenes. In particular the absorption intensity of the *K* band in the spectra of dienes with the structure $R-CH=CH-CH=CH_2$ is higher than for dienes with "central depression": $CH_2=\underset{\displaystyle R}{\overset{|}{C}}-CH=CH_2$. On the other hand, it has been shown than an increase of the bulk of the group R in $CH_2=\underset{\displaystyle R}{\overset{|}{C}}-CH=CH_2$ leads to the breakdown of the coplanarity of the vinyl fragments and a decrease of the π,π conjugation (Table 9).

Table 9. Parameters of the ultraviolet absorption spectra of alkyl-substituted dienes.

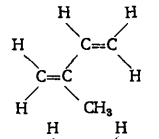
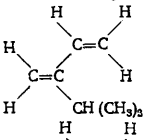
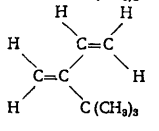
Compound	$\lambda(\varepsilon)$ in iso-octane, nm	$\vartheta°$
	223 (22100)	0
	223 (12000)	45
	224 (5400)	60

Table 9 shows that an increase of the size of group R increases the angle of deviation of the vinyl fragments from coplanarity (θ) and causes a corresponding decrease of the degree of conjugation in the $CH_2=CR-CH=CH_2$ molecule, reflected in a decrease of the absorption intensity.

The hindrance to π,π conjugation in diene molecules has a significant influence on the stability of their complexes with silver. It has been shown[73] that the stability of such complexes diminishes in the sequence buta-1,3-diene > 2-methylbuta-1,3-diene > 2,3-dimethylbuta-1,3-diene.

Apart from the steric hindrance to π,π conjugation, i.e. to electronic interaction between two or more multiple bonds, there is steric inhibition of σ,π conjugation in hydrocarbons. The electronic spectra of alkylbenzenes provide an example. The changes undergone by the electronic absorption spectrum of benzene as a result of the introduction of an alkyl group into the ring are due to a displacement towards the benzene ring of the electrons of the C–H bonds involving the α-carbon atom of the alkyl group, i.e. are a result of σ,π conjugation[74]. In the presence of steric hindrance in the molecule, the conjugation of the alkyl groups with the benzene ring is weakened; the absorption intensity diminishes and the electronic spectrum is displaced towards shorter wavelengths. On the other hand, a displacement of the spectrum towards longer wavelengths with increase of absorption intensity is evidence of an increase in the degree of conjugation of the system. It is interesting to note that the bathochromic shift of the characteristic absorption band and the increase of its intensity occur in the sequences *ortho-* < *meta-* < *para*- for dialkylbenzenes (Fig. 2), *cis-* < *trans*- for

olefins, and α- < β- for monoalkylnaphthalenes, in agreement with the decrease of the steric hindrance in these molecules.

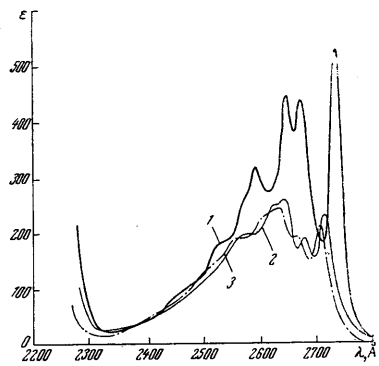


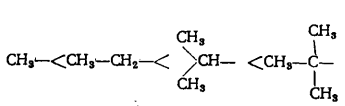
Figure 2. Ultraviolet absorption spectra of cymenes: 1) *p*-cymene; 2) *m*-cymene; 3) *o*-cymene.

Steric hindrance, which inhibits conjugation (electron delocalisation) in hydrocarbons, affects primarily the rates of their chemical reactions. Thus, in a study of the chlorination of alkylbiphenyl ring systems with molecular chlorine, de la Mare [75] established that the methyl groups in the *para*- and *meta*-positions increase sharply the rate of reaction. The chlorination rate constant for the *oo'*-dimethyl derivative of biphenyl, where there is steric hindrance to the electron shift (conjugation), is smaller by a factor of 16 compared with that for 4,4'-dimethylbiphenyl. A similar situation is observed in hydrocarbons with steric hindrance to σ,π conjugation. It has been found that the rate of abstraction by the trichloromethyl-radical of the α-hydrogen atom in the isopropyl group of *o*-cymene, in which there is steric hindrance to σ,π conjugation, is lower than in *p*- and *m*-cymenes, where there is no steric hindrance (Table 10). The same relative reactivities of cymenes have been observed in liquid-phase autoxidation [77].

Table 10. Relative rates of reaction of cymenes with the trichloromethyl radical.

Hydrocarbon	Relative rates
o-Cymene	0.44
m-Cymene	2.3
p-Cymene	2.5

According to the literature [2,79], steric hindrance increases with the degree of branching of the alkyl groups in the sequence:



and the bulk of the alkyl group as a whole does not have a steric effect as marked as branching at its α-carbon atom. The finding that small alkyl groups with maximum branching at the α-carbon atom give rise to more pronounced steric hindrance than bulkier alkyl groups but without such branching was already pointed out in earlier investigations. Alkyl groups can be arranged in the following sequence in terms of decreasing capacity for steric repulsion:

$$(CH_3)_3C- > (CH_3)_3C-CH_2- > (CH_3)_3C-CH_2-CH_2- \quad .$$

III. STERIC HINDRANCE IN THE SYNTHESIS OF HYDROCARBONS

1. Synthesis of Alkylbenzenes and Alkylnaphthalenes

Alkylation is one of the commonest methods of synthesis of hydrocarbons [80]. The addition of alkyl groups to the aromatic ring in the presence of acid catalysts takes place in accordance with the directing rules for the benzene ring [81,82]. Thus when toluene is alkylated with primary and secondary alcohols and alkyl halides in the presence of acid catalysts, the main products are *para*- and *ortho*-alkyltoluenes. Alkylation of toluene with tertiary alcohols and t-alkyl halides leads to the formation of *para*-t-alkyltoluene with only a low content of the *meta*-isomer. *p*-Xylene is not alkylated with t-butyl alcohol and t-butyl halides.

Baur [83], who alkylated *m*-xylene with t-butyl bromide in the presence of $AlCl_3$, and Noelting [84], who butylated the same hydrocarbon with t-butyl alcohol using sulphuric acid as a catalyst, obtained the same product: 5-t-butyl-1,3-dimethylbenzene.

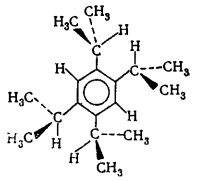
Despite the fact that the distribution of electron density in the aromatic ring of *m*-xylene (the concerted orientation of the two methyl groups) favours 1,3,4-substitution, steric hindrance to this mode of alkylation results in the formation of the symmetrical (anomalous) 1,3,5-isomer. It has been shown [85-88] that the alkylation product does not undergo subsequent isomerisation under the above conditions, i.e. it is the primary product of the addition of the t-alkyl cation. It is noteworthy that such substitution does not depend on the nature of the acid catalyst and takes place only with the t-butyl group, while the introduction of the s-butyl group into *m*-xylene under the influence of sulphuric acid and boron trifluoride gives rise to the formation of the 1,3,4-isomer.

The use of accurate modern analytical methods (capillary gas–liquid chromatography combined with infrared spectroscopy) in the study of the composition of the products of the alkylation of toluene and xylenes with various tertiary alcohols and alkyl halides in the presence of acid catalysts led to the demonstration of the absence or an extremely low content of *o*-t-alkyltoluenes and *o*-t-alkylxylenes [89-101].

It follows from the literature data [102] on this problem that the main reason for the anomalous behaviour of the t-alkyl group in alkylation reactions in the presence of acid catalysts is its bulk, which gives rise to considerable steric hindrance. However, on the basis of the bulk of the alkyl group alone, it is difficult to explain why, for example, the cyclohexyl group, which is bulkier than the t-butyl group, enters fairly readily the *ortho*-position relative to the methyl group [103].

Analysis of the structures of the *o*-dialkylbenzenes obtained by alkylation in the presence of acid catalysts showed that they contain at least one α-C–H bond in

adjacent alkyl groups. Owing to mutual repulsion, branched adjacent alkyl groups are oriented in such a way that their nearest interacting components become the protons of the α-C–H bonds, which is clearly illustrated by tetraisopropylbenzene as a model:



The minimum repulsion energy corresponds to this distribution of alkyl groups. In contrast to methyl, ethyl, and isopropyl groups, there is no similar possibility of orientation of the t-butyl group, so that its steric repulsion increases sharply [104]. A similar conclusion follows from an examination of the reaction mechanism and the geometry of the transition state.

The mechanism of the alkylation of aromatic hydrocarbons with olefins is known to involve electrophilic aromatic substitution. The mechanism of the alkylation with olefins in the presence of acid catalysts is usually treated on the basis of the hypothesis of the intermediate formation of active species: either alkyl derivatives of the acid or carbonium ions.

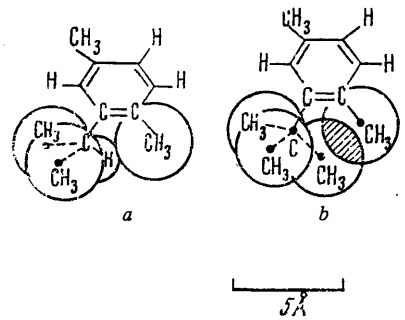
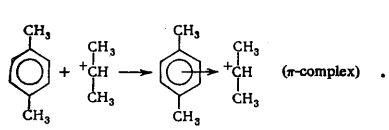
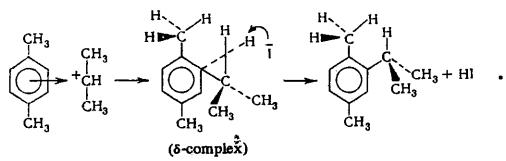


Figure 3. Molecular models: *a*) *o*-isopropyl-*p*-xylene; *b*) *o*-t-butyl-*p*-xylene.

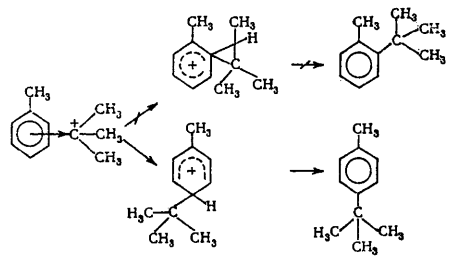
At the present time the carbonium ion theory of acid-catalysed alkylation reactions is the most popular. The existence of alkyl cations in strong acid solutions has been demonstrated by spectroscopic methods in many investigations [105,106]. Consequently alkylation of *p*-xylene takes place as follows:



The π complex rearranges to a σ complex which in the case of *ortho*-alkylation can be represented schematically as follows:



The scheme shows that the isopropyl group in the σ-complex transition state is oriented in such a way that the nearest interacting components of this group and of the methyl are the protons of the α-C–H bonds, which corresponds to the minimum repulsion energy between the *ortho*-alkyl groups. Evidently this state corresponds to the addition of any primary or secondary alkyl group. However, when a t-butyl group is introduced, then in the σ-complex transition state and in the resulting *o*-dialkylbenzene the steric repulsion effect increases sharply, as shown clearly in Fig. 3. Tending to reduce its potential energy to a minimum, the sterically strained molecule decreases the repulsive force by increasing the distance between the alkyl groups. Therefore, when the t-butyl group adds to toluene and *m*-xylene, the *ortho*-isomer is not formed:



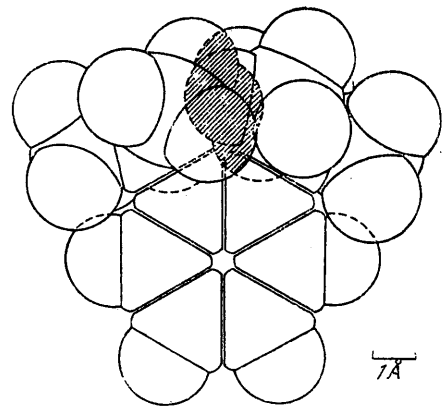


Figure 4. Molecular model of *o*-di-t-butylbenzene.

However, *o*-t-butyltoluene and 4-t-butyl-*m*-xylene were obtained by organomagnesium synthesis. Moreover, the t-butyl group was introduced into the ring by this method in the *ortho*-position relative to another t-butyl group [107]. Models for *o*-di-t-butylbenzene show marked overlapping of the van der Waals spheres of the alkyl groups (Fig. 4). The chemical properties of 1,2-di-t-butylbenzene have been investigated in detail. It is interesting to note that, on ultraviolet irradiation, it gives a mixture of the *m*- and *p*-isomers (20 and 80% respectively), which are more resistant to light; *o*-t-butyltoluene also isomerises under these conditions, but much more slowly.

Bulky adjacent groups undergoing a steric interaction with one another can actually alter the steric structure of the hydrocarbon. This has been confirmed by the finding that in 1,2,4,5-tetra-t-butylbenzene the ring is distorted so much that the boat conformation was assigned to it [108]. On irradiation with ultraviolet light, the compound isomerises to a derivative of "Dewar" benzene.

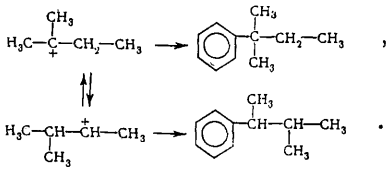
Thus in sterically hindered *o*-dialkylbenzene there is a strain in the π-electron system of the aromatic ring similar to the strain of the π-electron system of the double bond in strained *cis*-dialkylethylenes.

Steric hindrance due to t-alkyl groups arises also in the alkylation of naphthalene. However, here the hindrance is not caused by an adjacent alkyl group but by the "peri-hydrogen", which hinders the introduction of t-alkyl groups into the α-position of the naphthalene ring. Whereas t-butylmagnesium bromide reacts with bromobenzene, the reaction with α-bromonaphthalene does not occur [2]. The alkylation of naphthalene with isobutene in the presence of acid catalysts takes place anomalously, like the alkylation of toluene: only β-t-butylnaphthalene is obtained [109]. However, s-alkyl groups (isopropyl [110,111] and cyclohexyl [112,113] groups) enter the α-position of naphthalene fairly readily owing to the presence in these groups of the α-C–H bond, which permits a [favourable] orientation of the alkyl group relative to the "peri-hydrogen".

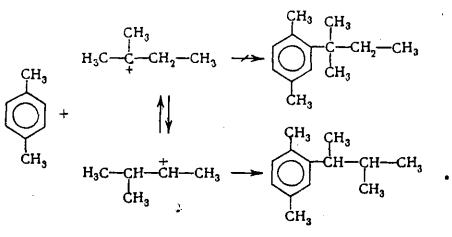
2. Anomalous Isomerisation of t-Alkyl Groups in the Alkylation of Hydrocarbons

Until recently, it was regarded as generally accepted and demonstrated that, in the alkylation of an aromatic ring with t-butyl halides, tertiary alcohols, and iso-olefins, there is no rearrangement of the resulting tertiary carbonium ions; the tertiary carbonium ion formed alkylates the aromatic ring with formation of t-alkylbenzenes [114].

However, it has been noted in a number of studies [115,116] that in the alkylation of benzenes secondary alkyl derivatives are formed together with tertiary derivatives. This is indicated, in particular, by the formation of a mixture of secondary and tertiary (main product) pentylbenzenes on alkylation of benzene with isopentyl chloride and pentenes in the presence of aluminium chloride at 0°C: [115,120]



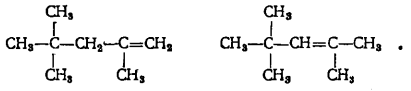
The equilibrium between the tertiary and secondary ions can be displaced towards the latter species under the influence of steric hindrance. Thus Friedman and Morritz [117], who alkylated *p*-xylene with isopentenes in the presence of BF_3 and $AlCl_3$ at 0°C, observed the formation (in yields up to 40%) of s-pentyl derivatives exclusively, which was confirmed by a careful analysis using infrared and mass spectrometry. They suggested that, when alkylation by tertiary ions (in the *ortho*-position of *p*-xylene) is hindered, the less sterically hindered secondary ions, in equilibrium with the tertiary ions, enter the ring:



3. Oligomerisation and Polymerisation of Alkyl- and Aryl-substituted Olefins

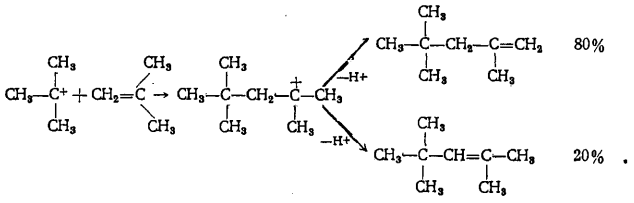
The first systematic studies on the reactivity of ethylene derivatives in the oligomerisation reaction were carried out by Lebedev and Filonenko [118], who observed that at room temperature in the presence of floridin only asymmetric di- and tri-substituted ethylene derivatives are polymerised. Further study of this problem and analysis of the accumulated experimental data enabled Korshak and coworkers [119,120] to conclude that steric effects as well as electron factors play an important role in the olefin polymerisation process.

The effect of steric hindrance is usually shown in two ways; (1) the rate of oligomerisation of olefins decreases with increasing number and bulk of substituents at the double bond and (2) the isomeric composition of the reaction products changes. In 1873 Butlerov [121] described the dimerisation of isobutene under the influence of sulphuric acid, which results in the formation of di-isobutene. The structure of di-isobutene was the subject of numerous investigations [122–125] which established accurately that this hydrocarbon is a mixture of two isomers:



The isomer with the double bond in the α-position predominates in the mixture.

On the basis of modern concepts, the dimerisation of isobutene may be represented by the following scheme:



The t-butyl cation adds to the isobutene molecule and forms a C_8 carbonium cation. The abstraction of a proton from the latter leads to the formation of two isomeric olefins in proportions of 4 : 1. The transition state in the reaction involving the abstraction of a proton from the carbonium cation contains a partial double bond (Fig. 5) stabilised by the hyperconjugation of the alkyl substituents with the electrons of the incipient π bond [126]. However, owing to steric hindrance, the formation of the β-olefin in the transition state is energetically unfavourable, as shown by the shaded part of the van der Waals spheres in the models (Fig. 5). Therefore the energetically more favourable α-olefin, in which there is no steric hindrance, is formed preferentially.

Similar steric hindrance in the transition state determines the composition of iso-olefins in the dimerisation of more complex hydrocarbons also, for example isohexenes. Thus a study of the oligomerisation of two isohexenes—2-methylpent-1-ene and 2-methylpent-2-ene [3,127]—revealed the preferential formation of isododecenes the double bond of which is remote from the quaternary carbon atom, i.e. 4,6,6-trimethylnon-3-ene and 3-ethyl-2,4,4-trimethylhept-1-ene and not 4,6,6-trimethylnon-4-ene and 3-ethyl-2,4,4-trimethylhept-2-ene (Fig. 6).

The relative contents of isododecenes with different hydrocarbon frameworks in the reaction products are determined by the concentrations of the individual hexenes in the mixture and their capacity for interaction with the

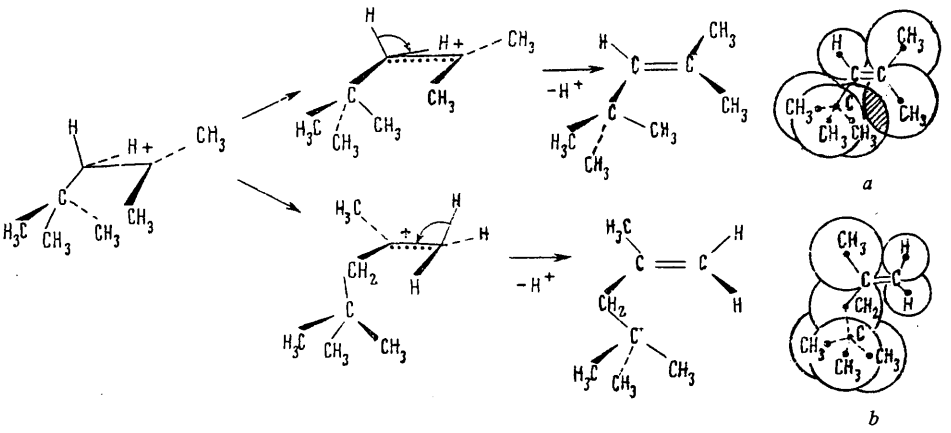


Figure 5. A three-dimensional scheme illustrating the formation of di-isobutenes and their models: *a*) 2,4,4-trimethylpent-2-ene; *b*)2,4,4-trimethylpent-1-ene.

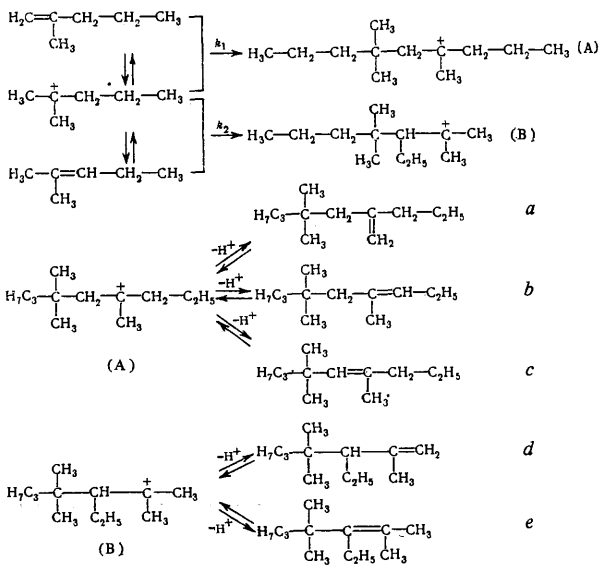


Figure 6. The mechanism of the dimerisation of isohexenes [127,128].

t-hexyl cation. It has been shown [127] that the rate of electrophilic addition of the t-hexyl cation to 2-methylpent-1-ene is five times faster than the rate of addition to 2-methylpent-2-ene, which can be explained by electronic and steric effects. The relative proportions of isododecenes with the same carbon framework but differing in the position of the double bond depend on their thermodynamic stabilities and the relative rates of abstraction of protons from different alkyl groups in the 4,6,6-trimethyl-4-nonyl cation (A) and 3-ethyl-2,4,4-trimethyl-2-heptyl cation (B).

The influence of structural factors on the rate and mode of reactions of carbonium ions has been the subject of controversy [129] and in the general case may be determined both by steric [130] and electronic effects [131,132]. A graphical representation of isododecene molecules (Fig. 7) with the bond lengths, valence angles, and actual radii of the substituents drawn to scale [59] shows that steric hindrance has a distinct effect on the structures of various isododecenes (on the basis of the overlapping of the spheres of groups not directly linked by valence bonds) (Fig. 7). Maximum steric hindrance, which occurs in the β-isododecene molecule and hence also in the transition state, results in the formation of α-isododecene as the main product of the abstraction of a proton from the 3-ethyl-2,4,4-trimethyl-2-heptyl cation (B). The insignificant formation of the β-olefin is caused by its lower thermodynamic stability owing to the marked steric hindrance arising as a result of the repulsion between the *cis*-methyl groups at the unsaturated and quaternary carbon atoms. The preferential formation of isododecene (*b*) compared with the olefin (*c*) on deprotonation of the 4,6,6-trimethyl-4-nonyl cation (A) can be explained similarly.

The literature and the present authors' experimental data [3] in Table 11 for the compositions of the oligomers should be regarded as confirmation of the hypothesis concerning the increasing role of steric effects in the formation of α-olefins on passing from the relatively low-molecular-weight C_6 hydrocarbons to the higher C_{12} hydrocarbons.

The introduction of a t-alkyl group in the β-position relative to the positively charged tertiary carbon atom increases sharply the yield of the α-olefin (Table 10). This is because, owing to the "cisoid repulsion strain" in the transition state, the formation of the β-olefin becomes energetically less favourable than that of the α-olefin, i.e. the energies of the σ,π conjugation of the alkyl substituents with the double bond of the olefin formed is no longer sufficient to overcome the steric hindrance.

The preferential formation of α-olefins, observed in the oligomerisation of olefins in the presence of acid catalysts, occurs [also] in the dehydration of alcohols and in the solvolysis of alkyl halides [139].

Thus steric factors are dominant in all elimination reactions leading to olefins if alkyl groups, at least one of which is tertiary, are present in the transition state in the *cis*-position relative to the double bond.

Molecular steric hindrance plays an important role in the polymerisation of olefins. Korshak [133] showed that the capacity for polymerisation of alkyl- and aryl-substituted olefins depends to a considerable degree on the screening of the double bond by substituents, i.e. on the steric hindrance caused by them. The influence of substituents is directly proportional to their bulk and their number.

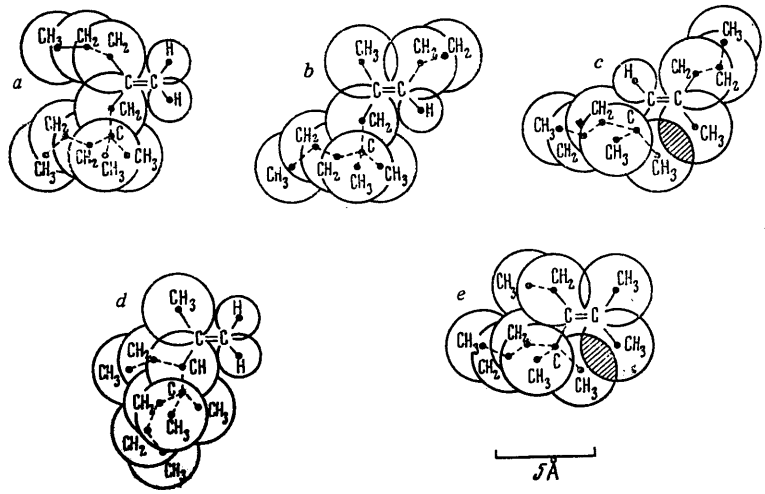
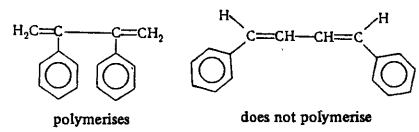


Figure 7. Molecular models of isododecenes: *a*) 4,4-dimethyl-2-propylhept-1-ene; *b*) 4,6,6-trimethylnon-3-ene; *c*) 4,6,6-trimethylnon-4-ene; *d*) 3-ethyl-2,4,4-trimethylhept-1-ene; *e*) 3-ethyl-2,4,4-trimethylhept-2-ene.

Table 11. The structures of carbonium cations and the concentrations of iso-olefins obtained from them.

α-Olefins	Wt. %	Carbonium cation	β-Olefin	Wt.%
$CH_2{=}C(CH_3){-}CH_2{-}CH_2{-}CH_3$	16	$CH_3{-}C^+(CH_3){-}CH_2{-}CH_2{-}CH_3$	$CH_3{-}C(CH_3){=}CH{-}CH_2{-}CH_3$	84
$CH_2{=}C(CH_3){-}CH_2{-}CH(CH_3){-}CH_3$	18	$CH_3{-}C^+(CH_3){-}CH_2{-}CH(CH_3){-}CH_3$	$CH_3{-}C(CH_3){=}CH{-}CH(CH_3){-}CH_3$	82
$CH_2{=}C(CH_3){-}CH_2{-}C(CH_3)_2{-}CH_3$	82	$CH_3{-}C^+(CH_3){-}CH_2{-}C(CH_3)_2{-}CH_3$	$CH_3{-}C(CH_3){=}CH{-}C(CH_3)_2{-}CH_3$	18
$CH_3{-}C(CH_3){=}CH{-}C(CH_3)_2{-}CH_3$	83	$CH_3{-}C^+(CH_3){-}CH(CH_3){-}C(CH_3)_2{-}CH_3$	$CH_3{-}C(CH_3){=}C(CH_3){-}C(CH_3)_2{-}CH_3$	17
$CH_2{=}C(CH_3){-}CH(CH_3){-}C(CH_3)(C_2H_5){-}C_3H_7$	90	$CH_3{-}C^+(CH_3){-}CH(CH_3){-}C(CH_3)(C_2H_5){-}C_3H_7$	$CH_3{-}C(CH_3){=}C(CH_3){-}C(CH_3)(C_2H_5){-}C_3H_7$	10

The concepts concerning steric hindrance developed by Korshak were confirmed also in the polymerisation of branched diene hydrocarbons. According to the mechanism established by Lebedev[134,137], butadiene polymerises with formation of carbon–carbon bonds in the 1- and 4-positions. Thus when the 1- and 4-carbon atoms are screened, polymerisation does not occur. On the other hand, if the 2- and 3-carbon atoms are screened, hindrance to polymerisation does not arise, which has been confirmed experimentally:



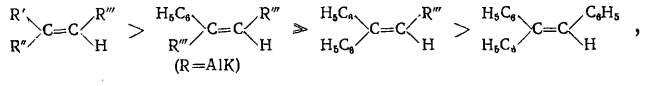
It is noteworthy that, apart from the steric factor, the conjugation effect apparently plays an important role in this case. In 1,4-diphenyl-substituted butadienes it is much more pronounced than in 2,3-diphenyl derivatives, since in the latter the phenyl groups are not included in the conjugated system of the diene.

Steric hindrance in the hydrocarbon molecule does not only retard but in some cases actually accelerates the radical polymerisation of olefins. Thus it has been established that the rate of polymerisation of α-vinylnaphthalene is higher[135] by a factor of 2.5 than the rate of polymerisation of styrene. This can be explained as follows: the vinyl group of α-vinylnaphthalene is displaced from the plane of the naphthalene ring system owing to the steric hindrance due to the "peri-hydrogen", which leads to a decrease of its conjugation with the naphthalene ring system. According to Bagdasar'yan's theory[136], a less conjugated olefin should give rise to a more reactive radical, which in fact is the reason for the higher rate of polymerisation. This leads to the following practical conclusion: in order to obtain the most reactive hydrocarbon monomers, it is necessary to synthesise hydrocarbons with a strained double bond.

4. Synthesis of Branched Alkanes

The screening of the double bonds by hydrocarbon substituents affects not only the polymerisation but also the

hydrogenation of branched olefins to alkanes. As early as the 1920's, Lebedev and coworkers[138] established that ethylene derivatives substituted to different extents are hydrogenated in different ways. The compounds R–CH=CH_2 are hydrogenated at the highest rate and CR_2=CR_2 at the lowest. This has been shown particularly convincingly by Kazanskii and coworkers[139,140], who established that in the presence of platinum black the rate of hydrogenation decreases in the following sequence:



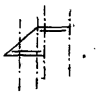
i.e. olefins with the double bond screened to a greater extent are hydrogenated at a lower rate. The rate of dehydrocyclisation of olefins is influenced more by their steric structure than by the position of the double bond[141]. The effect of the branching of the carbon framework of olefins on the yield of aromatic compounds has not in fact been investigated.

The first attempts to obtain by the Wurtz method fully methylated derivatives of higher ethane homologues were unsuccessful[142]. In general the synthesis of hexa-alkylethanes by the dimerisation of two tertiary alkyl groups is extremely difficult. The simplest analogue—hexamethylethane—was obtained from t-butyl chloride and sodium over a period of 10 days in a yield of 10%. In a number of studies[143,144], where t-alkyl halides were used in the Wurtz reaction, extremely low yields of branched alkanes were noted. Somewhat higher yields of these compounds are obtained in the organomagnesium synthesis. Therefore, for a successful synthesis of branched alkanes, it was necessary to seek ways whereby the effect of steric hindrance could be reduced to some extent[2].

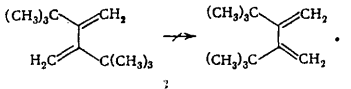
The steric hindrance in iso-olefin molecules promotes their decomposition on cracking. Thus Nazarov[142] established that the asymmetric di-t-butylethylene is readily cleaved at the site of addition of the tertiary group into lower olefins on distillation with traces of 2-bromonaphthalene-4-sulphonic acid. However, when one of the t-alkyl groups is replaced by a phenyl group, the resulting asymmetric t-alkylphenylethylenes become stable and are not cleaved even above 300°C.

5. Diels–Alder Synthesis

The Diels–Alder synthesis is a type of condensation in which a diene reacts with a dienophile in a coplanar cisoid conformation:



Naturally dienes in which such cisoid conformation of the double bonds does not arise under the experimental conditions owing to steric hindrance cannot enter into the Diels–Alder synthesis[145]. Thus Backer and Strating[146,147] showed that 2-t-butylbutadiene enters into the Diels–Alder synthesis normally, while 2,3-di-t-butylbutadiene does not react at all because it cannot assume the cisoid conformation necessary for the reaction, owing to the steric hindrance by the adjacent t-butyl groups[148]:



On the other hand, 1,3-di-t-butylbutadiene, in which the t-butyl groups are further apart and do not give rise to a steric effect, enters fairly readily[149,150] into Diels–Alder reactions. In general, if the formation of a coplanar cisoid conformation of the diene is interferred with by steric hindrance, the Diels–Alder synthesis as a rule takes place with difficulty and with low yields.

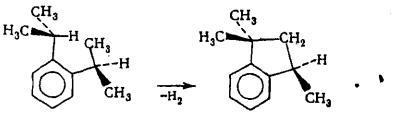
Table 12. The yield of indene in the cracking of cymenes (%).

Initial cymene	Indene
o-Cymene	3.6
m-Cymene	0
p-Cymene	0

6. The Formation of Indane–indene Structures

A characteristic feature of *o*-dialkyl derivatives of benzene is the formation of indene structures[151] (Table 12) on cracking.

The use of catalysts based on iron(III) oxide or aluminium oxide for the cracking of *o*-cymene increases the yield of indene. In the cracking of *o*-ethyltoluene, the yield of indene reaches 23%. Cyclisation of alkyl substituents as a result of their steric proximity with formation of indane derivatives was noted in the alkylation of isopropylbenzene with propene in the presence of aluminium chloride[152] according to the following mechanism:



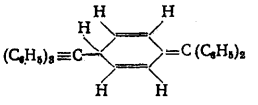
7. Dissociation of Hexa-arylethanes. The Structure of the Gomberg Hydrocarbon

In 1900 Gomberg[153] discovered the first free radical, which had an enormous influence on the further development of theory and practice in the field of organic free radicals. Gomberg obtained a free radical by treating chlorotriphenylmethane with metals (zinc, copper, and silver).

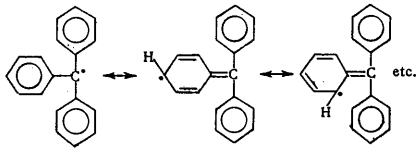
Numerous investigations led to the belief (Wieland, 1909) that chlorotriphenylmethane initially yields hexaphenylethane, which in benzene solutions consists of an equilibrium mixture of hexaphenylethane and triphenylmethyl radicals, the former predominating.

Markovnikov and Chichibabin[154] believed that the Gomberg hydrocarbon is not true hexaphenylethane but is merely identical with it [sic!].

Interesting studies on the dimer of the triphenylmethyl radical were published in 1968.[155–158] ^{1}H NMR and ultraviolet spectroscopy showed that the product of the association of the triphenylmethyl radicals obtained from chlorotriphenylmethane and silver is a hydrocarbon with the structure



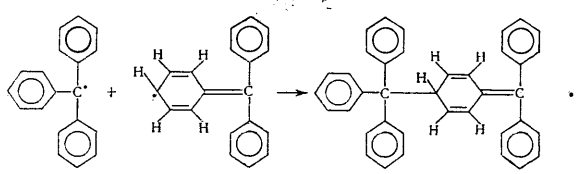
the formation of which can be understood bearing in mind that the triphenylmethyl radical can have several resonance forms:



The formation of hexaphenylethane on recombination of the classical form is difficult due to steric hindrance: under the influence of the *ortho*-hydrogen atoms, each phenyl ring is extended relative to the axis joining it to the central carbon atom which results in a propellor structure [159] in which the unpaired electron of the radical is screened by the *ortho*-hydrogen atoms.

Such radicals cannot approach one another to a distance sufficient for the formation of a C–C bond. It is interesting to note that at one time Gomberg also rejected the possibility of the dimerisation of triphenylmethyl radicals to hexaphenylethane. He wrote "...if the three valences of the carbon atom are occupied by three phenyl groups, it is difficult and probably actually impossible to introduce a complex species such as triphenylmethyl" [153]. Gomberg suggested that the association of triphenylmethyl radicals does not take place via the combination of the main (ethane) valences but in some other way.

On the basis of the above structure of the dimer of the triphenylmethyl radical, its formation actually takes place according to the following mechanism:



It should be noted that this structure of the triphenylmethyl radical dimer was proposed as early as 1905 by Jacobson [160], but, in view of the experimental difficulties involved in proving it, it remained neglected.

Thus the steric hindrance arising in the molecule play an important role here. As a result, hexaphenylmethane has still not been synthesised and [therefore] the field of triphenylmethane compounds should be thoroughly re-examined.

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Biochemical Importance of Lipid Peroxides†

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The review deals with the peroxides of unsaturated lipids; the process involving their formation is described and the catalytic action of lipoxidase and haematin compounds is illustrated. The modifying effects of various metals and their chelate complexes are discussed. The mechanism of their decomposition with formation of carbonyl, hydroxy-, epoxy-, and polymeric compounds is described.
The effect of these peroxides on haematin compounds protein thiols, enzymes, and vitamins of various types has been investigated. Various pathological changes induced by the introduction of polyunsaturated lipids and the toxicity of various oils and fats in food after heating in air have been examined. A study has been made of the damage caused by the formation of unsaturated lipid peroxides in various parts of the living cell, such as mitochondria, microsomes, lysosomes, and nuclei and of the toxicity of various types of lipid peroxides injected into living organisms, The appearance of lipid peroxides during photosynthesis and their involvement in the formation of cutin are described.
The bibliography includes 359 references.

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I. INTRODUCTION

An earlier paper by the present author and Viel dealt with the biochemical role of organic peroxides and their synthesis [1] and a paper by Latarjet [2] was concerned with their radiobiology. This review is devoted exclusively to lipid peroxides and covers publications up to 1970, the majority of which appeared in print after 1965. Thus, apart from the results of quite recent studies, the review considers certain questions relating to the effect of lipid peroxides on various types of enzymes and vitamins, their role in the breakdown of certain parts of the cell, and the inhibiting effect of vitamin E in the formation of lipid peroxides *in vivo*, i.e. problems which were only touched upon or not discussed at all in earlier publications.

It is noteworthy that the biochemistry of lipid peroxides constitutes a fairly well ordered and homogeneous field. The mechanisms of their formation and decomposition are known and many of the decomposition products have been identified. There is fairly accurate information concerning the effect of peroxides on haematin compounds, protein thiols, and various enzymes and vitamins, about the inhibiting effect of vitamin E and the changes occurring as a result of the formation of lipid peroxides *in vivo*, and also about the toxicity of various oxidised oils and fats in food. In view of all the above considerations, the author thought it necessary to write the present review dealing with lipid peroxides.

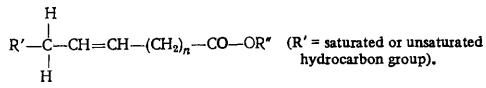
Lipid peroxides are formed as a result of the autoxidation of mono- and poly-unsaturated aliphatic acids which are present in the form of triglycerides in plant oils and animal fats. These acids can also exist in the form of phospholipids and sterol esters in various animal tissues. They are mainly oleic, linoleic, linolenic, and arachidonic acids containing respectively one, two, three, and four double bonds. Oleic acid is very common in both plants and animals and linoleic acid is particularly prevalent in plants. Linolenic acid is encountered much more rarely than the other acids but nevertheless its content is exceptionally high in linseed oil (50%) and in horse fat (16%). Arachidonic acid is present almost exclusively in animals, in which it is synthesised from linoleic acid introduced with food products. Apart from the acids enumerated above, tetra-, penta-, and hexa-enoic acids are present in animal tissues. Considerable amounts of a C_{20} acid with five double bonds and a C_{22} acid with six double bonds are present in cod liver oil‡.

At an elevated temperature and for higher degrees of unsaturation, the induction period in the autoxidation reaction becomes shorter and the rate of reaction increases. The mechanism of the autoxidation of unsaturated fatty acid derivatives has been described by Bolland [3] and Farmer [4,5] and has been discussed in detail in a number of other publications [6-9].

† The review was written originally in French specially for the journal "Uspekhi Khimii" and was translated into Russian by T. Va. Chernysheva. This is an English translation of the Russian version.

‡ Henceforth unsaturated acids will be designated by symbols such as 20 : 5 for the C_{20} acid with five double bonds, 22 : 6 for the C_{22} acids with six double bonds, etc. (Editor of Russian translation).

The first step is the abstraction of a hydrogen atom from the methylene group in the α-position relative to the double bond of the unsaturated compound:



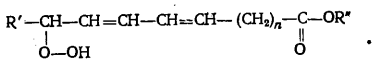
(R' = saturated or unsaturated hydrocarbon group).

The $R'-\dot{C}H-CH=CH-(CH_2)_n-CO-OR''$ radical formed in this way reacts with molecular oxygen, giving rise to the peroxy-radical $RO-O^{\cdot}$ [$R=R'-\dot{C}H-CH=CH-(CH_2)_n-CO-CR''$] which abstracts a hydrogen atom linked to the methylene carbon atom in the α-position of another lipid chain with formation of an α-methylene hydroperoxide and a radical $R^{\cdot}$:

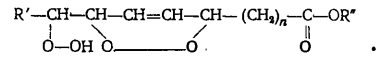
$$RO-O^{\cdot} + HR \rightarrow ROOH + R^{\cdot} .$$

The hydroperoxide in its turn decomposes into the radicals $RO^{\cdot}$ and $HO^{\cdot}$ which initiate new reaction chains.

The formation of the hydroperoxide is accompanied by the migration of the double bonds which are conjugated in polyunsaturated systems:



In the initial stages it may be accompanied by the formation of more complex derivatives of the hydroperoxide–peroxide type:



It is interesting to note that such structures were previously proposed for polyisoprene [10-18] and squalene [17] peroxides. Thus the term "lipid peroxides" refers to a mixture of several hydroperoxides (with a large number of conjugated double bonds), glycerides, phospholipids, and sterol esters of several unsaturated fatty acids incorporating in all probability peroxy-compounds of the hydroperoxide–peroxide type.

There are two main types of effective catalysts of the autoxidation of unsaturated lipids: lipidoxidase, which is highly specific for the determination of configurations, and haematin compounds—non-specific catalysts active in relation to many compounds undergoing autoxidation which are not unsaturated lipids. The speed of their action may be greatly altered in the presence of certain metals and their chelate complexes.

II. LIPOXIDASE

Lipoxidase is absent from animal tissues [19,20] but does occur in plants, particularly in Leguminosae (soya, peas, beans, wheat, groundnuts, clover, vetch, alfalfa, kidney beans, etc.). It has also been detected in radishes and in potatoes. According to quite recent studies, the wheat and pea lipoxidases [21] as well as the soya lipoxidase [22] contain several coenzymes. The presence of lipoxidase in microorganisms is doubtful. In fact *Pseudomonas fluorescens* and *Mycobacterium phlei* are the only bacteria which rapidly oxidase unsaturated fatty acids, but this oxidation is not catalysed by lipoxidase; it has been detected in the *Aspergillus* and *Rhizopus* moulds [23] but the actual oxidation catalyst was not determined exactly.

The preparation of pure lipoxidase from soya flour has been described in detail [24,25] and a new improved method [26] based on the extraction with water of defatted soya flour at pH 4.5 and room temperature was used recently. The enzyme is isolated after successive salting-out with aqueous ammonium sulphate solutions and subsequent electrophoresis.

Pure lipoxidase consists of colourless lamellar microcrystals with molecular weight ranging from 90 000 to 100 000. [25] Since it cannot be inhibited by fluorides, cyanides, azides, pyrophosphates, and diethyl dithiocarbamate prosthetic groups must be absent [26]. Similarly the absence of inhibition by mercury chlorobenzoate demonstrates the absence of SH groups, which is confirmed by chemical determinations [27].

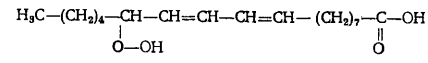
The catalytic activity of pure lipoxidase was studied in an aqueous 1.5×10^{-2} M solution of sodium linoleate in the temperature range from 0° to 37°C at different pH. [27] The results of this study showed that the maximum rate of oxidation occurs at pH 9.4, decreasing slightly at alkaline pH and diminishing appreciably at acid pH. Thus at pH 6.5 its activity is only one fifth of the activity at pH 9.4. The initial rate of oxidation at 37°C is higher than at 0°C but in the former case it decreases rapidly with time. Thus after 10 min the content of O_2 absorbed is identical for both temperatures, amounting to 0.15 mole mole^{-1}, but after 40 min it is only 0.4 mole mole^{-1} at 37°C and 0.6 mole mole^{-1} at 0°C.

The use of certain crude lipoxidases for the oxidation of derivatives of polyunsaturated acids at temperatures between 0° and 37°C has been described [20,28-36].

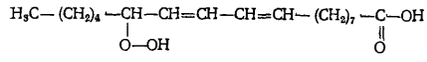
A comparative study [37] of the catalytic activities (at 20°C and pH 7) of soya, pea, groundnut, wheat, *Phaseolus mungo*, and *Phaseolus aurens* lipoxidases in the oxidation of linoleic and arachidonic acids by ammonium salts showed that none of the lipoxidases have prosthetic groups, while the *Phaseolus mungo* and *Phaseolus aurens* lipoxidases probably contain SH groups.

It follows from the above findings that lipoxidase is a highly specific catalyst in the oxidation of unsaturated lipids. Indeed it catalyses the oxidation of only penta-1,4-diene compounds $-CH=CH-CH_2-CH=CH-$ with the *cis*-configuration of the double bonds (as in natural fatty acids). It has been found that lipoxidase does not affect the rate of oxidation of mono- and di-unsaturated conjugated compounds or pentadiene compounds with the *cis-trans*- or *trans-trans*-configuration; it should be noted that the latter behave as inhibitors in oxidation reactions catalysed by *cis-cis*-pentadiene compounds. Moreover, the rate of oxidation of highly unsaturated compounds catalysed by lipoxidase is independent of the degree of their unsaturation. Thus the ammonium salts of linoleic, linolenic, and arachidonic acids are oxidised at the same rate [37]; the same can also be said concerning the esters of these acids [33,38]. Hence it follows that the catalytic action of lipoxidase diminishes with increasing degree of unsaturation of the substrate. The study [38] of the autoxidation and the oxidation catalysed by lipoxidase at 13°C of the ethyl esters of linoleic and linolenic acid showed that O_2 is absorbed (mole mole^{-1}) over a period ranging from 0.2–0.9 to 50 h in the autoxidation, while in the oxidation catalysed by lipoxidase it is absorbed over a period between 0.5 and 50 min for both esters.

A recent study [39] of the oxidation of soya, linoleic acid, and its methyl ester catalysed by lipoxidase demonstrated that O_2 attacks only the 13-C carbon atom with formation of a single conjugated hydroperoxide,



with the *cis-trans*-configuration (and not *cis-cis*), while in autoxidation and in oxidation catalysed by haematin compounds the attack is directed simultaneously to 13-C and 9-C, which leads to a mixture of two conjugated hydroperoxides:



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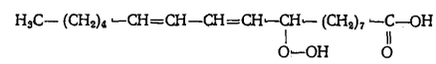
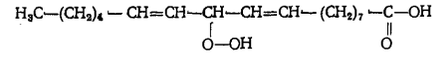


formed in equal amounts. Moreover there is a certain amount (of the order of 10%) of the non-conjugated hydroperoxide

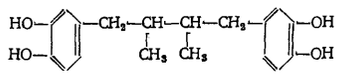


It is noteworthy that the hydroperoxides obtained on oxidation catalysed by lipoxidase are optically active in contrast to the hydroperoxides formed on autoxidation. These results demonstrate the stereospecificity of the catalytic action of lipoxidase.

The mechanism of the oxidation catalysed by lipoxidase has been discussed in detail [37]. Probably initially a transition enzyme–substrate complex is formed and in the second stage a free radical should be generated at the α-methylene carbon atom as a result of the capture of one electron by the lipoxidase protein. In the presence of molecular oxygens, this free radical should lead to the classical autoxidation reaction (the mechanism of which is quoted above).

The inhibiting effect of various phenolic compounds on the oxidation of a 7×10^{-3} M aqueous solution of sodium linoleate at pH 9 catalysed by soya bean lipoxidase has been studied [31] at temperatures ranging from $-6°$ to 30°C. The degree of inhibition (measured as a percentage decrease of the rate of absorption of O_2) increases with temperature. For nordihydroguiaretic acid at a concentration of 10^{-4} M, it amounts to 100% at 30°C and only 32% at 0°C. At 30°C and the same concentration, the relative degrees of inhibition for α-tocopherol, hydroquinone, propyl gallate, and nordihydroguiaretic acid are respectively 27, 38, 100, and 100% . Nordihydroguiaretic acid (NDGA) also proved to be very active in oxidation reactions catalysed by various crude lipoxidases, namely the oxidation of the ammonium salts of linoleic and arachidonic acids (at 20°C and pH 7). The use of propyl gallate, hydroquinone, and α-tocopherol led to different results depending on the nature of the lipoxidase [37].

NDGA, which will be frequently mentioned from now on, is 2,3-dimethyl-1,4-bis-(3,4-dihydroxyphenylbutane):



NDGA is widely used in the USA as an inhibitor of the oxidation of many food products at a concentration of the order of 10^{-4} M.

Apart from the studies described above, the catalytic action of lipoxidase is dealt with in four extensive publications which also contain important historical data [8,40–42].

III. HAEMATIN COMPOUNDS

Haemoglobin, myoglobin, haemin, and cytochrome c are the most important biological catalysts of the autoxidation of unsaturated animal lipids. They are involved in many physiological *in vivo* reactions and also in the oxidation of food products during storage (rancidity).

In contrast to lipoxidase (which catalyses the oxidation of pentadiene systems with the *cis-cis*-configuration only), haematin compounds catalyse the oxidation not only of all the unsaturated lipids, but also of many aliphatic-aromatic and alicyclic hydrocarbons [43]. However, their catalytic activity is shown only in a colloidal medium or in an emulsion but not in a homogeneous system (lipoxidase is active in both heterogeneous and homogeneous media). Thus in the oxidation of linoleic acid catalysed by haemin, the absorption of oxygen ceases on passing from an aqueous emulsion to a homogeneous solution (as a result of the addition of acetic acid, dioxan, or pyridine) and restarts when the heterogeneous medium is restored by the addition of water [44].

The rate of oxidation increases with the degree of unsaturation of the substrate. Thus in the oxidation of the methyl esters of oleic, linoleic, and linolenic acids (at a concentration of 2×10^{-2} M) in an emulsion at 0°C catalysed by haemin (at a concentration of 2×10^{-5} M), the rates of absorption of oxygen are respectively 1.3 and 6. [45]

The rate of oxidation is proportional to the square root of the concentration of the haematin compound. This was confirmed for the oxidation of an aqueous emulsion of 0.1 M ammonium linoleate catalysed by haemoglobin [45], cytochrome c [45], and myoglobin [46] with the catalyst concentration varying from 1×10^{-6} to 7×10^{-6} M.

It is very significant that at high concentrations (ranging from values of the order of 10^{-3} M to 10^{-2} M for 1 M substrate) haematin compounds inhibit the oxidation of unsaturated lipids. A study [46] of the oxidation of an aqueous emulsion of 17×10^{-3} M linoleic acid showed that haemoglobin, which is an active catalyst at a concentration of 4×10^{-6} M, becomes an inhibitor at a concentration of 4×10^{-5} M: haemin and cytochrome c also become inhibitors at concentrations in excess of 10^{-4} M. Likewise it has been found [47] that cytochrome c has an inhibiting effect at high concentrations in the oxidation of linoleic acid.

In the oxidation process catalysed by haematin compounds, the latter decompose with the liberation of iron. This has been observed in the oxidation of aqueous 0.2 M emulsions (pH 6.8) of linoleic and linolenic acid catalysed by haemoglobin and haematin [48].

The finding that the catalytic action of haematin compounds is not inhibited by carbon monoxide and changes only slightly on formation of haemochromes with nitrogenous bases despite an appreciable change in the oxidation-reduction potential suggests that the valence of iron (in the haematin compound) is not altered during the oxidation.

The usual autoxidation inhibitors such as phenols and amines proved to be active in the oxidation of various unsaturated lipids catalysed by haematin derivatives.

α-Naphthol, catechol, p-aminophenol, and dimethylalanine are effective inhibitors in the oxidation of aqueous emulsions of oleic acid and linseed oil at 38°C catalysed by haemin [49]. The action of various enolic inhibitors, α-tocopherol, NDGA, and 2,6-di-t-butyl-4-methylanisole was examined in a study [50] of the oxidation of colloidal sodium linoleate (0.2 M) at 37°C catalysed by haemoglobin and cytochrome c. The concentration of the haematin compound was 2×10^{-5} M. It was found that α-tocopherol

is a weaker inhibitor than NDGA. Indeed in the oxidation catalysed by haemoglobin a 30 m induction period is attained at an NDGA concentration as low as 2×10^{-5} M, whereas the concentration of α-tocopherol required to produce the same effect must be higher by a factor of 10. Similar results were obtained also with cytochrome c. The action of various enolic inhibitors and synergistic agents (such as aminoacids and ascorbic acid) on the oxidation of methyl oleate, methyl linoleate, pig fat, cod liver oil, and linseed oil at 37°C, catalysed by haemin, haemoglobin, and cytochrome c, has been examined in detail [50,51].

As in the previous case, the inhibiting effect of α-tocopherol is weaker than that of NDGA, 2,6-di-t-butyl-4-methylphenol, and 2,6-di-t-butyl-4-methylanisole.

In the oxidation of pig fat at 37°C, catalysed by haemoglobin, ascorbic acid proved to be an excellent synergistic agent over a narrow range of concentrations: 10^{-4} to 10^{-3} mole kg^{-1}. The optimum concentrations of the inhibitor and the synergistic agent are as follows in moles per kilogramme:

NDGA	10^{-3}	NDGA	10^{-4}
Ascorbic acid	10^{-3}	2,6-Di-t-butyl-4-methylphenol	10^{-4}
		Ascorbic acid	10^{-4} .

These compositions increase the induction period by factors of 85 and 300 respectively. The oxidation catalysed by haematin derivatives may be inhibited also by other compounds and not only the usual inhibitors of chain autoxidation. Thus in the autoxidation of a 0.1 M emulsion of oleic acid at 37°C, leuco-Methylene Blue (at a concentration of 10^{-3} M) increases the rate of absorption of oxygen by a factor of 20, while in the oxidation catalysed by haemin (at a concentration of 10^{-5} M) the rate decreases by 20%. Probably there is a coordination between the N and O atoms with formation of a complex more resistant to oxidation.

Haematin compounds catalyse the decomposition of hydroperoxides in an inert atmosphere. The decomposition [43] of a 0.1 M emulsion of the peroxide of sodium linoleate at 40°C, catalysed by haemin (at a concentration of 2×10^{-4} M), showed that the peroxide content decreases faster in the presence of haemin than in its absence, particularly at the beginning of the reaction. Thus after 10 h the corresponding degrees of decomposition are 70 and 40% and after 60 h 96 and 84%. The initial content of hydroperoxide was 0.08 mole per mole of linoleate.

The catalytic action of various haematin compounds (catalase, haemoglobin, haematin, and cytochrome c) in the decomposition of sodium linoleate hydroperoxide has been discussed [52]. The formation of RO· radicals in the decomposition process is explained by the high yield of the corresponding carbanions in the presence of compounds (hydrogen donors) such as polyphenols [53].

Thus the corresponding alcohol is formed in 94% yield from a mixture of methyl linoleate hydroperoxide (1 M), hydroquinone (2 M), and haemoglobin (5×10^{-3} M) when it is allowed to stand in alcoholic solution at room temperature [53]. Similar results were obtained for cumenyl hydroperoxide [53] but with a lower yield (80%) of cumenyl alcohol, owing to some decomposition of the $C_6H_5(CH_3)_2CO$· radicals.

The fact that the rate of the autoxidation reaction (catalysed by haematin compounds) is proportional to the content of hydroperoxide (formed or added) and that in an inert atmosphere haematin compounds decompose the hydroperoxide ROOH with formation of RO· radicals suggests that the hydroperoxide should be formed initially without the involvement of haematin compounds. Then, evidently, the hydroperoxide may decompose with formation of RO· radicals which probably initiate the oxidation reaction, the chain mechanism of which may be inferred from the action of the usual effective autoxidation inhibitors. Nevertheless the mechanism of the decomposition of the hydroperoxide formed differs somewhat from that of the reaction catalysed by variable-valence metals:

$$ROOH + M_n \rightarrow RO\cdot + {}^{-}OH + M_{n+1} .$$

The constant valence of iron in the oxidation process suggests that an electron is abstracted from the haematin protein and not from the metal, as in the preceding case.

Apart from the classical chain termination reaction $ROO\cdot + {}^{\cdot}OOR \rightarrow ROOR + O_2$, the peroxy-radicals probably also interact with haematin compounds [45], which leads to shorter chains and a higher content of carbonyl compounds than in simple autoxidation.

The mechanism of the oxidation catalysed by haematin compounds has been discussed in detail in several earlier publications [8,43,44,52-55].

IV. VARIOUS METALS AND THEIR CHELATE COMPLEXES

The oxidation of 0.017 M aqueous emulsions of linoleic and linolenic acids at 37°C in the pH range 4.5–7.5 catalysed by various metals and their chelate complexes has been the object of serious study [56]. Among the many metals tested, very few are active. Thus Co^{2+} and Mn^{2+} are very active, while Cu^{2+}, Fe^{2+}, and Fe^{3+} are much less active; at a concentration of 10^{-3} M (one mole for ten moles of linoleate) Fe^{2+}, Fe^{3+}, Cu^{2+}, V^{2+}, Mn^{2+}, and Co^{2+} increase the absorption of O_2 by factors of 2, 3, 9, 14, 136, and 170 respectively. The catalytic activity of Fe^{2+} ions has been investigated in the oxidation of colloidal linoleic acid (0.02 M) at 30°C and pH 7 as a function of their concentration [57].

We may note that the catalytic activity of Fe^{3+} increases markedly in the presence of a reducing agent such as ascorbic acid or cysteine and depends greatly on the pH, in contrast to haematin catalysis which is very little sensitive to changes in the pH. Thus in the presence of ascorbic acid the maximum rate of oxidation (which exceeds that of autoxidation by a factor of 54) occurs at pH 5 and Fe^{3+} and ascorbic acid concentrations of 10^{-2} and 10^{-3} M respectively.

In contrast to the behaviour in the presence of Fe^{3+}, the catalytic activity of haematin compounds is weakened in the initial stage as a result of the addition of ascorbic acid, the reaction becoming autocatalytic subsequently owing to the formation of free iron by the decomposition of haematin compounds.

Thus in the oxidation of linoleic acid catalysed by haemoglobin (5×10^{-6} M) or cytochrome c (10^{-5} M) the addition of ascorbic acid (10^{-3} M) gives rise to a 30 min induction period, while in its absence absorption of O_2 begins immediately. Moreover, ascorbic acid does not affect the catalytic action of Cu^{2+} but greatly inhibits that of Co^{2+}.

At a concentration in excess of 0.1 M, phosphates inhibit the catalytic action of Co^{2+} and the Fe^{3+}–ascorbic acid system but their optimum concentrations have not yet been determined.

The rate of oxidation of linoleic acid does not change in the presence of 8-hydroxyquinoline and $\alpha\alpha'$-dipyridyl, while o-phenanthroline (2×10^{-3} M) increases it slightly;

however, the rate does not change at all in the simultaneous presence of the metals and complex-forming agents mentioned above. All the metals were used at a concentration of 10^{-3} M (except for 5×10^{-4} M Co^{2+}) with the ratio

$$K = \frac{\text{moles of complex-forming agent}}{\text{gram-atoms of metal}}$$

varying from zero to 5.

When *o*-phenanthroline is employed, with K varying from zero to 2, the rate of absorption of O_2 increases by a factor of 60 for Fe^{2+} and decreases by a factor of 170 for Co^{2+}, the increase for Cu^{2+} being only by a factor of 2.

8-Hydroxyquinoline has a less pronounced modifying effect than *o*-phenanthroline. Indeed, when K is varied from 0 to 2, the rate of absorption of O_2 increases only by a factor of 16 for Fe^{2+} and decreases by factors of 2 and 4 for Cu^{2+} and Co^{2+} respectively.

Blood serum albumin and egg albumin (at a weight concentration of 1%) increase respectively by factors of 1.9 and 3.5 the rate of O_2 uptake in the oxidation of linoleic acid catalysed by the Fe^{3+} (10^{-3} M)–ascorbic acid (10^{-3} M) system.

The catalytic activity of Cu^{2+} also increases in the presence of certain proteins. In one of the studies[58] on the oxidation of 0.1 M colloidal solution of ammonium linoleate (0°C and pH 7) catalysed by Cu^{2+} ions (10^{-3} M) it was shown that egg albumin (10^{-4} M) increases the rate of absorption of O_2 by a factor of 5. This must mean that haemocyanin catalyses the oxidation of unsaturated fatty acids.

On the other hand, horse serum, even at a dilution by a factor of 50, greatly reduces the activity of the Fe^{3+}–ascorbic acid system and completely inhibits it at a dilution of 20. It shows a similar but less marked effect on the catalytic activity of Co^{2+}, while the catalytic activity of haematin compounds changes little in its presence. Apart from weakening the action of certain catalytic systems in the oxidation of linoleic acid, it has a very pronounced inhibiting effect on the formation of lipid peroxides (pH 7) in rat brain homogenate[59]. The inhibiting effect of this serum must be a consequence of the formation of a Fe^{3+} complex of serum siderophilin.

Among numerous aminoacids, only histidine and its derivative histidylhistidine proved very effective inhibitors of the oxidation of linoleic acid catalysed by Co^{3+} (2×10^{-4} M). The inhibiting action depends greatly on the pH, becoming completely insignificant in an acidic medium. For example at pH 7 histidine (4 moles per gramme atom of Co^{2+}) decreases by a factor of 50 the rate of absorption of O_2, while at pH 5 the rate of absorption of oxygen decreases only by 1%.

At pH 7 the catalytic action of Co^{2+} is also weakened by phenylalanine but to a much less extent than by histidine.

Cysteine acts in the presence of Fe^{3+} like ascorbic acid, the maximum acceleration occurring at pH 4 and becoming zero at pH 8. At pH 5 the Fe^{3+} (10^{-3} M)–cysteine (3.3×10^{-3} M) system increases the rate of oxidation of linoleic acid by a factor of 10.

V. NATURE OF THE COMPOUNDS FORMED ON DECOMPOSITION OF LIPID PEROXIDES

The unsaturated lipid with the general formula $R-CH_2-CH=CH-R'$ (R' = saturated or unsaturated groups) initially gives rise to the hydroperoxide $R-\underset{\underset{O-OH}{|}}{CH}-CH=CH-R'$, which undergoes homolytic decomposition into the radicals $R\dot{C}H-\underset{\underset{O\cdot}{|}}{CH}=CH-R'$ and ·OH.

The ·OH radicals can interact with the initial lipid, attacking double bonds with formation of the dihydroxy-compound $R-CH_2-CHOH-CHOH-R'$, which may lead to the corresponding hydroxyketone and diketone as a result of dehydration.

The ·OH radicals can also attack the α-methylene carbon atom with formation of H_2O and the $R-\dot{C}H-CH=CH-R'$ radical (which is involved in the chain oxidation reaction).

The $R-\underset{\underset{O\cdot}{|}}{CH}-CH=CH-R'$ radicals can participate in the chain reaction, attacking the initial lipid with formation of the monohydroxy-compound $R-CHOH-CH=CH-R'$ and regeneration of the $R-\dot{C}H-CH=CH-R'$ radical. They can also decompose in two ways: (1) with dissociation of the double bond in the α-position and formation of the aldehyde RCHO and the radicals ·CH=CH–R', which combine with the ·OH radicals to give the unstable enol HO–CH=CH–R', isomerising into the aldehyde OCH–CH_2–R'; such dissociation leads to the formation of two unsaturated aldehydes (with a saturated group R'); (2) with dissociation of the double bond in the β-position and formation of the radicals R· and the aldehyde O=CH–CH=CH–R'.

The radicals R· combine with ·OH radicals to give the alcohol ROH. The greater content of carbonyl compounds compared with alcohols, particularly at low temperatures is probably due to the greater ease of dissociation in the α-position compared with the β-position.

The aldehydes thus formed undergo in turn degradative oxidation via two parallel reactions. Thus the C_n aldehyde with the general formula RCH_2CHO may be oxidised to the peroxide $R-CH_2-\underset{\underset{O}{\|}}{C}-O-OH$, which then decomposes into the C_{n-1} alcohol RCH_2OH and carbon dioxide[60–62] (or reacts with the initial aldehyde to form the acid RCH_2COOH).

The aldehyde can be also oxidised to an aldehyde hydroperoxide:

$$R-\underset{\underset{O-OH}{|}}{CH}-CHO .$$

The peroxide decomposes homolytically with subsequent elimination of hydrogen atoms from the α- or β-position relative to the carbonyl group[63]. Dissociation in the α-position leads to a C_{n-1} aldehyde and formic acid:

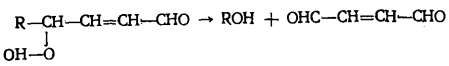
$$R-\overset{\overset{H}{|}}{\underset{\underset{O-OH}{|}}{C}}-CHO \rightarrow RCHO + HCOOH .$$

Dissociation in the β-position yields a C_{n-2} alcohol ROH and glyoxal.

With a C_n α-unsaturated aldehyde $R-CH_2CH=CH-CHO$, a hydroperoxide should be formed in the α-position relative to the double bond (i.e. in the γ-position relative to the carbonyl group), which can probably decompose owing to the dissociation in the α-position into a C_{n-3} aldehyde R–CHO and malonic dialdehyde:

$$R-\underset{\underset{O-OH}{|}}{CH}-CH=CH-CHO \rightarrow R-CHO + HO-CH=CH-CHO \rightarrow OCH-CH_2-CHO$$

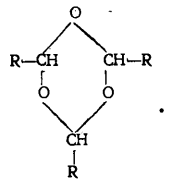
or into a C_{n-4} alcohol ROH and fumaric dialdehyde as a result of dissociation in the β-position:



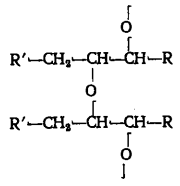
The aldehyde α-hydroperoxide $R-\underset{\underset{O-OH}{|}}{CH}-CHO$ can also decompose into H_2O and an α-ketoaldehyde RCOCHO.

The foregoing considerations account for the formation of a large number of carbonyl and hydroxy-compounds with short chains as well as formic acid in the oxidation of many unsaturated lipids. Malonic dialdehyde merits particular mention; its reaction with thiobarburic acid results in a red colour. This reaction has been frequently used for a quantitative determination of peroxides in biological media and has been discussed[64]. Mention should also be made of the formation of formates[65] which are probably produced as a result of the esterification of alcohols by formic acid.

In the presence of formic acid, aldehydes can lead to the formation of simple or mixed trioxans:

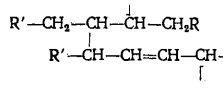


Polymers of two types may be produced. In the first case two carbon atoms are linked via an oxygen atom; the polymers correspond to the general formula



and are formed as a result of the dehydration of dihydroxy-compounds. They are produced in the presence of oxygen at a moderate temperature.

In the second case a bond is formed between carbon atoms:



In this case polymers are produced as a result of the action of dihydroxy-compounds on the olefinic compound with elimination of water. They are formed in the thermal decomposition of the hydroperoxide in an inert atmosphere. It should be noted that the polymers may contain in their chain functional groups (HO, CO) produced as a result of attack on the α-methylene carbon atom or the double bond.

At a high temperature (>250°C) and even in the absence of O_2, polymers with cyclohexene rings may be formed owing to the Diels–Alder addition of a conjugated polyolefinic compound to the initial non-conjugated polyolefinic compound. The mechanism of the formation of various types of polymers and also their determination have been the subject of a publication with 60 literature references[66].

The autoxidation of unsaturated lipids is discussed in a long paper with 192 references[67]. Another publication deals with various peroxides of unsaturated fatty acid esters[68].

Among monounsaturated lipids, the oleic acid derivatives have been most thoroughly investigated. The hydroperoxide of methyl oleate has been isolated with a purity of 85% and its properties have been described[68-70]. It is a colourless and odourless liquid readily soluble in organic solvents, decomposing slowly at room temperature, rapidly at 120°C, and in 15 min at 150°C. The autoxidation of methyl oleate has been studied[71-81] and it has been shown[78] that the *cis*-form (oleate) is converted into the *trans*-form (elaidate) during the autoxidation process.

It is clear from the above studies that the principal compounds formed in the autoxidation of methyl oleate are water, mono- and di-hydroxymethyl sterates, saturated C_7-C_9 aldehydes, C_{10} and C_{11} unsaturated aldehydes, and the hemialdehydes of suberic and azelaic acids. We may mention that α-undecenal is the main compound formed by the direct decomposition of the hydroperoxide of methyl oleate at 150°C. The formation of the above carbonyl compound can be accounted for on the basis of the considerations described in the preceding section, since the OOH group can occupy positions ranging from the 7th to the 12th as a result of double bond migration. Apart from the products mentioned above, numerous hydroxy- and carbonyl compounds are produced in consequence of the subsequent autoxidation of the aldehydes produced in the initial stage of the hydroperoxide decomposition.

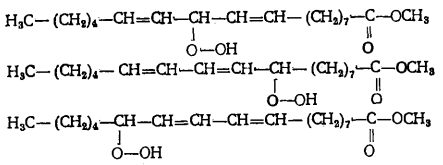
The polymer chains formed in the autoxidation of methyl oleate at 65°C [in the presence of cobalt(II) oleate] contain ester linkages[79]. The polymers obtained in the decomposition of hydrogen peroxide at 210°C[82] consist of carbon chains.

The autoxidation of oleic acid esters which are higher homologues of methyl, ethyl, and propyl oleates has also been investigated[83], but the corresponding hydroperoxides were not isolated. It is noteworthy that the maximum concentration of hydroperoxide at a given temperature decreases with increasing molecular weight of the ester. The autoxidation of oleic acid has been examined in a number of investigations[73-81,84-86]. In the latest study[86] carried out in thin layers at 60–80°C special attention was paid to the isolation and characterisation of the volatile products formed in the autoxidation.

The autoxidation of higher homologues of oleic acid and their methyl esters has also been the subject of several investigations. One fo them concerns the autoxidation of erucic acid and its methyl and propyl esters[87] and another deals with the autoxidation of brassidic acid[88]. The investigations have shown that, as with oleic and elaidic acids, the *cis*-isomer (erucic acid) undergoes autoxidation faster than the *trans*-isomer (brassidic acid). Dihydroxy-behenic acid was detected among the autoxidation products. A further investigation dealt with the autoxidation at 40°C of the methyl esters of oleic, elaidic, erucic, and α-undecenoic acids[89]; it showed that the rate of autoxidation decreases in the sequence indicated above. In a recent study[90] on the autoxidation of methyl undecenoate at 50°C, a hydroperoxide (in two stereoisomeric forms) and the corresponding epoxy-compounds were characterised.

The autoxidation of methyl linoleate has been the subject of several investigations[72,91-95]. The last study was concerned with the action of various inhibitors on the autoxidation of the *cis-cis*- and *trans-trans*-isomers. In the dark at 40–60°C there is an induction period of 15 min, while at 80°C the autoxidation begins almost at once.

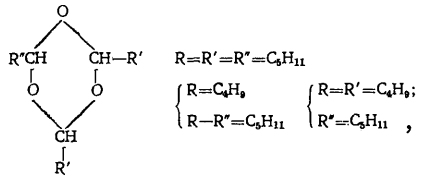
The corresponding hydroperoxide has been isolated [91-93] with purities of 84, 92, and 92% respectively. It consists of a mixture of three isomers with the following formulae:



The isomers with a conjugated diene group having the *cis-trans*-configuration constitute 90% of the total amount of hydroperoxide. Nevertheless, according to a recent investigation [94] of the autoxidation of methyl and ethyl linoleates at 60°C in chloroform solution, conjugated diene groups appear only when the hydroperoxide content is of the order of 100–200 millimoles per kilogramme of ester.

The primary decomposition products of the peroxides of methyl linoleate consist of saturated aldehydes (hexanal, pentanal), octenal, deca-2,4-dienal, and the hemialdehydes of suberic and azelaic acids.

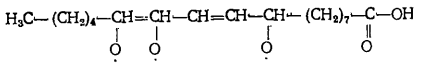
The above aldehydes were isolated also in the autoxidation at 37°C of an aqueous 2×10^{-2} M solution of ammonium linoleate [96]. The aldehydes obtained in the first stage of the decomposition of the above hydroperoxides may condense into trioxans, may be oxidised to the corresponding acids, or can undergo further oxidative degradation with formation of various carbonyl and hydroxy-compounds with lower molecular weights. The formation of 2,4,6-trialkyl-1,3,5-trixoans, simple or mixed, corresponding to the general formulae



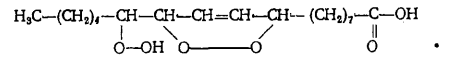
was observed in the oxidation of methyl linoleate in a thin layer at room temperature. The trioxans were obtained as a result of the polymerisation and copolymerisation of pentanal and hexanal. Among the decomposition products of the initial aldehydes, special mention should be made of the dicarbonyl compounds consisting of glyoxals, a C_6 ketoaldehyde, fumaric dialdehyde, and hex-3-ene-1,6-dial, which were isolated in the oxidation of methyl linoleate at 45°C. [97-99].

The polymers formed as a result of the autoxidation of methyl linoleate at 4°C [82] consist of a mixture of dimers and trimers with linkages via oxygen atoms. Each chain contains C=O and O–H groups and a certain number of double bonds. The polymers obtained [100] as a result of the autoxidation of methyl linoleate at 33°C and subsequent decomposition at 100°C in an inert atmosphere also consist of a mixture of dimers and trimers but here the linkages are between carbon atoms.

The autoxidation of linoleic acid was studied recently by several investigators [101-103]. The first two studies were concerned with the identification and isolation of numerous volatile compounds and the third with the kinetic relations for autoxidation at low O_2 pressures in the presence of various inhibitors. In autoxidation in thin layers at 20° and 40°C, [101,102] saturated aldehydes ranging from C_2 to C_7, alcohols ranging from C_1 ot C_5, and esters [65] (mainly formate esters with pentyl formate predominating) were isolated. Apart from the above compounds obtained in the decomposition of the monohydroperoxide, trihydroxy-, triketo-, and hydroxyketo-compounds may also be formed as a result of the disproportionation of the radicals:



The latter are products of the homolytic cleavage of the hydroperoxide–peroxide



The autoxidation of ethyl linoleate has also been the subject of several investigations [3,104-106], in which a hydroperoxide was isolated [3]. The structure of the polymers formed in the autoxidation is similar to that of the polymers produced from methyl linoleate with linkages via oxygen atoms [106].

Two studies [107,108] have been made on the autoxidation of methyl linolenate at 37°C with isolation of the corresponding hydroperoxide having a purity of the order of 80%.

The hydroperoxide is monomeric and has three double bonds, two of which are incorporated in the conjugated group; the *cis-trans*-transfiguration predominates (the amount of the *trans-trans*-configuration is insignificant). Since the OOH group can occupy the 16-, 13-, 12-, and 9-positions, the primary decomposition products of the hydroperoxide consist of propanal, pentanal, and hepta- and octa-2,4-dienals.

The dicarbonyl compounds produced as the result of a subsequent autoxidation of the above aldehydes consist of malonic dialdehyde [109] and hex-3-ene-1,6-dial [110]. The formation of carbonyl compounds in the autoxidation of methyl linolenate (and also oleate and linoleate) is discussed in two large publications [111,112]. The structure of the polymers formed during autoxidation at 30°C is similar to that of the polymers from the linoleate hydroperoxide (linkages via oxygen atoms). Saturated C_2–C_6 aldehydes, 2,4-diethyl-6-propyltrioxan, 2,4-diethyl-6-pentyltrioxan, pentanal, acids ranging from C_1 to C_6, and their various esters were isolated quite recently in a study of the autoxidation of linolenic acid at 20° and 40°C. [113] Hydroperoxides derived from methyl linoleate, methyl linolenate, ethyl arachidonate, methyl eicosapentenoate, and ethyl esters of menhaden§ fat were obtained in 95% purity in a recent investigation [114].

The autoxidation of esters was initially carried out at 4°C over a period of 80 days and then at room temperature for 148 h until the content of hydroperoxides reached 28 moles for 100 moles of ester. The peroxides were isolated from the autoxidation product thus obtained with the aid of thin-layer chromatography.

In two important investigations [115,116] of saturated lipids, a study was made of the autoxidation at 60°, 150°, and 200°C of very pure methyl palmitate. It was found that at 60°C hydroperoxide was not formed over a period of 56 days, while at 150°C its content reached 300 millimoles per kilogramme after 3 h, and at 200°C only hydroxycarbonyl compounds and carboxylic acids formed as a result of the decomposition of the peroxide could be detected. It follows from these observations that the attack of the saturated esters by molecular oxygen at 150°C leads primarily to the formation of a double bond as a result of dehydrogenation. Although probably all the carbon atoms are attacked, the hydroperoxide is formed preferentially in the centre of the molecule. The above

§ Menhaden is a fish of the herring family (Clupeidae) (Editor of Russian translation).

two papers criticise all previous investigations and quote numerous references to studies on the autoxidation of saturated lipids.

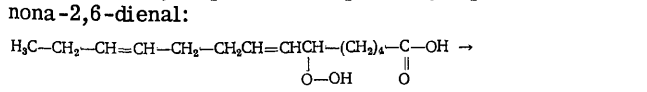
Natural fats and oils consist of triglycerides with various contents of saturated and unsaturated acids depending on their nature. Thus carbonyl compounds, formed in oxidative degradation, are of the type which would probably be formed simultaneously from oleic and linoleic acids and in some cases also from linolenic and arachidonic acids.

A lipid containing a relatively small amount of linoleic acid and in particular linolenic acid can give rise to considerable amounts of carbonyl compounds, derived from these polyunsaturated acids, in consequence of a much less extensive autoxidation of oleic acid.

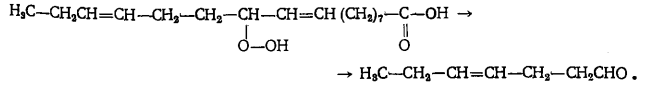
There are publications [111,112] with detailed data on saturated aldehydes, unsaturated aldehydes, and dienals formed from mutton, beef, and pork fats, cocoa oil, and also from ground nut, soya bean, and linseed oils (as well as from methyl oleate, trioleate, and linolenate and ethyl linoleate). These lipids were subjected to autoxidation at room temperature and under ultraviolet irradiation until the formation of different amounts of hydroperoxide; they were then decomposed at room temperature or at 165°C.

Hexanal, oct-2-enal, and deca-2,4-dienal were obtained by the decomposition at 100°C of autoxidised cotton seed oil (with a peroxide content of 125 millimoles per kilogramme) [117]. Numerous saturated aldehydes, unsaturated aldehydes, and dienals, as well as oct-1-en-3-ol and oct-1-en-3-one were obtained from sunflower seed oil autoxidised at 37°C. [118] Saturated aldehydes ranging from C_2 to C_9, unsaturated aldehydes from C_5 to C_9, 2,4-dienals (from C_6 to C_{10} except C_9) were isolated from the autoxidation products of soya bean oil [119]; the configuration of hexa- and octa-2,4-dienals has been discussed [120]. Hexanal, oct-2-enal, and deca-2,4-dienal have been isolated [121]; the last probably consists of a mixture of two stereoisomers—2-*trans*-4-*cis*-(28%) and 2-*trans*-4-*trans*-(72%). Numerous aldehydes, ketones, and hydroxy-compounds have been identified [122,123] as well as *cis*-hex-3-en-1-al. [124] The formation of 2,4-dienals from autoxidised pork fat has been studied [125]. The isolation of octadecadienoic acids (the 11,15-isomer and a small amount of the 10,15-isomer) from beef and mutton fat is noteworthy [126]. The autoxidation was carried out at 37°C until the attainment of a peroxide content of 2 millimoles kg^{-1} with subsequent decomposition at 140°C in an inert atmosphere.

The first hydroperoxide is probably a precursor of nona-2,6-dienal:



and the second is a precursor of hept-4-enal:



Probably the above unsaturated aldehydes are partly responsible for the odour of green cucumbers which appears in beef fat during its storage.

An attempt has been made to relate certain chemical characteristics to the organoleptic parameters of alimentary fats [127]. It was found that a very small peroxide content may be very important for the estimation of the freshness of these fats. Thus the appearance of an unpleasant taste was noted for a peroxide content of 0.10 millimole kg^{-1}.

VI. EFFECT OF LIPID PEROXIDES ON VARIOUS SUBSTRATES

The formation of epoxy-compounds and α-epoxy alcohols as a result of the decomposition of α-olefinic hydroperoxides was observed with cyclohexene [128] and many olefins [122,129]. The autoxidation of unsaturated fatty acids at the double bonds has been the subject of an intensive investigation [130–132] which established the following facts.

In the presence of haemin (weight concentration 2×10^{-5}) in a stoichiometric mixture of oleic acid and the peroxide of ethyl oleate (at room temperature and at a reduced pressure), the degree of unsaturation of the acid gradually diminishes, with an accompanying decrease of the overall content of active oxygen.

In addition the ratio

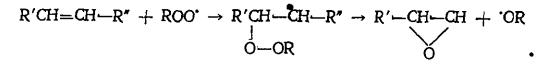
$$r=\frac{\text{unsaturated acid content}}{\text{active oxygen content}}$$

becomes close to unity.

In a mixture of unsaturated fatty acids (with an iodine number of 126) and the peroxide of oleyl alcohol, the peroxide oxygen is transferred to the double bonds of the acid. Quantitatively this phenomenon depends greatly on the nature of the haematin catalyst (weight concentration 3×10^{-3}). Thus at room temperature after 1 h the ratio $r = 0.31$ in the absence of a haematin catalyst or in the presence of oxidised cytochrome; r becomes 0.96 in the presence of reduced cytochrome [131].

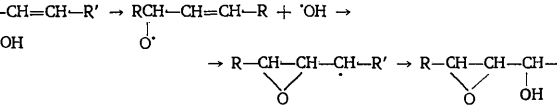
The role of reduced cytochrome in the transfer of peroxide oxygen to the double bonds of unsaturated fatty acids has been discussed in detail by Dubouloz and coworkers [133].

Epoxides may be formed immediately in the autoxidation process in consequence of the addition of ROO· radicals to the double bond:

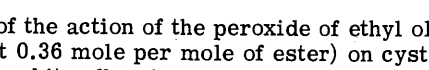


The reaction mechanism has been discussed in detail [134].

Epoxyalcohols are probably formed in the decomposition of the hydroperoxide with subsequent addition of ·OH radicals to the double bond [53]:



The epoxidation of unsaturated compounds in the presence of haematin compounds by hydroperoxides probably takes place via the addition of ROO· radicals to the double bond, since the latter are formed as a result of a series of reactions [135]:



The study [136] of the action of the peroxide of ethyl oleate (peroxide content 0.36 mole per mole of ester) on cysteine and degraded egg white albumin showed that the thiol groups of the protein enter fully into the reactions in the presence of an excess of the peroxide. The reaction products consist of disulphides and their derivatives containing oxygen. The biological importance of this reaction has been discussed in detail and the methods employed have been criticised [136].

Another study [137] dealt with the autoxidation in emulsion of linoleic acid (2×10^{-3} M) at 37°C and pH 7.4, catalysed by haemin (10^{-5} M) or haemoglobin (2×10^{-6} M) in the presence of 10^{-3} M cysteine or glutathione. The rate of

degradation of the SH groups of the last two compounds is proportional to the content of peroxide in the emulsion. The cysteine oxidation product consists of cysteine, cysteic acid, and cysteine disulphoxide.

The action of an aqueous 2×10^{-3} M emulsion of linoleic acid peroxide (37°C and pH 7.4) on various enzymes has been the subject of a major investigation[138]. It was shown that the activity of all enzymes with SH groups as well as that of cholinesterase, choline dehydrogenase, glyoxalase, β-amylase, succinate dehydrogenase, and urease is strongly inhibited. Fairly strong inhibition occurs also with other enzymes not containing SH groups, for example lipase, invertase, pepsin, trypsin, papain, and cytochrome oxidase, while xanthine oxidase, tyrosinase, catalase, and α-aminoacid oxidase are not affected. It is noteworthy that enzymes such as cholinesterase, lipase, invertase, and pepsin are also inhibited by an aqueous emulsion of palmitic acid. Here the inhibition is probably caused by the nautralisation of the positive charges of the proteins by the negative charges of the acid. Attempts have been made several times to relate the degree of inhibition of the enzymes to the content of peroxide in the emulsion. Thus an 80% degree of inhibition obtains for papain and urease at peroxide concentrations of 0.22×10^{-3} and 0.12×10^{-3} M respectively. In another study an emulsion of fatty acids from linseed oil was employed instead of the emulsion of linoleic acid. We may note that the inhibition under irradiation is more pronounced in the presence of linoleic acid than in its absence.

Thus after 2 h succinate dehydrogenase was inhibited only to the extent of 14%, while in the presence of an emulsion of linoleic acid (4×10^{-7} M) the degree of inhibition reached 63%. The degree of inhibition of succinate dehydrogenase (at a linoleic acid concentration of 4×10^{-7} M) was investigated as a function of time and it was shown that the degree of inhibition reaches 20% after 15 min, 60% after 45 min, and then tends asymptotically to 80%.

It is interesting that these enzymes can be protected from the action of peroxides by more labile enzymes containing SH groups. The protection of urease by cysteine against the action of peroxides formed in the autoxidation of linseed oil has been discussed[138]. A study has also been made[139] of the inactivation of glyceraldehyde-phosphate dehydrogenase by linoleic acid hydroperoxide and of the inactivation of ribonuclease by the same hydroperoxide[140].

A special investigation[141] of the inactivation of enzymes with SH groups by peroxy-acids has been made.

The degradation of carotene in the autoxidation of unsaturated lipids catalysed by soya bean lipoxidase has been the subject of numerous investigations[142-144]. The degradation occurs in alfalfa on storage in the field[145] as a result of the action of peroxides formed in the autoxidation of unsaturated lipids catalysed by the lipoxidase of this plant.

The study of the autoxidation[146] of colloidal methyl linoleate (3.4×10^{-2} M) initiated by X-rays in the presence of vitamin A showed that the degree of degradation of vitamin A increases with the peroxide content. Thus at a peroxide concentration of 5×10^{-5} M, only 33% of the initial vitamin A remains. The degradation of vitamin A does not occur solely under the influence of X-rays in the absence of linoleate.

The study of the autoxidation of ethyl linoleate[147] (25° and 37°C) in petroleum ether solution in the presence of carotene (weight concentration 2.5×10^{-4} in relation to linoleate) showed that the decomposition of carotene is complete over a period of 48 h. Certain autoxidation inhibitors proved effective in the stabilisation of carotene. Thus pyrogallol, hydroquinone, and α-tocopherol at a weight concentration of 3×10^{-5} relative to linoleate (at 37°C over a period of 48 h) prevent oxidation to the extent of 100, 74, and 76% respectively). A gradual breakdown of vitamin A occurs in margarine during its autoxidation at room temperature. Thus the degree of decomposition of vitamin A, reaching 6.5% for a peroxide content of 0.7×10^{-3} mole kg^{-1}, becomes 43% when the peroxide content is 10^{-2} mole kg^{-1}.[148]

The degradation of vitamin A in halibut-liver oil during its oxidation at 25°, 80°, and 98°C and also its protection by NDGA alone or NDGA in the presence of a synergistic agent have been investigated in detail[149].

The study of the degradation of vitamin A during the autoxidation of olive oil at 55°C in thin layers showed[150] that vitamin A decomposes gradually. Thus after 2 h the degree of its degradation is 69%, while in the presence of 0.048% of α-tocopherol it amounts to only 5%, reaching 36% after 10 h. Another study[151] dealt with the degradation of carotene in the autoxidation of ground nut oil at different temperatures (from 4° to 98°C) and also its protection against oxidation with the aid of α-, β-, and γ-tocopherols and gossypol.

A large publication[152] has been devoted to the degradation of carotene at 35°C under the influence of the peroxides of ethyl oleate, methyl linoleate, methyl linolenate and cotton seed, ground nut, and soya bean oils as well as to protection against oxidation with the aid of α-, β-, and γ-tocopherols and gossypol. The protective action of α-, β-, and γ-tocopherols against the degradation of carotene and bixin by the peroxide of methyl linoleate is also examined in two other papers[32,153].

In a study of the degradation of vitamin A and carotene[154] during the autoxidation at 37°C of a colloidal solution of ammonium linoleate (0.2 M, pH 7) catalysed by 2×10^{-5} M haemoglobin or cytochrome c showed that, following the absorption of 500 cm^3 of oxygen, the degree of degradation of vitamin A and carotene is respectively 88 and 53%, while in the presence of 5×10^{-3} M α-tocopherol, the degree of degradation is only 63 and 5% respectively.

Another study[50] dealt also with the question of the protection of vitamin A and carotene with the aid of α-tocopherol in the course of the autoxidation of an aqueous emulsion of oleic acid (37°C, 0.1 M, pH 7) catalysed by haemin (2×10^{-5} M). After 3 h, 1400 cm^3 of oxygen is absorbed and the degree of degradation of vitamin A is 88%, while in the presence of 6×10^{-3} M α-tocopherol the degree of degradation is only 63% and 300 cm^3 of oxygen is absorbed. The behaviour of carotene is similar to that of vitamin A. When 1400 cm^3 of oxygen has been absorbed, carotene is degraded to the extent of 63%, while in the presence of 5×10^{-3} M α-tocopherol the degree of degradation is only 5%.

Usually diets rich in unsaturated lipids but deficient in vitamin E and A cause a diminution of the vitamin A reservoir in animal livers. The addition of α-tocopherol and other antioxidants to the diet has a protective effect in relation to vitamin A, as shown by the following findings.

After seven months the vitamin A reservoir in the livers of male albino rats maintained on a diet containing 5% of pork fat and deficient in vitamins A and E is almost completely exhausted. The addition to the diet of each rat of 1 mg of α-tocopheryl acetate over a period of one week leads to a degree of degradation of vitamin A of only 71% during the same time.

The addition of α-tocopherol, leuco-Methylene Blue, phenothiazine, and tetramethylthiuram disulphide to a diet including 10% of cod liver oil and deficient in vitamin E increases the vitamin A content in chicken livers compared with the diet free from additives [155].

The addition of Methylene Blue or phenothiazine to a diet including 10–20% of cod liver oil and deficient in vitamin E increases the content of vitamin A in rat livers over a period of 14 weeks compared with the diet free from additives. The effect of the additives diminishes markedly when cod liver oil in the diet is replaced by pork fat [156,157]. The protective action of vitamin E, promoting the retention of vitamin A in rat livers, has been described in two papers [158,159].

Ethyl linoleate peroxide (250 millimole kg^{-1}) in contact with crystalline biotin leads to 96% degradation of the latter at 37°C after 12 h. As for vitamin A, α-tocopherol has a protective effect: the degree of inhibition is 44% in 48 h at a 4% concentration of this compound. Another study [160] also demonstrated the degradation of biotin at 25° and 37°C in the presence of the peroxide of corn oil (100 millimole kg^{-1}) and in the case of diets containing 5% of lipids of which 3% is cod liver oil and 2% cod liver fat; the overall peroxide content in the diet is 5 millimole kg^{-1}.

A study of the action of pyridoxine and riboflavin [161] showed that riboflavin decomposes lipid peroxides and thereby protects pyridoxine from their action.

VII. THE ROLE OF LIPID PEROXIDES IN THE DETERIORATION OF FOOD PRODUCTS

It has been already seen that carbonyl and mono- or poly-functional hydroxy-compound may be formed from lipid peroxides. The monocarbonyl compounds consist of a mixture of saturated and unsaturated aldehydoacids and in all probability are responsible for oxidative rancidity and reversion. These frequently encountered phenomena have been discussed in detail in a number of publications [11–15,162].

Cow's milk. The overall composition of the acids constituting milk lipids is as follows [163]:

Unsaturated acids (60%): 12% of acids ranging from C_4 to C_{12}, 11% of myristic acid, 28% of palmitic acid, and 9% of stearic acid.

Unsaturated acids (40%): 34% of oleic acid, 5% of linoleic acids, and 1% of others.

Acids entering into the composition of phospholipids [164]: 41% of saturated acids, 40% of mono-olefinic acids, 2.3% of conjugated and 8.8% of conjugated diolefinic acids, 3.6% of triolefinic acids, 2% of tetraolefinic acids, and 2.2% of pentaolefinic acids.

Evidently milk phospholipids have a higher content of polyunsaturated acids than glycerides.

It has been shown [165] that the content of peroxide in powdered milk allowed to stand in air increases with time. In the same study [165] it is recommended that various antioxidants (particularly of the phenolic type) be employed at a weight concentration of 10^{-4}. The formation of peroxides has been investigated in various specimens of powdered milk during storage at 2° and 38°C over periods ranging from 4 months to 1 year [13,113]. When the peroxide content is of the order of 6–10 millimoles per kilogramme of lipids, a rancid odour appears. The maximum content of peroxide formed over a period of 4 and 9 months is 5 and 14 millimoles per kilogramme of lipids.

C_2–C_{18} saturated aldehydes, C_5–C_{11} unsaturated aldehydes, C_8 and C_9 2,4-dienoic aldehydes, oct-1-en-3-one, and oct-1-en-3-ol were identified in the lipids of sour milk [166–168]. Alkyl methyl ketones $RCOCH_3$ ranging from C_1 to C_{13} are also formed [169]. Probably they are derived mainly from myristic and palmitic acids.

The nature and mechanism of the formation of various compounds in the autoxidation of milk lipids have been discussed in detail [166–174]. One of the papers [172] criticises preceding investigations.

Data on the content of peroxides and carbonyl compounds in various animal fats and edible vegetable oils as a function of storage and irradiation conditions have been published [13,175,178]. The study of the storage of raw vegetables, in particular peas [179–182], showed that the content of glucides and nitrogen remains more or less constant.

No changes occur also in blanched vegetables, i.e. those subjected to the action of boiling water which decomposes lipidoxase. On the other hand, the peroxide content and acidity of the lipid component of raw vegetables may greatly increase [181]. There is also a possibility of a decrease of the iodine number—for example, in raw peas it decreases from 98 to 89 in 5 years. We may also note that chlorophyll is degraded in peas to the extent of approximately 30% in 5 years.

Lipids, which constitute only about 0.3% of dry potato [183], contain 75% of polyunsaturated fatty acids, 53% of 18 : 2 acid, and 22.5% of 18 : 3 acid. The saturated component consists almost entirely of a C_{16} acid (17.4%). After exposure to oxygen at room temperature for 5 months, C_2–C_6 saturated aldehydes and C_1–C_5 saturated hydrocarbons were isolated. The latter are probably formed from aldehydes:

$$R{-}CHO \rightarrow RH + CO.$$

Potato chips fried at 185°C in a mixture consisting of 50% of cotton seed oil and 50% of corn oil and stored at room temperature in air were very carefully investigated [179]. 18 different carbonyl compounds were isolated from freshly fried potato chips and 19 from less fresh specimens. During ageing, the content of saturated aldehydes (particularly hexanal), α-unsaturated aldehydes (more of C_7 than C_8), and alkyl methyl ketones (more of 2-pentanone than 2-hexanone) increases. On the other hand, there is a rapid decrease of the content of deca-2,4-dienal.

On storage pork frequency becomes rancid [184]. The rancidity is accompanied by a change in colour, which becomes greyish-brown instead of pink. The rancid meat has an unpleasant odour and taste and is somewhat toxic. The rancidity is a consequence of the oxidation of oleic acid triglycerides and small amounts of polyunsaturated acids (particularly linoleic acid) and subsequent degradation of haemoglobin and myoglobin accompanied by the liberation of inorganic iron compounds. This reaction is catalysed by haematin compounds of the meat itself. The very rapid deterioration of horse meat in the presence of air is probably a consequence of an analogous phenomenon, which, however, is much more rapid owing to the higher content of linoleic acid (16%) in horse fat.

VIII. CHANGES IN LIVING ORGANISMS INDUCED BY LIPID PEROXIDES AND THEIR DECOMPOSITION PRODUCTS

The presence of peroxides at a concentration of several tens of millimoles per kilogramme of dry material was observed in the lipid component of green leaves of certain plants: sunflower, wheat, peas, beans, waterweed (Elodea) [185], and white lucerne [186]. Peroxides could not be

detected in the stalks, roots, and seeds of these plants [185]. The localisation of peroxides in the leaves and their decomposition under conditions where photosynthesis but not tissue respiration ceases suggests that photosynthesis is closely related to the formation of peroxides. This hypothesis is based on the finding that a flavin-lipoprotein compound containing iron and manganese and capable of reducing carbon dioxide was isolated from lucerne leaves [186]. The reduction was accompanied by the formation of a peroxide of the lipid component of the leaf. The role of peroxides of glycolic and glyoxylic acids in the decomposition of chlorophyll has been examined [187,188]. It is interesting that the leaves, seedlings, and seeds of certain oil-bearing plants contain substances capable of causing the decomposition of peroxides [189-191].

The polymers obtained as a result of the decomposition of lipid peroxides the formation of which is catalysed by lipoxidase, are probably components of cutin [160], an impermeable film coating part of the plants, which had been acted upon by air.

Even a balanced diet containing between 5 and 20% of highly unsaturated lipids and with a low content of vitamin E may cause the pathological changes enumerated below, which may vary depending on the type of animal [162,192,235]:

1. Yellow colour of fatty tissues.
2. The formation of the ceroid pigment in rat livers.
3. Brown colour of the rat uterus.
4. Atherosclerosis and peripheral damage of the viens in man.
5. Exudative diathesis in chickens.
6. Encephalomalacia in chickens.
7. Decrease of the capacity for egg bearing and embryo generation in hens.
8. Depigmentation of incisor teeth in rats.
9. Muscular dystrophy in ruminants.
10. Liver necrosis and pulmonary haemorrhage.

These ten pathological changes have been discussed in two large reviews [233,234]. Certain pathological changes, such as, for example, the yellow colour of the fatty tissue in certain animals, the brown colour of the rat uterus, the formation of the ceroid pigment in rats, and the appearance of exudative diathesis and encephalomalacia in chickens may be directly linked to the action of the oxidation products of unsaturated lipids on tissue proteins which results in their damage. The differences between the behaviour of chickens and rats in relation to diets with a high polyunsaturated lipid content are probably a consequence of the different structures of their capillary vessels. In other diseases, for example in muscular dystrophy or liver necrosis, which occur also in the absence of lipids from the diet, the role of polyunsaturated lipids is less clear. However, in liver necrosis the decomposition of sulphoaminoacids under the influence of lipid peroxides probably plays a considerable role. It is quite likely that muscular dystrophy is a consequence, at least partly, of the decomposition of vitamin E under the influence of these peroxides.

It is noteworthy that different antioxidants such as NDGA, Methylene Blue, diphenyl-*p*-phenylenediamine, phenothiazine, and tetraethylthiuram may be replaced in the diet by vitamin E and play a protective role against one or several of these diseases. For example, selenium compounds (at a concentration of $10^{-7}-10^{-6}$ M) can fulfil a protective role against liver necrosis and exudative diathesis but not against encephalomalacia. The action of these different antioxidants has been reviewed [233,234] and has been described in a special paper on the action of SeO_2. [235]

IX. PATHOLOGICAL CHANGES INDUCED *IN VIVO* BY A DIET CONTAINING VARIOUS LIPIDS HEATED IN THE PRESENCE OF AIR

Edible lipids consist of a mixture of triglycerides of stearic, palmitic, oleic, and linoleic acids. Animal fats contain much more of unsaturated acids (40–60%) than vegetable oils (10–30%) and much less of linoleic acid. Beef and mutton fats contain between 1 and 2% of this acid and pork fat contains 6–10%, while in many vegetable oils its content reaches 60%. Horse fat, which contains, apart from a small amount (4.5%) of stearic acid, 5.3% of linoleic acid and a considerable amount of linolenic acid (16%), is an exception.

Various fried products sold commercially are heated at 180–200°C. Under these conditions, there is usually an increase of the content of hydroxy-compounds, free acids, esters, conjugated dienes, and particularly polymers (the initial content of which is low, namely 1–2%). The content of carbonyl compounds initially increases to a maximum and then falls and that of peroxides is more or less constant. This can decrease or increase slightly but remains insignificant, its concentration rarely exceeding 10 millimole kg^{-1} (provided that the food product had not been subjected to preliminary ionising irradiation).

The degree of overall unsaturation (iodine number), and particularly the content of linoleic acid, decreases appreciably. These chemical changes are reflected in an increase of the refractive index, the dielectric constant, and particularly the viscosity [236-239].

The physicochemical changes occurring during the frying of various food products containing lipids have been discussed in a number of publications [240-244], the last of which is devoted to different types of meat.

Apart from temperature and the duration of frying, the content of the peroxides and lipids and their decomposition products is influenced by the area of contact between the lipid and air, which is determined by the shape, dimensions, and material of the frying-pan and also the duration of the preliminary heating and cooling. Indeed, peroxides are formed during the preliminary heating and then decomposed during frying and are reformed during cooling. Thus, evidently, the content of different peroxide derivatives will be higher if the heating is interrupted than when it is carried out continuously and will increase with the number of preliminary heating and cooling cycles. Nevertheless, we may note that carbonyl compounds may be partly eliminated by evaporation or can undergo further oxidative degradation: this in fact accounts for their maximum content when the heating process is of limited duration. Thus, when corn oil [236] was heated for 24 h at a constant air flow rate of 150 $cm^3\ kg^{-1}\ min^{-1}$, the content of peroxides at 120°, 160°, and 200°C was respectively 40, 3, and 1 millimole kg^{-1} (the initial content was 0.5 millimole kg^{-1}). After 24 h at 200°C (at an air flow rate varied from 0 to 2400 $cm^3\ min^{-1}$), the content of carbonyl compound changed from 86 to 116 millimole kg^{-1} (with a maximum of 122 millimole kg^{-1} for an air flow rate of 1200 $cm^3\ min^{-1}$).

When cotton seed oil was heated continuously at 175°C for 62 h [238] and with interruptions (heating for 7–8 h followed by 12–16 h of storage at room temperature), the results presented in Table 1 were obtained.

Lipid peroxides introduced into the alimentary canal by a probe gradually disappear during digestion. Thus the content of the peroxide of ethyl oleate after 5 h was only 12% of the initial value, which was 10^{-4} mole [245].

Moreover, lipids originating from various parts of the organism, particularly from the lymph (specimens of which were removed during digestion), contain no peroxides at all [245-247].

Table 1.

Substance	Content, millimole kg^{-1} heating	
	continuous	interrupted
Peroxides	2.3	3.6
Carbonyl compounds	158	155
Hydroxy-compounds	130	241
Free acids	280	560
Polymers (%)	14.8	13.8
Iodine number	103	98

Probably the peroxide of the lipid ester or triglyceride is hydrolysed by lipase with retention of the OOH functional group, which is then partly reduced by the pancreatic secretion. The above facts and also the absence of peroxides from excrement suggest that lipid peroxides are mainly decomposed on the mucous membrane of the intestine [245].

Experiments [248] performed on rats fed on a diet containing 10% of *Vernonia* oil containing 70% of 12,13-epoxyoleic acid showed the presence of this acid in adipose tissues, the liver, kidneys, and the heart and also in excrement. On the other hand, epoxides were absent from these tissues when *Vernonia* oil was replaced by corn oil. These findings suggest that epoxides are not decomposed in the digestive organs (which is surprising in view of the presence of 0.1 *N* HCl in the stomach and the sensitivity of epoxides to acid hydrolysis) and are normally stored in various tissues together with other lipids.

Hydroxy- and carbonyl compounds are readily absorbed [249]; thus the content of carbonyl compounds in the lymph may increase by a factor of 10.

A diet containing 10–20% of lipids heated in air usually causes a retardation of growth, a decrease of the degree of assimilation of food, and its efficiency, and also an increase of the amount of water required.

On such a diet, certain animal organs, particularly the liver, greatly increase in size. However, it should be noted that the restoration of a normal diet leads to the recovery of the sick animals. Vitamins (including vitamin E) ameliorate but do not eradicate these diseases. Fresh lipids as well as proteins also have a favourable effect.

The toxicity of heated lipids increases with the content of linoleic acid (with the exception of horse fat, the content of the 18 : 3 acid in normal lipids is very low), as shown by the results obtained in two studies on rats [250-252] fed on a diet containing 20% of lipids.

The toxicity increases with the number and duration of preliminary heating and cooling cycles (consequently one should avoid using the same oil in several successive frying operations) and decreases as a function of the weight of the lipid. For example, the harmfulness of various heated lipids employed in commercial frying involving large amounts of product is much less than that of lipids heated in the laboratory in much smaller amounts, as shown by studies [253-259] on rats fed on a diet containing 23% of lipids.

Since the mucous membrane of the intestine decomposes lipid peroxides, their intrinsic action must be restricted to the level of digestive enzymes. Apart from the enzymes mentioned above [138], the inhibition of xanthine oxidase by the peroxide of soya bean oil has been demonstrated [247]. Such decomposition of enzymes should be reflected in a reduced assimilability of food, which entails a retardation of growth. Thus the content of peroxides in lipids treated at 200°C is low, and consequently their role in the overall pattern of the induced diseases is very small.

However, on heating at lower temperature (60–100°C), when the content of peroxides is fairly high, their presence may be responsible for the overall toxicity of the heated lipids. Thus the inhibition of the growth of rats fed on a diet containing 20% of soya bean oil subjected to autoxidation at 60°C increases with the peroxide content [247,259]. A study on cotton seed oil autoxidised at 60°C showed that the incidence of illness increases when the maximum peroxide content is reached [240].

The relation between toxicity and the content of peroxides was observed not only with cotton seed and soya bean oils autoxidised at 60°C but also with the ethyl esters of the highly unsaturated fatty acids in the fat of the cuttle fish. The autoxidation products obtained at 30° and 100°C contained respectively 970 and 75 millimole kg^{-1} of peroxides and proved to be very toxic to rats [260].

In other studies lipid peroxides introduced via the alimentary canal proved to be non-toxic. For example the hydroperoxide of methyl oleate introduced in an amount of 5% into the diet of rats is altogether non-toxic [261,262].

Thus there is no definite relation between the degree of toxicity of the heated lipid and its peroxide content, particularly for the same lipid at low heat-treatment temperatures in the initial autoxidation stage.

It should be noted that in pathological cases, where the regeneration of the intestinal epithelium (decomposed by lipid peroxide) is slow, lipid peroxides can apparently overcome the protective effect of the intestine [263]. Studies during which methyl linoleate labelled with ^{14}C at 1-C was introduced via the digestive tract, showed that this peroxide is extensively decomposed in the intestine and the decomposition products are incorporated into various tissue lipids.

The epoxides which are deposited together with other lipids in various cell tissues are not toxic at first sight. Indeed, the introduction of 5% of methyl *cis*-epoxystearate [261,264] or 7% of epoxyoleic acid (in the form of 10% *Vernonia* oil) [248] into the diet of rats is not harmful. However, according to other investigations [265], epoxides appear to be carcinogenic.

Hydroxy-compounds, at least those with long chains, are not toxic. For example, methyl mono- and dihydroxystearates are not harmful to rats when their content is 5%. [261]

Carbonyl compounds are probably to some extent responsible for the overall toxicity of heated lipids, which decreases after their treatment with semicarbazide. They can act on digestive enzymes, since they inhibit the activity of lipase. One should examine the effect of each type of aldehydes as a function of the degree of their unsaturation; probably aldehydes with conjugated double bonds should be more toxic.

Polymers are usually toxic. Their activity evidently depends on the degree of diene conjugation or, in other words, on the content of linoleic acid in the initial lipid. This has been demonstrated for pork fat and cotton seed oil after their heat treatment in air at 95°C for 300 h and after distilling off the autoxidation products, obtained in

this way, at 300°C at a very low pressure [264]. The residue from cotton seed oil (40% of the total quantity of the oil), introduced in an amount of 20% into rat diet, caused in one week the death of all the animals, while the residue from pork fat (17% of the total quantity) does not cause death but inhibits growth [264]. We may also note that the distillation residue may contain thermal polymerisation products with cyclohexene fragments which are not formed in frying on a commercial scale [266] but the present author believes that they can be formed in the decomposition of polymers at 300°C.

On the other hand, the degree of assimilation of toxic polymers decreases with increase in molecular weight. Therefore the heaviest fractions are not always the most toxic.

Table 2. Composition of certain animal fats (%).

Fat	Acids				
	18:0	16:0	18:1	18:2	18:3
Mutton fat	34	24	44	2	traces
Beef fat	21	32	45	2	traces
Pork fat	16	30	45	7	traces
Chicken fat	7	26	38	20	traces
Horse fat	5	26	34	5	16
	(+5% 14:0)		(+7% 16:1)		

Table 3. Composition of cod liver fat (%).

Acid		% in fat	Acid		% in fat
20% of unsaturated triglycerides	18:0	3	2% of triolefinic acids	18:3	
	16:0	12		20:3	
	14:0	3		22:3	
	15:0	1	tetraolefinic acid	18:4	2
	17:0	1			
45% of mono-olefinic triglycerides	18:1	25	10% of pentaolefinic acids	20:5	9
	20:1	13		22:5	1
	22:1	6	hexaolefinic acid	22:6	9
	14:1	traces			
	16:1				

Table 4. Composition of certain vegetable oils (%).

Acid	Linseed oil	Soya bean oil	Cotton seed oil	Safflower oil	Corn oil	Groundnut oil	Olive oil
18:3	47—60	4—8	traces	traces	1.5	traces	traces
18:2	15—24	49—56	40—50	77	58	20—3	4—12
18:1	15—19	24—34	20—30	13	27	50—60	70—85
Saturated	10—15	12—17	20—30	10	12.5	10—20	7—17

In addition, one must bear in mind the existence of trioxans, particularly derivatives of 2,4-dienoic aldehydes, such as deca-2,4-dienal, in which corn oil heated at 200°C becomes enriched [237]. The importance of 1,3-conjugation has been emphasised by Holman and Greenberg [267], who discuss all compounds with two conjugated double bonds, for example the hydroperoxide of ethyl linoleate, and its reduction and decomposition products, as well as ethyl linoleate derivatives which are not involved in the normal metabolism of linoleic acid [267]. The biochemical activity of various fractions of linseed oil [266,268], herring oil [269,271], and pork fat [271] has been investigated. Several excellent papers have been devoted to the toxicity of heated lipids [249-252,256,272,273]. The compositions of various lipids are given by Hilditch and Williams [274]. The compositions of the main animal fats and vegetable oils according to the literature data [111,274] are quoted in Tables 2, 3, and 4.

X. CHANGES IN TISSUE CELLS OCCURRING ON FORMATION OF PEROXIDES

Earlier it was stated that lipid peroxides administered to rats with food are largely decomposed by the mucous membrane of the intestine and only their traces can be detected in the lymph.

Nevertheless the conditions for the formation of lipid peroxides are favourable even in the mammalian organism in consequence of the simultaneous presence in vascular endothelium also of light unsaturated lipids (in the form of an emulsion), haematin compounds, and oxygen [245]. The capacity of the tissue for the formation of lipid peroxides increases with the content of unsaturated acids and the degree of their unsaturation as well as in the presence of catalytic systems such as haematin iron or non-haematin iron together with ascorbic acid, and decreases in the presence of inhibitors, for example vitamin E.

It is noteworthy that the composition, particularly as regards polyunsaturated lipids, not only of the triglycerides of the fat reserves but also of the phospholipids in various tissues is greatly influenced by the type of lipids in the diet. Thus an increase in the content of linoleic acid in the diet increases simultaneously the content of linoleic acid in the storage lipids and the content of linoleic and arachidonic acids in various tissues. Polyunsaturated acids (other than the main acids), such as those of the 20:5 and 22:6 type, in cod liver oil are deposited in various animal tissues without change.

The correlation between the degree of unsaturation of lipids entering into the composition of tissues and the degree of unsaturation of lipids in the diet accounts for the pathological changes observed *in vivo* under the influence of a diet enriched in polyunsaturated lipids.

However, we may note that the formation of polyunsaturated 20:3 acids may occur also in tissues if the diet is deficient in linoleic acid and includes saturated lipids such as those of coconut oil. The composition of lipids in various tissues as a function of the type of lipids in the diet has been discussed in detail [275-279].

The presence of peroxides in connection with various pathological changes in tissues occurring due to a diet with a high content of polyunsaturated lipids and deficient in antioxidants has already been mentioned. Lipid peroxides were also detected after the exposure of a live animal to ionising radiation in the presence of atmospheric oxygen [280-286].

The formation of lipid peroxides under the influence of ionising radiation is in all probability initiated by $^{\cdot}OH$ and $^{\cdot}OOH$ radicals formed in the aqueous phase [13]. The analogy between the diseases caused by ionising radiation and lipid peroxides, in particular the decomposition of various enzymes, has been discussed in detail [2,287]. The detection of peroxides in the tissues of live animals has

been questioned in two publications [288,289]. Indeed, when lipids were extracted in an inert atmosphere, even traces of peroxides could not be detected in any of the organs of rats (the chromatographic method was used [290]) subjected to preliminary irradiation with X-rays in air or fed on a diet containing 20% of fresh soya bean oil or its peroxide [288]. Similar results were obtained in the study of various organs from chickens fed on a diet containing 10% of cotton seed oil. Blood lipids, which induce the formation of small amounts of a very unstable peroxide, are an exception. A study [289] based on 33 different tissues confirmed the validity of earlier results [288].

Hence it probably follows that live tissues do not contain peroxides (or at most traces in adipose tissues) and that the latter are formed *in vitro* during extraction in contact with an atmosphere from which oxygen has not been completely exhausted. A deficiency of vitamin E in the tissue probably appreciably increases the rate of formation of the peroxide *in vitro*.

Whereas the presence of lipid peroxides in live tissues is doubtful, the formation of peroxides *in vivo* is indicated by the products obtained on decomposition of lipid peroxides and the fact that such formation is prevented by vitamin E and other antioxidants. In this case lipid peroxides probably undergo gradual transformations from the instant of their formation, which lead to various physiological (decomposition of protein thiols and various enzymes) and structural changes (rupture of membranes in mitochondria and lysosomes).

When aqueous emulsions of lipid extracts from various rat organs were exposed to ionising radiation (5–100 krad), the formation of peroxides with a lipid content of several tens of millimoles per kilogramme was observed.

Peroxides are also formed during aerobic incubation of various live tissues at 37°C. However, in the majority of investigations the peroxides were determined only indirectly with the aid of a colour test for malonic dialdehyde (one of the decomposition products of lipid peroxides) with thiobarbituric acid. This very sensitive test yields interesting results in comparative studies, but does not reflect the true content of peroxides (see the discussion in Wills's paper [292]).

The considerations concerning the formation of peroxides *in vivo* and the catalysis of the oxidation of aqueous emulsions of linoleic acid by metal chelate complexes are applicable, in broad outline, to the determination of the capacity for the *in vitro* formation of endogenic peroxides in various live tissues in the presence of atmospheric oxygen, particularly when one considers the catalytic activity of various forms of iron (haematin and non-haematin) and ascorbic acid and the effect of chelating agents and of phosphate concentration. The rate of formation of peroxides in the tissue increases with its overall iron content as well as with the content and degree of unsaturation of its component lipids. In the presence of non-haematin iron, the content of ascorbic acid in the tissue is very important. Thus the onset of the formation of the peroxide on addition of ascorbic acid to homogenates of various tissues is explained by the presence in them of non-haematin iron. It has been shown [293] that in various tissues of scorbutic guinea pigs, less peroxides are formed than in the tissues of healthy guinea pigs and that the addition of ascorbic acid to tissues affected by scurvy restores their normal capacity for the formation of peroxides. It is interesting to note that tissues in a state of constant cell division, such as bone marrow, the mucous membrane of the intestine, and cancer cells, do not form peroxides.

Discussions concerning the formation of peroxides as a result of the *in vitro* aerobic incubation of various tissue homogenates have been published [292–299]. The formation of endogenic peroxides in the homogenates of various rat organs and also the catalytic effect of these homogenates in the autoxidation of linoleic acid in emulsion was discussed in detail in one of these papers.

Mitochondria usually contain considerable amounts of polyunsaturated lipids (particularly in the form of phospholipids) derived from acids with 3,4,5, and 6 double bonds, such as 18:3, 20:3, 20:4, 22:4, 22:5, and 22:6 acids. The distribution of lipid molecules in the vicinity of various cytochromes makes them particularly susceptible to autoxidation.

The composition of the liver and heart mitochrondria in various sea fish and birds and also several marine mammals has been described [301,302]. Data have also been published [302] on the composition of the mitochondria in the chicken liver and the ox heart. The composition of rat liver mitochrondria has been studied [303,304].

Suspensions of mitochrondria at 37°C in a sucrose or sodium chloride solution (with a phosphate buffer) absorb oxygen with subsequent formation of malonic dialdehyde. Ascorbic acid usually catalyses these reactions and vitamin E inhibits them.

The phenomena described below are accompanied by the degradation of enzymes such as succinate dehydrogenase, TPNH cytochrome reductase, choline oxidase, and amino-acid oxidase (on the other hand, the liver alkaline phosphatase and brain cholinesterase resist the formation of this peroxide). The degradation of the enzymes is revealed by a weakening of the oxidative phosphorylation and oxidation of α-oxoglutaric acid.

Apart from the degradation of enzymes, the mitochondrial membranes swell and are lysed with liberation of free fatty acids and soluble proteins.

Vitamin E, introduced *in vitro* into suspensions of mitochondria, decreases the absorption of oxygen and the formation of malonic dialdehyde, protecting thereby the above enzymes against oxidative degradation and the membrane against swelling and lysis. The introduction of 0.47 and 4.7% of vitamin E into mitochrondria from rabbit heat tissue decreases the rate of absorption of oxygen by factors of 7 and 28 respectively [305]. It is noteworthy that the capacity of mitochrondria for the formation of peroxides depends also on the composition of polyunsaturated lipids and antioxidants (in particular vitamin E) in the diet. Thus when a diet deficient in vitamin E and containing 3% of pork fat and 2.5% of fish fat is administered, the rate of absorption of oxygen and the amount of malonic dialdehyde formed decrease respectively by factors of 2.5 and 10 when 10 mg of α-tocopherol is added to the diet [306].

Degradation of mitochondrial enzymes has been discussed in Refs. 307 and 308 and the swelling and lysis phenomena in Refs. 309 and 310. The last two papers deal with the role which ascorbic acid plays in the occurrence of these processes.

The formation of peroxides in the mitochondria of rat liver and rabbit heart cells has been thoroughly investigated [305,306]. The inhibiting effect of vitamin E (in relation to the formation of peroxides in the mitochondria of rabbit heart cells and rat and rabbit liver cells) has been studied [311–313].

Microsomes contain 30–40% of lipids, particularly phospholipids, and twice as much of polyunsaturated lipids (in relation to nitrogenous bases) as in mitochondria. Certain molecules of these lipids are located near cyto-

chrome molecules, which gives them a particularly high capacity for the formation of peroxides [314].

Applications to rat liver cell microsomes of the same methods as for mitochondria [305] led to the discovery that the absorption of oxygen accompanied by the formation of malonic dialdehyde takes place.

The formation of peroxides in microsomes leads to a modification of the synthesis of nucleic acids and proteins and to a decrease of the synthesis of ascorbic acid and also to an inhibition of the activity of gulonolactone oxidase [315]. The microsomes themselves degenerate, their altered shape being clearly visible through an electron microscope.

As for complete homogenates and mitochondria, vitamin E plays the role of an inhibitor. Thus addition of α-tocopherol (0.25 g/gN) leads to degrees of inhibition of 72 and 69% respectively in the absorption of oxygen and the formation of malonic dialdehyde.

The formation of peroxides in the microsomes of rat liver and rabbit heart cells has been described in broad outline [314]. The inhibition of gulonolactone oxidase has been investigated [315,316], the second study [316] being concerned in addition with the dependence of the degree of inhibition of the synthesis of ascorbic acid on the content of malonic dialdehyde. The effect of TPNH and ATP on the formation of peroxides in microsomes has been studied [317].

Although lysosomes contain less lipids than mitochondria and microsomes, they nevertheless have only a simple membrane. They form peroxides with difficulty but the membrane is easily ruptured on formation of peroxide even in insignificant amounts. Thus the rupture of the membrane in rat liver cell lysosomes under the influence of ultraviolet light and γ-radiation and the product of the autoxidation of methyl linoleate is accompanied by the liberation of hydrolytic enzymes: cathepsin, glucuronidase, acid phosphatase, and aryl sulphatase. The addition of ascorbic acid increases and that of vitamin E decreases the amount of such liberated enzymes.

The formation of peroxides in lysosomes associated with the liberation of enzymes has been discussed [318-320].

The haemolysis of red blood corpuscles is associated with the rupture of membranes as a result of the formation of lipid peroxides. The haemolysis is promoted by a diet deficient in vitamin E, while the introduction of vitamin E or other antioxidants, for example reduced Methylene Blue, into the diet interferes with haemolysis. The haemolysis of red blood corpuscles has been discussed in a number of publications [321-325].

The inhibition of cell division under the influence of ultraviolet light is probably also induced, at least partly, by the action of lipid peroxides [326].

Indeed, in a study of the fertilised eggs of the worm *Chaetopterus pergamentaceus* and the sea urchin (*Lytechornus variegatus*), it was established that ultraviolet light and irradiated methyl linoleate inhibit cell division. Probably such inhibition is a consequence of the repression of the activity of the enzymes and of the depolymerisation of nucleoproteins.

Vitamin E is the usual component of the majority of living organisms. It is encountered in the tissues of all animals and is widely distributed in plants. It has also been found in unicellular organisms such as yeasts and moulds. Its antioxidant activity, which is usually shown in an increase of the duration of the induction period and in a decrease of the rate of absorption of oxygen and the rate of formation of hydroperoxides and their decomposition products, has been frequently noted in this review.

A similar situation obtains in the oxidation of linoleate catalysed by lipoxidase and haematin compounds and in the oxidation of mitochondria and microsomes.

Although α-tocopherol behaves as a weaker antioxidant *in vitro* than other tocopherols, it accumulates in the animal organism (particularly in phospholipids) and therefore under *in vivo* conditions exhibits a pronounced antioxidant activity. Its distribution in various animal fats and vegetable oils as well as in various rat organs has been discussed in two publications [16,327].

Various tocopherols do not exhibit synergism but form strongly inhibiting systems with ascorbic, citric, and phosphoric acids, which probably also play a very important role in the stabilisation of tissue lipids [326,328,329].

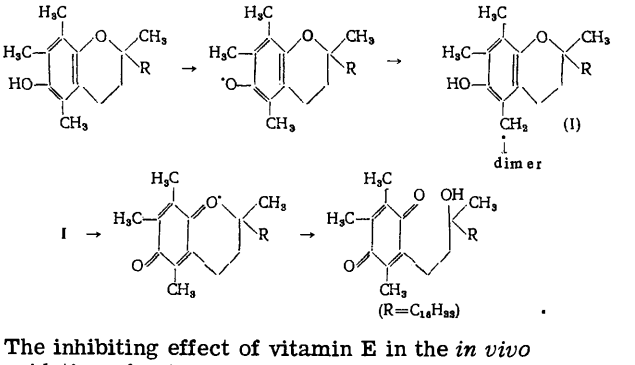
The degree of degradation of α-tocopherol in tissues usually increases with the content and degree of polyunsaturation of lipids in the diet. However, the loss of tocopherol from a tissue on a diet from which it is absent greatly depends on the nature of the tissue. We may note its very tenacious retention by the brain [330]. The decomposition products of α-tocopherol *in vivo* consist of α-tocopherylquinone (formed as a result of the opening of the pyran ring) and dimeric α-tocopherol (with an unaffected heterocyclic structure).

Indeed the presence of tocopherylquinone was established in the liver and in the muscles of mice and pigs [331] and its content in adipose tissues increases with the degree of unsaturation of lipids in the diet. (It is higher by a factor of 3 for methyl linoleate than for coconut oil [332].)

The simultaneous presence of the dimer and the quinone was also observed in the livers of mice and rats after intra-abdominal injection of α-tocopherol into animals which had been fed for a year on a diet deficient in vitamin E. [331,333] The dimer and the quinone are also formed on simultaneous oxidation (60° and 100°C) of α-tocopherol and methyl linoleate by atmospheric oxygen [334].

The effect of ROO· radicals formed as a result of the action of iron(III) salts on the hydroperoxide of methyl linoleate and the peroxides of methyl linolenate, ethyl arachidonate, and methyl eicosapentanoate on α-tocopherol has been investigated [335] and kinetic data have been published.

α-Tocopherol is converted into α-tocopherylquinone as a result of the abstraction of a hydrogen atom (from the OH group) followed by the rupture of the pyran ring, rearrangement, and fixation of the OH group [335]:



The inhibiting effect of vitamin E in the *in vivo* autoxidation of polyunsaturated lipids has been examined [16,233,234,336-338].

Ubiquinone, which is usually found in mitochondria in larger amounts than α-tocopherol, can be reduced to ubiquinol [339,340]. On the other hand, the latter can be

reoxidised by peroxides to ubiquinone. Ubiquinol proved to be an inhibitor approximately as effective as α-tocopherol in the oxidation of an emulsion of arachidonic acid catalysed by 2×10^{-6} M haemoglobin (37°C, pH 7.4) and also in the photochemical oxidation of the mitochondria in ox liver cells. These findings suggest that ubiquinol and ubiquinone can play a very important role as antioxidants for mitochondria.

Squalene [341], which is present in considerable amounts in fish lipids, can behave as an antioxidant, at least at the beginning of the reaction. In fact, a comparative study [341], of the autoxidation of methyl linoleate and methyl oleate at 63°C in the presence of 0.02% of tocopherol or squalene showed that in the first five days the content of the hydroperoxide is lower in the presence of squalene than in the presence of added α-tocopherol; after this period the formation of the peroxide in the presence of squalene is faster and after 8 days it is as rapid as in the absence of inhibitors.

We have already seen that inorganic compounds [337,338,342-344] introduced with food can prevent certain pathological changes induced by a diet with a high content of polyunsaturated lipids and deficient in vitamin E. A study [337] has shown that Na_2SeO_3 introduced into the diet gradually reduces the formation of peroxides in the liver, heart, and muscles of chickens. Selenocystine and selenomethionine were detected in the hydrolysate of liver proteins.

In addition various aminoacids containing selenium at concentrations of 10^{-4} and 2×10^{-4} play the role of inhibitors, which may be compared with α-tocopherol in the oxidation of an emulsion of methyl linoleate catalysed by haemoglobin.

These findings suggest that selenium introduced with food in the form of inorganic compounds is deposited in various tissues of the chicken as selenoproteins which *in vivo* probably behave as antioxidants. The mechanism of inhibition by selenium compounds consists mainly in the decomposition by these compounds of the hydroperoxide formed, but not via a radical mechanism. In addition, selenium compounds, which decompose peroxides, protect coenzyme A in the absence of cystine [343].

The role of selenium compounds in metabolism has been discussed in detail [338,343] and the mechanism of their interaction with hydroperoxides has been considered in another study [344].

Apart from α-tocopherol, which is widely distributed in plants [16,327], many polyhydroxy-compounds, such as simple aromatic polyphenols or heterocyclic derivatives (hydroxychromans, hydroxycoumarones [345]) can play a fairly important role in inhibition. In certain special cases their inhibiting activity may be the main function, as in the case of NDGA, the antioxidant activity of which *in vitro* has been considered in this review.

A thorough study has been made [346] of the toxic effect of various types of lipid peroxides administered intravenously and intra-abdominally to rats and chickens. It was shown that the toxicity depends to a large extent on the nature of the compound in which the lipids are bound and on the method of injection. Thus, peroxides of the triglycerides derived from olive and nut (groundnut?) oils are much less toxic than free fatty acids. Their ester and phospholipid peroxides, which are of the same type, are much more toxic when administered intravenously than intra-abdominally.

The retention of lipid peroxides by various tissues depends also on the type of peroxy-compound and the nature of the emulsifying agent. Probably it is greater the lower the toxicity of the peroxide. The peroxides of triglycerides are retained to a considerable degree by blood, lungs, the liver, the spinal column, kidneys, and the intestine. A moderate amount is retained in the heart and the muscles and a very insignificant amount in the brain, the pancreas, and in adipose tissues. The degree of retention in the blood is very considerable over a period of 1 h, is insignificant after 2 h, and becomes zero after 500 h.

Possibly the mechanism of the elimination of triglyceride peroxides differs from that for peroxides of other types. It is interesting to note that intravenous administration yields identical results with chickens and rats but after intra-abdominal administration the retention of triglyceride peroxides by various rat organs is less than by chicken organs.

We may note that in the presence of 0.5 millimole per kilogramme of the hydroperoxides of ethyl linoleate and $(CH_3)_3COOH$ [t-butyl hydroperoxide], symptoms of methaemoglobinaemia appear.

Numerous quantitative data concerning the retention of various types of peroxides by rat and chicken organs as a function of the dose administered and time and also as a function of the content of methaemoglobin in the case of ethyl linoleate and $(CH_3)_3COOH$ have been published [346].

The toxicity of certain autoxidation products of lipids and of certain organic peroxides administered to rats intra-abdominally only has been examined [2,347]. According to the data of the second study, the hydroperoxide of methyl linoleate and particularly of $(CH_3)_3COOH$ should be less toxic than was suggested in another investigation [346]. Nevertheless, it follows from the above studies [346,347] that lipid peroxides (and probably other peroxides) are much more toxic when introduced with food, which is reasonable, bearing in mind their decomposition by the mucous membrane of the intestine, which occurs in such a way that only some of their decomposition products pass into the lymph. Their toxicity when introduced by injection is undoubtedly a consequence of the combined effects resulting from attack on double bonds (which entails the degradation of the principal fatty acids, namely the 18:2 and 20:4 acids) and the degradation of haematin nuclei, protein thiols, various vitamins (particularly vitamins A and C), various enzymes, and membranes (which may lead to the haemolysis of red blood corpuscles).

Oxidation catalysed by variable-valence elements has been examined in two papers [348,349] and the general theoretical questions concerning the inhibition of autoxidation have been considered by Knorre et al. [350] Moreover, several papers and publications on synthesis after 1960 were devoted to organic peroxides in general [351-359], some of which [351-353] analyse various methods of their determination.

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New Ideas Concerning the Strength of Adhesive Joints of Polymers†

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The review was written by J.J.Bikerman specially for "Uspekhi Khimii". Bikerman is one of the leading U.S. specialists in the theory and practical aspects of surface phenomena and adhesion in polymers and solids and therefore the presentation of his views on the nature and strength of adhesive joints is of very considerable interest.
It is noteworthy that the views developed by the author depart widely from those common in the USSR and therefore his review is of special interest for the Soviet reader. Putting forward a number of interesting and well founded postulates of the rheological theory of adhesion, the author essentially ignores the molecular nature of adhesion phenomena, the chemical nature of adhesives as such, and the polymer nature of adhesives, which are not discussed in the review at all. Also ignored are the thermodynamic criteria of adhesion, the effects of the flexibility of the polymer chain and its structure on adhesion, etc. All these factors make the author's approach to adhesion somewhat one-sided and biased. However, this is compensated by a purposeful approach to the problem, a polemical presentation, and a number of postulates which are of very great practical value for all those concerned with adhesion and adhesive joints.
The bibliography includes 75 references.

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I. STRENGTH OF ADHINTS AND MOLECULAR ADHESION

In 1959 a valuable review on "Modern Views on the Adhesion of High Polymers" was published[1] in "Uspekhi Khimii". In the present paper an altogether different approach to the problem is employed. The author's views on the reason for the strength of adhesive joints (or adhints as they will be called henceforth for brevity) are described in the book which has been published in two editions[2]; readers who find this review too compressed and incomplete are referred to this monograph.

The mechanical rupture of an adhint requires the application of a stress f (g cm^{-1} s^{-2} or kg m^{-1} s^{-2}) or a force F (g cm s^{-1} or kgf m s^{-2}) and the performance of a certain amount of work W (g cm^2 s^{-1} of kg cm^2 s^{-2}). The problem of the factors which determine these quantities can be expressed also in a somewhat different form. Each adhesive joint contains several components; in the simple case there are two—the adhesive and the adherend—but there may be as many as five: the first adherend, the first boundary layer, the adhesive, the second boundary layer, and the second adherend. It is necessary to find a relation between the experimental values of f, F, or W on the one hand and the properties of these components and the geometry of the adhint on the other.

The second formulation of the problem may appear strange to unprepared readers and therefore it must be justified immediately. For many years everyone believed and even now it is still frequently believed that it is necessary to overcome *adhesion* in order to rupture an adhesive joint. Theoretical or molecular adhesion is by definition the attractive force A (per unit area) between the atoms or molecules of a substance A and the atoms and molecules of a substance B along the boundary between the phases A and B. It is assumed that the mechanics of rupture is fairly unimportant. If a stress f proves to be necessary in repeated experiments for the rupture of a joint between an adherend B and an adhesive A, the implication is, according to some theoreticians, that the adhesion A between A and B is equal to f. Thus one can obtain curves relating A to, for example, the chemical composition of A and B if the breaking stress f has been measured as a function of this composition. The geometry of the adhint and the mechanics of the experiment are disregarded, since the experimenter believes that he measures molecular adhesion, which is independent of external conditions such as the kind and direction of the breaking force, the form and size of the adhesive joint, etc.

In fact the resistance to rupture (f) is never and under no conditions equal to A. One can create fairly artificially an imaginary relation between f and A, as stated in section III, 1, but it is in all cases insignificant. The identification of f with A constitutes the apex of a pyramid made up of several strata of erroneous assumptions. The principal stratum or the principal error is the hypothesis that the theoretical adhesion A may be determined by mechanical measurements on adhints. The second unjustified hypothesis is that the force responsible for rupture is equal to the external force F applied to the adhesive joint. The third error consists in the fact that the macroscopic stress is assumed to be equal to the microscopic stress. The fourth stratum involves the assumption that the microscopic stress necessary to initiate rupture is equal to molecular adhesion.

The considerations set out in the previous paragraph may be elucidated using peeling as an example. In Fig. 1, A represents a rigid adherend, R a flexible ribbon, and G a layer of glue. A force F is applied to the free end of the ribbon. Evidently the force does not act directly on the edge E of the adhesive. Thus the first task of the investigator is to calculate or measure the force and moment acting on this edge and the crack formed in it; when the crack grows, the adhint gradually disintegrates.

† Edited by Yu.S. Lipatov.

The relation between the external force F and local stresses in the adhesive and at its boundary with air depends on the thickness and nature of the ribbon, on the thickness and nature of the layer of glue, etc; a mathematical expression for this relation is given in section V, 4. If the local stresses have been determined correctly, the second of the errors enumerated above is eliminated.

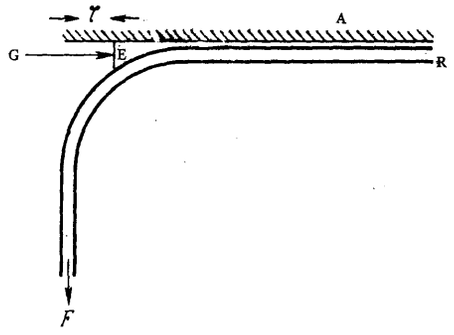

Figure 1. Peeling of a ribbon R from a rigid adherend A; G = adhesive; E = its edge.

All solids are inhomogeneous. They contain cavities, impurity inclusions, crystal lattice defects, and other flaws. Usually each flaw gives rise to a concentration of stresses in its vicinity. If the *average* stress along the cross-section of the solid is σ (g cm^{-1} s^{-2} or kgf m^{-1} s^{-2}), then the stress at the flaw may be 100 σ or even 1000 σ. The true *local* stress σ_m, which should be defined as "local at a square" [locally in a cross-section ?Ed. of Translation] is much greater than σ and a crack is initiated at the point where σ_m is particularly high. This is in fact, why for a given average stress σ, σ_m varies from point to point and solids disintegrate via a crack growth mechanism and not immediately into individual atoms or molecules. As long as the investigator bears firmly in mind the radical difference between σ and σ_m, he avoids the third error.

If the description of peeling described here is correct, then it is clear why one cannot employ the fourth stratum as a basis. The crack arises and spreads in the adhesive layer. In many systems its distance from the interface (adhesive — adherend) exceeds by a factor of hundreds and thousands the "radius of molecular action"; thus the phenomena which occur along the crack cannot depend on forces acting across its boundary.

Here one must ask the obvious question why cracks cannot originate and grow exactly between two solid phases. In this case one might expect the equality or at least a close relation between σ_m and A. The answer is that interfacial rupture is altogether unlikely. Fig. 2 illustrates the boundary between two solids; the circles represent the molecules of one solid and the crosses those of another. The [dotted] lines show that the crack spreading from left to right may be propagated in different ways. If the probabilities of all three ways are equal, the probability that the rupture will occur *between* the two phases is 1/3. The probability that the crack will occur between two phases at a distance equivalent to 11 molecules is $(\frac{1}{3})^{10}$, i.e. approximately 1 : 59 000; in other words an interfacial crack with a length equivalent to 11 molecules can be expected in only one adhint out of 59 000. The probability is even smaller if the attraction between the adhesive and the adherend (if the adherend is a material with strong cohesion) is mostly greater than the attraction between the molecules of the adhesive; this follows from the familiar general expression for van der Waals constants a: $a_{12} \simeq \sqrt{a_1 a_2}$, where a_1 is the constant for two molecules of type 1, a_2, the constant for two molecules of type 2, and a_{12} the constant for a molecule of type 1 and a molecule of type 2. If $a_1 > a_2$, then $a_{12} > a_2$. In a metal — adhesive — metal system, the numeral 1 refers to the metal and the numeral 2 to the adhesive.

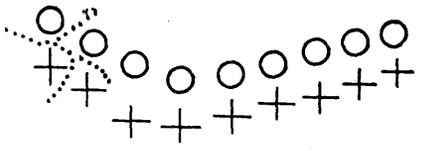

Figure 2. The growth of a crack (dotted lines) between two solid bodies.

The impossibility of rupture exactly along the interface can be proved also in a different way. Since the probability of finding a particularly weak spot in a solid is greater the larger the specimen, the breaking stress (and hence $\sigma_m : \sigma$) usually increases if the thickness of the plate undergoing rupture is reduced. The thickness of the adhesive layer is rarely below 0.01 cm and the "thickness of the slits" between different molecules in Fig. 2 may be estimated as 10^{-9} cm; evidently, for equal molecular forces, a smaller stress is needed to rupture a thicker layer.

Since material A cannot be separated from material B exactly along their boundary, the forces acting between A and B are not involved in the separation process; rupture takes place far from the boundary and the stress necessary for it cannot yield any information about the true adhesion between A and B. Thus the first postulate on which the upper part of the pyramid of errors rests is as misleading as the second. A more detailed examination of the problem of the value of A for the strength of adhints may be found in the author's book[2].

II. HOOK-TYPE ADHINTS

The main conclusion of the first section of this review is that the experimental values of f, F, and W are independent of the molecular adhesion A and cannot be used for its determination. The breaking stress is determined by the mechanical (and not chemical) properties of the components of the adhint and by the geometry of the system. The significance of this general rule can be more conveniently considered separately for each class of adhesive joint. From the standpoint of the mechanism of strength, there are three such classes. The simplest to understand and probably the oldest class is that of hook-type adhints, which occur in consequence of "mechanical adhesion". Their adherends are fibrous or porous solids (fabrics, paper, natural wood, etc.). During the formation of such joints, the liquid adhesive flows round the

fibres or filaments of the adherend and after solidification forms hook or loops around each fibre. When, say, a postage stamp is stuck to the envelope, the mechanism of joint formation differs little from the mechanism responsible for the joint between two fabrics sewn together. As in sewing, molecular contact between the adherend and the adhesive is not required in hook-type adhints, which constitutes an extremely favourable factor, since extensive purification of materials such as paper, cardboard, or wood is almost impossible even in the laboratory let alone in industry.

When a breaking force is applied to a hook-type adhint, one of the two components (the fibres of the adherend or the filaments of the adhesive) breaks because they cannot be separated in any other way; in certain systems the break occurs partly in one material and partly in the other. At any rate, f, F, and W are fully determined by the mechanical strength of the fibres which are intrinsically weak or at which the external force is concentrated; unfortunately a mathematical formulation of the strength of hook-type adhints does not as yet exist.

Generally speaking, in order to obtain satisfactory hook-type adhints, it is necessary to ensure that the adhesive penetrates the space between the adherend fibres and solidifies there. Thus the incorporation of the adhesive in the adherend is the most significant process in the life of a hook-type adhint. This process was investigated several years ago[3,4]. Two questions were investigated: (1) to what depth the adhesive should penetrate into the fibrous body in order that the strength of the adhint should reach its maximum possible value for the given system and (2) what time is necessary for such incorporation. Different types of paper and cardboard served as adherends and the extreme inhomogeneity of these materials has been the main source of the inaccuracy and the poor reproducibility of the quantitative results.

A clear answer to the first question was obtained for filter paper which is much more homogeneous than many other varieties. It was glued on one side to a thick metallic plate and on the other to an aluminium foil; the foil was peeled off after the solidification of the adhesive. For small amounts of glue (m, g m^{-2}), the resistance to peeling increased with m, but, when m exceeded 15 or 20, the resistance no longer depended on m. For this paper, 20 g per m^2 corresponded to a thickness of penetration to a depth of approximately 30 μm. The average diameter of the fibres in the paper was $8-10$ μm. Thus it was sufficient to engage by the adhesive hooks two or three fibres in the bulk of the adherend in order to attain the maximum resistance possible for the given paper.

In these experiments the adhesive employed was a melt of poly(vinyl acetate). When an aqueous solution of dextrin was employed instead, the liquid penetrated into the adherend to a considerable depth, but left behind fewer hooks after the removal of solvent, so that peeling from paper glued with dextrin was easier for all values of m than when the melt was employed.

When the foil was stripped from a laminate cardboard, the results depended on whether the foil was glued to the edge or to the centre of the cardboard rectangle. In the first case the resistance was smaller, since the external force was transmitted immediately to the loosest of the layers and the crack passed along this layer. In the second case the cleavage had to begin in an external layer, which is usually denser and stronger than the others; therefore a much greater force was required to initiate peeling. As long as the experimentor believes that he is measuring molecular adhesion between the glue and the cardboard, it will not occur to him to alter the site of the joint from the edge to the centre and vice versa.

In order to answer this question, a polyethylene vessel containing a measured amount of glue was turned upside down with the opening pointing downwards towards the paper and was then drawn along the paper at a constant velocity (u, cm s^{-1}). The depth of penetration of the glue (τ, cm) was then measured with the aid of a microscope. If the diameter of the aperture is b (cm), each point on the surface of the paper remained in contact with the glue over a period b/u seconds. During this time, the glue penetrated into the adherend to a depth τ (cm), so that the average rate of penetration was $\tau u/b$ (cm s^{-1}). The measured values confirmed the simple hydrodynamic description of the process for simple liquids.

III. IMPROPER ADHINTS

The second class of adhesive joints is also of respectable antiquity but its nature was understood only several years ago. Improper joints contain weak boundary layers. The concept of weak boundary layers is as significant for the modern ("rheological") theory of adhesive joints as the rejection of the idea that rupture takes place exactly at the interface, as stated in the first section. The adherends in improper adhints either do not contain any pores and voids capable of being filled with glue or they have at least a dense surface layer: for example, paper coated with varnish or a dyed wooden plate may be incapable of being impregnated with glue; the usual metals, glasses, and plastics are also incapable of forming hook-type adhints. The absence of voids is a general property of adherends in improper and proper adhints.

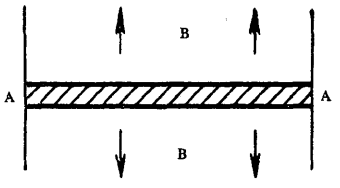

Figure 3. A proper butt joint. A = adhesive; B = adherends.

When it is said that two cylinders of a substance B are glued together with an adhesive A, only two materials are mentioned. In the schematic representation of such an adhint (Fig. 3) only two materials are indicated. In improper adhints there is at least one more substance, which is located on the boundary or along both boundaries between A and B (Fig. 4). When a breaking force is applied to the adhesive joint shown in Fig. 4, a crack arises in the boundary layer if its strength is less than that of the materials A and B. Thus the adhint is ruptured in the material which is not even mentioned in the description of the system and is determined by its properties.

According to their origin, weak boundary layers can be divided into seven groups, since three phases are involved in the formation of an adhesive joint: the medium (usually air), the adhesive, and the adherend. The material of

the weak layer can enter the adhint from the medium (air) (a), from the adhesive (b), from the adherend (c), from air and the adhesive (d), from air and the adherend (e), from the adhesive and the adherend (f) and from all three phases (g). Certain examples of these types will be described in the present section.

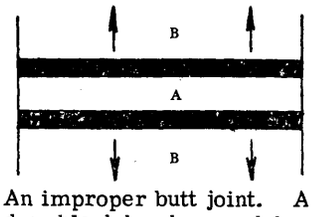

Figure 4. An improper butt joint. A = adhesive; B = adherends; black bands—weak boundary layers.

1. Weak boundary layers of the *first group* are frequently encountered. When the liquid adhesive spreads on the surface of the adherend, it must displace air from each hollow on the rough surface. If the displacement is incomplete, bubbles of air remain between the adherend and the solidified adhesive, as shown schematically in Fig. 5. Each bubble concentrates stresses in the adjoining regions of the solid; this effect was already mentioned in the first section and it is expressed by Eqn. (4) in the fifth section.

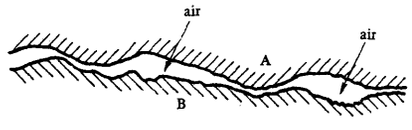

Figure 5. Air bubbles between an adherend B and an adhesive A which has not achieved complete contact with the adherend.

Air remains between the adhesive and the adherend either because the wetting of the adherend by the liquid adhesive is poor or because the adhesive joint was prepared hastily and sufficient time was not allowed for the liquid to flow into all the pits and grooves. Wetting is determined by the contact angle θ or more accurately the advancing contact angle θ_A. A modern treatment of contact angles was recently given in a book by the present author[5] but it is outside the scope of the present review. One need only point out that, when the equilibrium contact angle is zero and the advancing contact angle is negligibly small, one should employ as far as possible only adhesives giving $\theta = 0$ on the surface of the adherend.

One sometimes encounters the view that the requirement for $\theta = 0$ arises because the liquid wetting the solid has a strong affinity for it; it is believed that the liquid A displaces air from the surface of the adherend B because the molecular adhesion between A and B is high. This approach is unconvincing. The contact angle depends not only on the attraction of B to A but also on the attraction or air (or generally speaking a third phase) to A and to B. If, say, water wets poorly a solid surface, one cannot conclude that the attractive forces between these two phases are small; if the solid is heated in mercury until all the gases have volatilised and is then treated with water, the latter can readily displace mercury so that an impression will be created that the attraction of water to the adherend is high. One can appropriately mention here the mechanism of soldering. If a drop of liquid solder is deposited on what appears to be a metal the drop does not spread. Supporters of molecular adhesion have concluded that in this case the attraction between the metal and the solder is so weak that no adhesive joint is obtained. In reality liquid solvent does not displace air from the surface of the oxide but it does readily displace fused rosin from the surface of the metal.

An example resembling soldering was investigated by Nicholas and Poole[6]. Oxygen-free copper gave $\theta = 20°$ at 1200°C on tungsten and f for joints between tungsten and copper was approximately 1900 bars (1 bar = 10^6 g cm^{-1} s^{-2}). When there were 251 parts of oxygen per million parts of copper, θ reached 70° and f did not rise above 320 bars. A dark layer, the composition of which probably corresponded to the oxide WO_3, could be seen in this system as the boundary between copper and tungsten (a magnification of 450). The oxide did not behave itself as a weak boundary layer but copper did not wet it; this cavities remained between copper and the oxide after solidification.

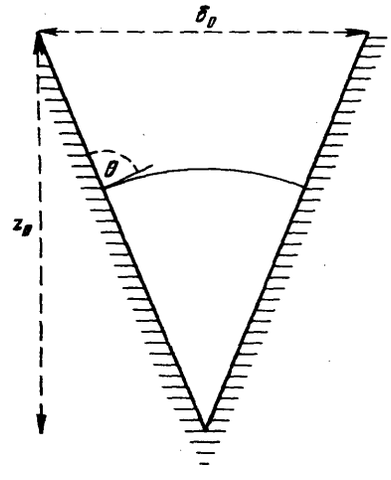

Figure 6. Displacement of air from a scratch by an adhesive flowing downwards. Maximum width of scratch—δ_0; depth—z_0; contact angle (in liquid adhesive)—θ.

In all probability the unwettability of polytetrafluoroethylene is the main reason why nothing can be glued to this polymer. There exists yet another possibility: namely that it contains impurities which act like those in polyethylene (see section III, 2), but it is difficult to reconcile this with the observation that PTFE copolymers fused and cooled on a clean metal surface (in air) form with the latter very strong adhesive joints.

The displacement of air by a liquid adhesive always requires some time and in many systems the time is very long. Hollows in solid surfaces usually have an irregular shape which is not susceptible to mathematical treatment. It is therefore necessary to resort to models. Fig. 6 shows a channel with a depth z_0 (cm) and a width at the top δ_0 (cm); a liquid fills it above and forms with the walls an advancing contact angle θ_A; the thin continuous lines indicate the position of the meniscus t seconds after the beginning of the experiment. The shortest distance between this line and the top of the channel is designated by the symbol z. If the surface tension and the viscosity of the liquid are denoted by the symbols γ (g s^{-1}) and η (g cm^{-1} s^{-1}) respectively, the following approximate formula is valid:

$$z_0 \ln \frac{z_0}{z_0 - z} - z = \frac{\delta_0 \gamma \cos \theta_A}{6\eta_m^{z_0}} t . \quad (1)$$

It is readily seen that z will equal z_0, i.e. the liquid will reach the bottom, only after an infinite time t whatever the values of γ and η. This result is obtained because the walls of the channel are assumed throughout to be ideally straight; since in reality they are rounded near the bottom, $z_0 - z$ reaches zero for finite values of t; at any rate, it is clear that haste in the preparation of adhints can result in the formation in the latter of weak boundary layers of the first group.

The flow of liquid may be accelerated by an external pressure[7], but this pressure P must be greater than the product $2\gamma\cos\theta_H/\delta_0$ (g cm^{-1} s^{-2}) in order to affect seriously the rate of flow; when θ_0 is small, i.e. the channel is a crack, the required P is much too high for practical purposes. The usual adhesives are non-Newtonian liquids, i.e. their viscosity depends on the rate of flow; estimates of this correction may be found in the literature[7,8]. The viscosity of the adhesive very often increases with the time it takes to fill the hollows in the adherend because of the evaporation of the solvent, the cooling of the melt, or a chemical reaction; if the rate of this increase is comparable to the rate of flow, the adhesive may solidify without reaching the bottom of the channel, so that air bubbles remain between the glue and the adherend[9].

2. Weak boundary layers of the *second group* consist of a substance which was previously contained in the adhesive. Industrial polyethylenes are the most thoroughly investigated representatives of this group. When the usual polyethylene is fused on a clean metal, glass, etc. support and is allowed to set, the solidified drop can be readily scraped off with a fingernail. Printing ink sticks to polyethylene but readily splits off from the latter on removal of the solvent. This lack of capacity of polyethylene for "adhesion" was previously explained, and even now continues to be explained[10], by the fact that the force field generated by the alkane chain $-CH_2-CH_2-CH_2-$ is weak; the attraction of methylene groups to solids is so weak that it can be readily overcome by a negligible external force.

The myth of the inadequate molecular adhesion of polyethylene was destroyed and the true cause of the weakness of polyethylene adhints was discovered in a series of investigations[11-15].

Firstly, technical polyethylene was purified by dissolution in boiling toluene or xylene and precipitation with acetone or butanone. The precipitate, which usually contained more than 95% of the initial polymer, did not contain polar groups (for example carbonyl groups) which can be almost always found by examining the infrared spectra of unpurified polyethylenes. The content of branched chains (for example isopropyl groups) was lower than in the initial material. Thus after purification the composition of polyethylene was closer than before to that of the ideal compound $-CH_2-CH_2-CH_2-$; nevertheless it proves to be an excellent adhesive and was used successfully to glue metals to metals, glasses to glasses, and glasses to metals[11]. All adhesive joints with purified polyethylene were made in an atmosphere of nitrogen in order to avoid oxidation.

In certain cases purification increased the tensile strength by a factor of 50. Such enormous increase of "adhesive capacity" could not be accounted for by a physical change in the material, since the density, wettability, and other measured properties did not alter appreciably as a result of purification. The author concluded that crude polyethylene contains impurities soluble in the liquid polymer and eliminated from it during solidification and crystallisation. Some of them accumulate in the surface layer. If they are almost liquid at the experimental temperature or their strength is reduced, the surface layer as a whole is characterised by a low resistance to rupture. Adhesive joints prepared with crude polyethylene must be represented by Fig. 4 and not Fig. 3; when a tearing axial force (arrows in Fig. 4) is applied, the weak boundary layer is split in two and the strength of this layer alone (and not of the polyethylene itself) determines the experimental strength of the adhint. Purified polyethylene contains almost no insoluble impurities, does not form weak boundary layers, and gives rise to strong adhesive joints.

Secondly, the resistance to rupture of the compounds just mentioned was compared[12] with the strength of polyethylene itself. If weak boundary layers are absent, the system consists of only two components: the adherend and the adhesive and rupture naturally occurs in the weaker phase. In all cases this was purified polyethylene, since the adherends were only metals (steel, copper, and aluminium) and glasses. Since the crack arose and spread in polyethylene, the rupture of the adherend — polyethylene — adherend system was largely analogous to the rupture of polyethylene itself. Fig. 7, which presents some of the results obtained by the present author and his coworkers[12,15], does indeed show that the strength of polyethylene adhesive butt joints is almost equal to the strength of polyethylene rods (the dashed line on the right-hand side of the diagram) when the layer of adhesive is fairly thick (for example 150 μm). The reason why the breaking stress f (expressed in bars in Fig. 8) increases when the thickness δ of the adhesive diminishes is explained in section V, 1. At any rate, it is clear that f is determined by the strength of the adhesive and has nothing in common with molecular adhesion between the adhesive and the adherend. Polyethylene could be seen with the naked eye or with the aid of the microscope on both rupture surfaces.

Thirdly, a low-molecular-weight substance was mixed with purified polyethylene in order to restore it to the "anti-adhesive" or non-glueing state[13]. Oleic acid, which is a typical polar compound, proved to be suitable for this purpose. On the basis of the molecular theory of adhesion, oleic acid should increase the "adhesive capacity" of non-polar polyethylene. In fact the admixture of 1 mg of the acid in 1 g of purified polyethylene reduced its resistance (Γ, g s^{-2}) to peeling (of aluminium foil glued with polyethylene to glass) and when the added concentration reached 1%, Γ fell to 10 kdyn cm^{-1} from 65 kdyn cm^{-1} for the uncontaminated polymer.

Fourthly the accumulation of oleic acid on the surface layer was confirmed by electrical measurements[14]. Purified polyethylene and its mixtures with 0.1, 0.2%, etc. of oleic acid were placed in an atmosphere of moist ammonia and the surface conductivity of the polymer was measured. The curve relating the surface conductivity $1/\chi$ to oleic acid concentration c was found to resemble very closely the $\Gamma = f(c)$ curve mentioned in the previous paragraph; when the concentration was raised from 0.1 to 0.4, $1/\chi$ fell by a factor of 6. Probably the limiting solubility of oleic acid in the solid polyethylene investigated is approximately 0.1%; when c is above this minimum, the excess acid accumulates near the surface, where it reacts with ammonia and forms ions responsible for the enhanced conductivity.

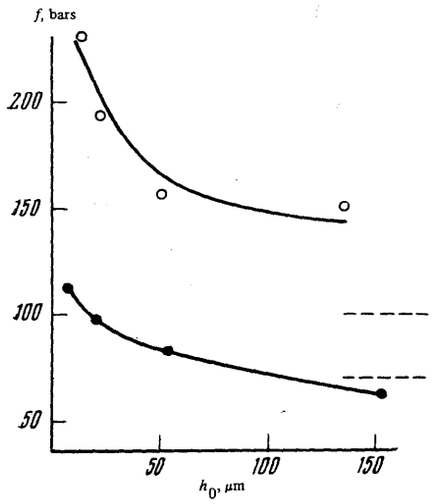

Figure 7. Resistance to rupture of "glass — purified polyethylene — glass" adhints (upper curve) and "steel — purified polyethylene wax — steel" adhints (lower curve). Abscissa—thickness of the layer of adhesive in micrometers. Ordinate—breaking strength in bars. The dotted lines indicate the tensile strength of the free polyethylenes.

Fifthly, the accumulation of the impurity near the surface and hence the formation of a weak boundary layer was eliminated by increasing the solvent power of solid polyethylene[15]. Petrol and water are almost immiscible, but their complete mixing can be achieved by adding sufficient acetone. By analogy, when polyethylene is treated with a substance soluble in solid polyethylene and capable of dissolving oleic acid, the acid will cease to accumulate in the surface layer and to reduce the strength of the adhesive joint. Ethyl palmitate $C_{15}H_{31}COOEt$ was found to be such a substance. The breaking stress for specimens with a "pin" was less than 1 bar when the adhesive was a mixture of 99 parts of polyethylene and one part of oleic acid, while the adhesive consisting of 94 parts of polyethylene, one part of oleic acid, and five parts of palmitate was ruptured following the application of a stress of 75 — 95 bars, i.e. was almost equal to the resistance of the purified polymer.

This example is particularly instructive if it is compared with the predictions of the molecular theory of adhesion. According to this theory, polar molecules increase adhesion. In fact polar oleic acid caused a catastrophic decrease of f; ethyl palmitate, the dipole moment of which is equal to that of oleic acid, does not alter f at comparable concentrations in purified polyethylene and its admixture in polyethylene contaminated with oleic acid sharply increases f. The resistance to rupture depends on solubilities and not on polarities.

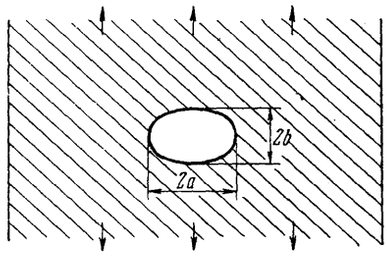

Figure 8. Concentration of stresses at an elliptical opening in the film. Axes of the ellipse—$2a$ and $2b$.

In the disintegration of systems containing weak boundary layers of the second kind, part of the layer remains on the adhesive and the remainder on the adherend. This separation has been demonstrated by simple weighing[13] and by electron microscopic observations[16].

It is clear from the foregoing that the formation of weak boundary layers of the second kind may be prevented either by removing harmful impurities from the adhesive or by increasing their solubility in the solid polymer. The third method is widely used in industry: impurities are decomposed by oxidation or by some other chemical reaction. In the fourth method they are polymerised. Polyethylene is subjected to an electric discharge in helium or another inert gas[17]. This results in the cross-linking of short molecules on the surface layer, which sometimes becomes several times stronger than the main bulk of the adhesive. Adhesive joints with such polyethylenes are ruptured in the polyethylene and for them f is determined by the strength of the polymer.

Other examples of weak boundary layers of the second group were apparently observed by Buiko and Zinchenko[18], Foster and Winn[19], etc.

3. Weak boundary layers on the adherend are also a common phenomenon. The aim of the cleaning of metallic surfaces before varnishing, enamelling, etc.[20] is to remove such layers. Since chemical contamination of the surface does not impair its mechanical properties, cleaning is unnecessary: adhesive joints with aluminium are formed daily and can be maintained indefinitely although the surface of the metal is covered by a continuous oxide film from edge to edge.

The effect of a random contamination of the metallic surface on the strength of adhints has been described in Buchan's book[21]. The attachment of rubber to brass is frequently performed in industry but is sometimes unsuccessful. Buchan studied the surface of electrolytic brass

specimens to which it was difficult to attach rubber. The complex salt $[Zn(NH_3)_6]\{Zn_3[Fe(CN)_6]_2\}$, which probably in fact formed the weak zone, was detected on some specimens. Theoretically, the cyanide electrolytes from which brass was precipitated contain no iron but sufficient iron ions entered the bath from the tubes and instruments employed in the manufacture to make possible the synthesis of the above salt.

The effect of adhesive butt joints of the type "steel — epoxy-resin — dye — tinplate — epoxy resin — steel" was investigated as a function of the purity of the tinplate[22]. Stearic acid deposited on the plate in an amount of 0.004 mg per cm^2 reduced the resistance to rupture f by 30 — 40%; when the surface concentration of the acid was raised to 0.04 mg cm^2, f was 50% below the value for the clean plate. In the presence of contaminations, the rupture surface passed along the boundary between the dye and the tinplate, i.e. in a weak boundary layer.

An example of a non-metallic surface is mentioned by Kamenskii[8]. The attachment of an unvulcanised rubber mixture to old vulcanised rubber yields adhints with low values of Γ. If the brittle and oxidised surface layer of vulcanised rubber is removed by brushing with a wire brush, the breaking stress increases, say, by a factor of 6.

A later example refers to polypropylene[23]. A double metallic plate — epoxy-resin — polypropylene film — epoxy-resin — metal adhesive lap-joint was ruptured readily and the rupture surface did not differ in any way from the initial surface of polypropylene. However, it was sufficient to treat the film with trichloroethylene vapour for several seconds to increase the resistance to rupture by a factor of 6 and to shift the rupture plane from the surface to the bulk of the film.

Industrial polycaprolactam apparently constitutes an even more striking example of weak boundary layers than polypropylene or polyethylene. It contains up to 12%, of the monomer[24], which is seen on certain films as a crystalline deposit. As long as the monomer is present on the surface of the polymer, neither polychloroprene nor polyisobutylene (deposited on a fabric ribbon) form strong adhints with polycaprolactam; however, the resistance (Γ) to rupture increases several times after the extraction of the monomer with water[25]. Unfortunately the authors did not compare the experimental Γ with the theoretical values, so that the reader finds it difficult to judge how complete the purification of polycaprolactam has been. Different elastomers form with unpurified polycaprolactams adhesive joints which have different resistances Γ. It would be instructive to compare the sequence of these elastomers in terms of increasing Γ with their sequence in terms of increasing capacity to dissolve the monomer; possibly the two series will be similar.

4. A weak boundary layer formed on interaction between the adhesive and the medium was observed when purified polyethylene was employed as the adhesive. As already stated, all polyethylene adhints described in section III, 2 were formed in an atmosphere of nitrogen. When similar adhints are prepared in air, polyethylene is oxidised (becomes yellow) at a high temperature and the oxidation products form a weak boundary layer, so that the strength of the adhint decreases.

5. Weak boundary layers of the *fifth group* are formed most often when an adhesive joint prepared in an inert medium is then introduced into a corrosive environment. Silicate glasses swell in water. Glass filaments in glass laminates also swell if the access of water to them is not prevented. Swollen glass is a weak material; in glass laminates ruptured underwater the crack usually arises in the swollen interfacial layer. Bitumen protects aluminium from corrosion simply by preventing the access of water to the metal. If water nevertheless reaches it, a phase, which may be called an aluminium hydroxide gel, gradually grows between the metal and the protective coating and bitumen is readily separated from aluminium[26].

In both examples just quoted the mechanical effects of swelling probably play a decisive role. The specific gravity of swollen glass is lower than that of dry glass and the specific gravity of aluminium hydroxide is lower than that of the metal. Thus a weak boundary layer splits the adhesive away from the adherend like a wedge. Unfortunately this mechanism has not yet been subjected to mathematical analysis.

It may be that swelling also weakened adhesive lap joints of the type "aluminium — epoxy-resin — aluminium", which were prepared in various atmospheres and were allowed to remain in the same medium for 1 h.[27] After such ageing, their f values were measured. In dry argon the resistance was only 5% lower than before ageing but in an atmosphere comprising 80% of argon and 20% of oxygen with a relative humidity of 50%, ageing reduced f by a factor of 2.

6. Weak boundary layers of the *sixth kind* are formed most frequently when the adhesive reacts chemically with the adherend. Long ago it was already noted that a highly alkaline casein glue forms weak adhesive joints of the type "wood — glue — wood". Alkali corrodes (hydrolyses) wood and gives rise to a weak zone between the adhesive and the unaffected wood. Clearly similar difficulties arise if an acid adhesive is employed to cement copper, zinc, iron, and other metals sensitive to acids. Less obvious examples are also known[28].

When rubber is vulcanised on brass, the joint will be weak in those cases where the brass surface is immaculate (see section III, 3). In many cases it is sufficient to introduce an excess of sulphur into the rubber mixture (for example 10% instead of 2%); the excess sulphur reacts with copper in the brass and forms copper sulphide, which is segregated in the form of a powder between the two main phases[21]. The excess sulphur may be harmful also in the absence of copper. A mixture of sulphur and raw natural rubber was placed on the surface of a synthetic vulcanised rubber, the entire system was heated, cooled, and the film of natural rubber (now vulcanised) was peeled off. The resistance to peeling fell when the system was heated too long; probably sulphur diffused from the mixture to vulcanised rubber and increased the brittleness of its surface layer[29].

The examples just quoted are particularly instructive, since there are still investigators[30] who believe that the chemical bond between the adhesive and the adherend may be the cause of strong adhesive joints. It is much more likely that the chemical reaction weakens the adhint instead of stabilising it.

The chemical reaction yields a new substance which is frequently insoluble in the starting materials and is independent of them; it is neither willing nor able to couple, in the words of Lucretia, the two adjacent phases.

The adhesive and the adherend do not form weak boundary layers solely via chemical reactions; sometimes diffusion is also sufficient. Two relevant examples will be quoted.

If a metal K in contact with a metal M is heated, the diffusion of the atoms of K into the lattice of M may be faster than the diffusion of M into K. Then cavities

remain in the metal K near its boundary with M; initially they are of atomic dimensions but subsequently they merge into pores, which are visible under the microscope. In other words, a weak boundary layer is produced. It was noted[31,32] on prolonged heating (25 days at 800°C) of a copper plate coated with brass or aluminium bronze (93% Cu, 7% Al). Cavities with diameters up to 0.001 cm were observed in these alloys at the very boundary with copper.

Gold filaments welded to aluminium were difficult to tear off and the rupture apparently occurred along the boundary between the two metals. In order to elucidate the mechanism of the phenomenon, the system was maintained at 450°C for 2 h and then the transition layer between aluminium and gold was investigated[33]. It was found to contain seven phases: aluminium, $AuAl_2$, AuAl, Au_2Al, Au_2Al_2 (?), Au_4Al, and gold, and numerous pores were visible along the boundary between the Au_5Al_2 (?) and Au_4Al phases. The crack spread in the region of the pores and not between the two different metals. This example too is instructive. Supporters of the molecular theory of adhesion would calculate the attraction between the ideal crystals of gold and the ideal crystals of aluminium in an ideal contact and would compare the adhesion thus calculated with the experimental strength of the weld. How remote is reality from academic theories!

7. All three phases present in the formation of the adhint participate in the creation of weak boundary layers of the *seventh group*. Such systems were studied by Black and Blomquist[34]. When the adhesive lap joint consisted of an adhesive and two aluminium plates, the breaking stress at room temperature was approximately 122 bars. The adhesive was a mixture of eight parts of phenolic resin and one part of epoxy-resin. After the system had been heated (288°C) for about 100 h, f (still at room temperature) decreased to 65 bars, so that the system may be regarded as comparatively temperature resistant. The strength of adhints of the same dimensions but with stainless steel adherends was fully comparable, before heating, with the value of f for aluminium joints, but after heating f was negligibly low. In order to reduce f almost to zero, the system had to be heated in air or oxygen; heating in nitrogen had little influence on f. The authors concluded that a component of stainless steel accelerates the oxidation of the adhesive by gaseous oxygen, i.e. catalyses the reaction. Systematic experiments showed that copper, the classical accelerating agent for the oxidation of organic compounds, is responsible.

The disintegration of the adhint began at a three-phase boundary where air, the adhesive, and the metal meet; a visible strip of oxidised adhesive gradually spread along the metal surface. All three phases were involved in the formation of a weak boundary layer: the layer did not arise when the metal contained no copper or the gas contained no oxygen and when the adhesive was a polyamide or a butadiene — acrylonitrile copolymer.

What lesson can we draw from this section? Along the boundary between the adhesive A and the adherend B, there are in many systems weak materials, different from both A and B; cleavage or rupture occur within the bulk of these materials. If the experimenter does not suspect their existence, he may decide that the disintegration was of the adhesive type, i.e. that the crack occurred exactly between A and B and that his task may be to strengthen the mutual attraction between these two substances. In fact he must discover with what kind of weak boundary layer he is dealing (the first group? the second group?...) and how the formation of such a layer can be prevented. Weak boundary layers can never be disregarded with impunity.

IV. LOCATION OF RUPTURE

The concept of weak boundary layers permits a more critical approach to the main problem of adhesive joints already discussed from the theoretical standpoint in the first section of the review. If the rupture of the adhint is seen with the naked eye to occur along the interface, the question arises of whether one is dealing with an adhesional failure or a cohesional rupture of a weak boundary layer. As just stated, the answer to this question is extremely important: the entire plan of future work on the improvement of adhints depends on it.

The conclusion that the rupture of adhesive joints hardly ever occurs exactly between the adhesive and the adherend has unfortunately been confirmed by only a few experiments undertaken to test it. It is difficult to make such experiments convincing. Generally speaking, molecular forces decrease very rapidly with distance from a given molecule or a given solid. The molecular attractive forces between two bodies A and B may be neglected compared with the forces between A and C and between C and B when the thickness of the third substance C between A and B exceeds several ångstroms; the majority of studies leading to the opposite conclusion are based on an erroneous interpretation of experimental data. Thus one can assert that experimental results confirm the above conclusion even if the residual adhesive (or one of its components) on the adherend after rupture is not thicker than several ångstroms; in other words, the monomolecular third substance on the rupture surface of the adherend already demonstrates that the failure was not adhesional. The molecular layer of the adherend (or one of its components) on the surface of the adhesive after rupture is of course also instructive.

Analytical detection of monomolecular layers on the surface of a solid is very laborious. Methods whereby it is possible to detect surface contaminations with a thickness of 100 or 1000 Å may prove to be unsufficiently precise. This remark, applies, for example, to luminescence analysis, whereby it is possible to demonstrate transition layers (at the boundary between two polymers) with a thickness of 1 μm [35] and which clearly reveals the difference between an uncontamined surface and a surface coated with a film having an average thickness of 10 μm.[36] Unfortunately the difficulties are not confined to purely analytical problems. In many cases it is not known what should be sought. If, for example, there is a weak boundary layer of the second kind, the impurities migrating onto the adherend may be chemically quite different from the main component of the adhesive. Thus, after the rupture of an aluminium — polyethylene adhint, not even a trace of polyethylene was detected on the metal but this does not imply that the rupture occurred exactly along the boundary: we may suppose that, instead of the polymer, the antioxidant added to the polymer passed onto the adherend and since the experimenter did not look for it at all he did not find it. The situation is even worse in the case of weak boundary layers of the first group. If before rupture air occupies a considerable proportion of the interface, it cannot be distinguished from the air which penetrated the space between the adhesive and the adherend at the instant of rupture. Here the presence of a weak layer must be inferred from the breaking stress f. We shall suppose that an adhesive which wets freely an adherend B_1 forms with the latter adhints the value of f for which is 100 (in terms of arbitrary units). If the same adhesive in an adhesive joint of the same type and of the same dimensions gives $f = 1$ with an adherend B_2 and no traces of the adhe-

sive can be detected on the rupture surface of B_2, one can conclude with a considerable degree of certainty that a layer of air almost separated B_2 from the adhesive even before the rupture of the adhint.

We shall consider five experimental studies on the mechanism of apparent adhesional failure. Huntsberger[37] treated ribbons of an alkyd resin (with a thickness of 4 μm) with a solution of polyisobutylene from which a film approximately 25 μm thick was obtained after evaporation of the solvent and then one ribbon was peeled from the other. The thickness of the alkyd film after rupture was the same as initially. This result is unconvincing, since it was not shown how the solvent affected the alkyd film—whether or not it became stretched during rupture, whether a certain amount of the alkyd resin remained on polyisobutylene, and what was the effect of the surface roughness on the measured thickness.

Johnson[38] rubbed the rupture surface with a potassium bromide powder and measured the infrared spectrum of the powder scraped off the surface. If the powders from the surfaces of the adhesive and the adherend were identical, then clearly the rupture occurred in a particular material and not *between* two different materials. This happened, for example, when a varnish film (of unknown composition) was deposited from solution onto an organic adherend (also insufficiently characterised). The resistance to rupture was very low and both spectra showed absorption lines due to the phthalate esters employed as plasticisers. Evidently the failure, which at first sight appeared to be typically adhesional, consisted in the splitting off of a surface phthalate film. When polymers without a plasticiser were employed, both spectra were still almost identical. They corresponded to one of the polymers slightly contaminated with the other. In a third system, a dye, i.e. plastic + pigment, was coated with the solution of another polymer. After drying and peeling, the spectra were found to be different. Unfortunately none of the above systems was investigated in detail. Four tacky plasters were clamped to five adherends, were peeled from them at two different rates, and the contact angles θ of a drop of water in air (at 50% humidity) on the adherend were determined[39]. Of the 49 results obtained, only four are quoted here; the changes in contact angle were in the same direction as in all other systems. The angle θ on glass was 11° before contact with the plaster. When the plaster was stripped off rapidly, $\theta = 36°$ was obtained; after slow peeling, θ was 44°. Water on the plaster gave $\theta = 92°$. Thus θ changed in all cases in the direction from the adherend to the adhesive and was closer to θ for the adhesive when the peeling was slow and there was more time for the adhesive to displace air from the hollows on the surface of the support. In this study measurements were made of the contact angle of water which one must suppose did not alter (or only slightly altered) the properties of the organic adhesive (polyacrylate in the preceding example). It is incorrect to employ for the estimation of wettability liquids which are good solvents of traces of the adhesive remaining on the adherend. Clearly a drop of solvent in a volume of perhaps 1 cm^3 very rapidly removes contaminations weighing 0.000001 g per square centimetre[40].

If the adhesive contains labelled atoms, its traces on the support after rupture can be comparatively readily determined[41]. Aluminium plates were covered with a solution of polyurethanes, the solvent was removed at 60°C over a period of 16 h, and the polyurethane films were peeled from the metal. When the average roughness of aluminium was 0.76 — 1.02 μm, the average thickness of the residual adhesive on it was approximately 200 Å and for a roughness of 0.38 — 0.51 and 0.13 — 0.25 μm, the average thickness of the contaminant τ was 120 and 80 Å.

In the most valuable investigation, the thickness of the residue and the resistance to rupture Γ were measured on the same specimens[42]. Radioactive polypropylene was clamped to glass at 60°C and then peeled at room temperature. When the duration of contact at 60°C was 10 min, Γ amounted to 113 kdyn cm^{-1} and the thickness τ was equivalent to 2.4 monomolecular layers; after 60 and 120 min of contact, Γ was 236 and 226 kdyn cm^{-1} and τ was equivalent to 3.4 and 5.5 monolayers. Consequently, as long as τ remained small, τ and Γ increased together. One may conclude that $\tau = 0$ only when $\Gamma = 0$; when the adhesive is separated from the support without leaving a residue, no force is required for the rupture.

The electron microscope has so far proved relatively unsuitable for the determination of τ. The reason is that usually the method of replicas has to be employed. Traces of adhesive on the adherend may dissolve in the polymer from which the replica is made or in its solvent; in all such cases the material in which the experimenter is interested becomes invisible. Even if one chooses for the replica a high-molecular-weight compound which does not mix with the adhesive, one cannot rely on the pattern obtained. The general scientific principles of adhesion are applicable to replicas as well as to any other coating. If the replica comes into true molecular contact with the adherend, it cannot be separated from it exactly along the interface. The replica can be stripped readily only if there is never any true contact. It may be that the surface of the replica which before peeling was directed towards the adherend does not reproduce its profile in all details. The differences may be insignificant in those cases where an error of 100 or 200 Å is acceptable but the method is inapplicable when monolayers are considered.

V. PROPER ADHINTS

Improper adhints are frequently encountered in the laboratory but fortunately they constitute a rare exception among adhesive joints produced industrially on a large scale. In proper joints failure occurs either in the bulk of the adherend or in the bulk of the adhesive; there is no doubt that it is "cohesional" and not "adhesional". With the exception of a negligible percentage of adhints deliberately ruptured in laboratory tests, proper joints may be said to be immortal. An old table or an old aeroplane is scrapped when the adhesive joints between the leg and the frame in the first object or between two pieces of aluminium in the second are still in an excellent state. The deterioration of other components made the whole object valueless.

If the adherends in adhesive joints are made of metal or glass and the adhesive is an organic polymer, failure occurs much more often in the bulk of the adhesive than in the bulk of the adherend. Henceforth it will be assumed that the adhesive always breaks. The adherends in proper joints have no pores in an amount sufficient to assign the adhint to the hook type described in the second section; only in rare cases is it difficult to decide to which type the given adhint belongs.

Since rupture occurs in the adhesive, the measurement of the resistance to rupture of a proper adhint reduces essentially to the measurement of the tensile strength f_M of the adhesive. This strength can be of course found quite independently of any adhesive joints. It would

appear that f_M is a characteristic property of the polymer such as its density or chemical structure; it would also appear that the resistance to rupture f of the adhint is always identical with f_M of the given adhesive. In such a case there would be no need to measure f; the strength of all adhesive joints made with a particular adhesive would be equal to the tensile strength f_M of the polymer. In fact f_M is not a very constant quantity and f usually differs appreciably from f_M. The approximate equations

$$f = \frac{1}{\alpha}\left(\frac{\xi}{\beta} - s\right) \qquad (2)$$

and

$$f_M = \frac{\xi}{\beta_M} - s_M \qquad (3)$$

probably provides the clearest illustration of the foregoing statement. Here ξ denotes the theoretical cohesion of the adhesive, β and β_M are the stress concentration factors due to the inhomogeneity of all solids, α is an analogous factor due to the difference between the mechanical properties of the adhesive and the support, and s and s_M are residual stresses. Only ξ is the same in both equations; β is not necessarily equal to β_M and s may differ from s_M. The longest section of the author's book[2] is devoted to the difference between f and f_M which, incidentally, is pointed out at the very beginning of the present review; below this difference is discussed in an abbreviated form.

1. The factors β and β_M are equal to the ratio σ_m/σ in the layer of adhesive and in the free rod of the adhesive; as in the first section, σ_m is the maximum "local stress at a square" and in the bulk of the material and σ is the stress averaged over the entire cross-section of the specimen.

If in a solid sheet or in a solid film there is a fairly wide elliptical aperture (Fig. 8) located in such a way that the major axis of the ellipse ($2a$) is perpendicular to the external force (indicated by arrows) and the minor axis ($2b$) is parallel to it, then the stress τ_m at the right-hand and left-hand edges of the ellipse is

$$\sigma_m = \sigma\left(1 + \frac{2a}{b}\right). \qquad (4)$$

Numerous formulae for apertures of more complex shapes are quoted by Savin[43]. If the ellipse is greatly extended, i.e. resembles a crack, the ratio $2a/b$ should be very large. For example, if $a = 100b$, then σ_m/σ, i.e. the stress concentration factor β is 201. In such cases, even when the average stress σ is quite inadequate to overcome the cohesion ξ of the material, the stress σ_m may prove to be greater than the cohesion and consequently can cause the growth of the crack and the rupture of the specimen.

Clearly the probability of encountering an aperture for which the ratio a/b is large enough to give $\sigma_m > \xi$ is greater the larger the specimen. This is one of the main reasons and perhaps the most important reason for the increase of f when thinner films of adhesive are employed, as shown in Fig. 7. The greater the bulk of the adhesive, the greater the maximum value of the a/b ratio.

2. Butt joints. The coefficient α depends on the geometry of the system. Adhesive joints between the end-faces of two rods or pins would appear to be most suitable for the determination of the breaking force having a general significance. If the cross-section of the rod is S (cm²) and the external force required for rupture is F (dynes or newtons), one might conclude that the stress giving rise to the growth of a crack is F/S. Such a conclusion would be erroneous.

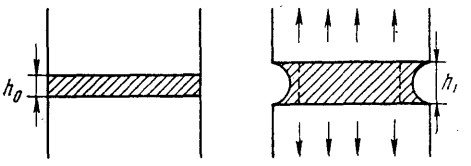

Figure 9. Concentration of stresses induced by the deformation of an adhesive "fillet". Left-hand diagram—butt joint before stretching; thickness of "fillet"—h_0. Right-hand diagram—ditto after stretching; thickness—h_1.

Fig. 9 illustrates a typical adhesive butt joint. The thickness of the adhesive layer has been increased by a factor of 20 in order to show more clearly its deformation on extension of the system. The left-hand and right-hand diagrams illustrate the system respectively before and after extension almost to rupture; the modulus elasticity of both rods is assumed to be so high that a change in their shape may be neglected. When the external force (arrows!) extends a flat cylinder of adhesive, its radius diminishes; this is Poisson compression. Fig. 9 shows that the compression cannot be homogeneous, since the adhesive is attached to adherends and its layer adjoining the adherends cannot be compressed as long as the adherends are not compressed. If this limitation did not exist, the profile of the adhesive cylinder would be as shown by the dashed line. Its true profile is indicated by the continuous curve. Clearly the cylinder is "unnaturally" extended not only along its axis but also in a perpendicular direction; it may be that both tensile and compressive stresses operate in it and the true stress σ at each point must be calculated from the theory of elasticity (or on the basis of more complex theories if the adhesive does not obey Hooke's law). This calculation has probably not as yet been performed with sufficient accuracy but the effect of the deformation of the adhesive on the distribution of stresses may be estimated roughly on the basis of the three special examples discussed below.

Suppose that the thickness of the adhesive before extension were h_0 and in the extended state h_1. We postulate that the profile of the extended cylinder is fairly close to an ellipse, the vertical half-axis of which is evidently $0.5\,h_1$; the horizontal half-axis is designated by the symbol a. We also postulate that the system was heated before deformation, so that its residual stresses s were reduced to zero. Then the volume of the adhesive will be also almost equal to the initial volume $\pi r^2 h_0$, where r is the radius of the adherend and of the initial "fillet" of the adhesive. It follows from the equality of the volumes that the half-axis a is

$$a = \frac{2r}{\pi} \cdot \frac{h_1 - h_0}{h_1}. \qquad (5)$$

On substituting this value of a in Eqn. (4) remembering that $b = 0.5\,h_1$ in this equation, we find that the stress at the

bottom of an elliptical hollow is greater than the average value by a factor α and that

$$\alpha = 1 + \frac{8r}{\pi} \cdot \frac{h_1 - h_0}{h_1^2} \quad (6)$$

Thus a purely geometrical departure of the layer of adhesive from the initial shape is sufficient to determine the stress concentration. For example, if $r/h_1 = 100$ and $(h_1 - h_0)/h_1 = 0.1$, then $\alpha = 26$. The greatest stress in the system is 26 times larger than F/S.

The above hypothesis that the layer of adhesive is free from residual stresses is invalid in the usual tests on adhesive joints. Almost always two opposed forces act along the boundary between the adherend and the adhesive. The adherend attempts to extend the adhesive in a radial direction and the adhesive attempts to reduce the radius of the adherend. If both materials obey Hooke's law and the modulus of elasticity of the adherend is many times greater than the modulus of the adhesive, the tensile stress P (g s^{-2}) acting per unity length of the boundary between the adhesive and the adherend is to a first approximation[2]

$$P \simeq \frac{h_1^{1.5} f}{2r^{0.5}} , \quad (7)$$

where h_1 and r have the previous values and $f = F/S$. Suppose that h_1/r is again 0.01; then $P \simeq 0.05\, h_1 f$. When the thickness of the adhesive layer (in the extended state) is 0.1 cm, $P \simeq 0.005\, f$ (g s^2). This tensile stress is distributed throughout the thickness of the layer, which is determined by the roughness of the interface. In this case, when the average roughness dimension is about 1 μm, the radial stress is not far from $50\, f$ (g cm^{-1} s^{-2}). In this example the maximum stress is not observed at the bottom of the elliptical hollow but at its boundary with the adherend and exceeds the average stress by a factor of 50. Its experimental estimate may be found in the paper by Mylonas[44].

Eqns. (6) and (7) are applicable, since Hooke's law holds for all parts of the system. If the adhesive is an ideal plastic material, i.e. is not deformed at all as long as the shear stress is below a characteristic value (kg cm^{-1} s^{-2}), and flows freely when the stress exceeds k, then

$$f = \frac{wk}{h_0} , \quad (8)$$

for an adhesive joint consisting of two rigid plates with a width w (cm) and a layer of adhesive with a thickness h_0 (cm). If the adherends are cylinders with a radius r, then[45]

$$f = \frac{2kr}{3h_0} . \quad (9)$$

It is remarkable that f is inversely proportional to the thickness h_0. Adhints with a very thin layer of adhesive should have an enormous strength when plastic adhesives are employed; this conclusion has been confirmed experimentally, for example by Mossatt and Wulff[46]. The effect of the thickness h on the strength of such systems is much greater than for the purely elastic adhesives discussed in section V, 1.

In principle, the critical shear stress k is a constant of the material of the same kind as the cohesion ξ. Eqns. (2), (8), and (9) show that the breaking stress f is never equal to ξ or k even when the rupture undoubtedly takes place within the bulk of the adhesive. The path from molecular forces to resistance to rupture is long and thorny.

3. Lap joints. It would appear that when the upper plate of the adhesive joint illustrated in Fig. 10 is pulled to the right and the lower plate to the left, purely tangential stresses (shear stresses) will arise in the layer of adhesive between both plates. In fact the distribution of stresses is much more complex in this case also.

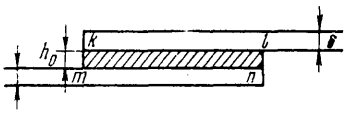

Figure 10. Concentration of stresses in a lap joint.

Firstly, the lines of force should undergo a sharp change of direction on passing from the upper plate to the adhesive and from the adhesive to the lower plate. Therefore near the points k, L, m, and n, there is a concentration of stresses analogous to that which arises at the corners of a square cut in a sheet or a film (instead of the ellipse shown in Fig. 8). The coefficient α of this concentration increases as the ratio of the thickness h_0 of the adhesive layer to the thickness δ of the solid plate diminishes; in the usual adhints α may easily reach values of 10.

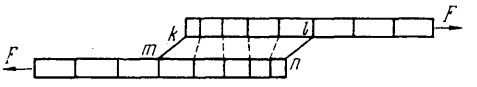

Figure 11. Differential stretching of plates in a lap joint.

Secondly, the external forces (arrows in Fig. 10) extend the plate unequally along its length, so that the film of adhesive is not only extended but also bent. This is illustrated in Fig. 11. To the right of the point l in the upper member and to the left of the point m in the lower member, the entire force F acts on the plates and their relative deformation is high. At the points k and n, i.e. at the free ends of the plates, there can be no stress. It may be that the relative deformation gradually diminishes from l to k and from m to n, as shown schematically in Fig. 11. If both the plates and the adhesive obey Hooke's law, it is possible to derive an approximation expression for the maximum coefficient α of the concentrations of tangential stresses at the ends of the layer of adhesive:

$$\alpha = \left(\frac{G_1}{2E\delta h_0}\right)^{0.5} L , \quad (10)$$

where G_1 is the modulus of shear elasticity of the adhesive, E the modulus of elasticity of the adherend on extension, δ the thickness of the plate, h_0 the thickness of the adhesive, and L the length of the overlap, i.e. the distance $\overline{kL}$ or $\overline{mn}$. Since the dimensionless ratio $L/(\delta h_0)^{0.5}$ reaches 100 in many adhints, the coefficient α due to the deformation under consideration may sometimes be actually higher than the coefficient calculated above.

Thirdly, plates are bent when an external force is applied, as shown in Fig. 12. The left-hand side shows a system subjected to a force so weak that deformation is still not observed. Clearly the force pulling one of the plates upwards does not act along the same line as the force equal in magnitude and pulling the other plate downwards. A twisting moment is generated, which leads to the deformation shown on the right-hand side of the Figure; here both forces act along the same straight line but the two plates are bent. The deformation of the plates causes the deformation of the adhesive between them. Evidently the distance between the adherends near the points m and n is greater than in the centre of the adhesive film, so that the adhesive is extended not only in the vertical direction but also its thickness near the ends is appreciably greater than before and greater than the thickness of the middle sections in the present case. The stresses in the adhesive near the ends of the film are similar to the stresses responsible for peeling (see section V, 4).

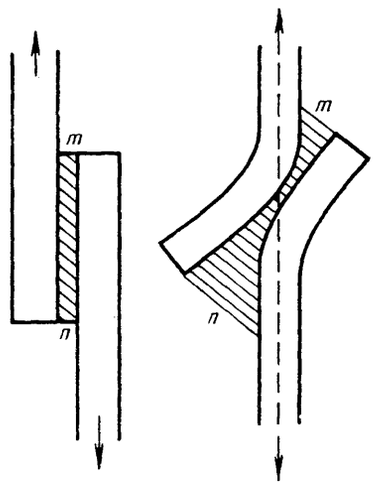

Figure 12. Bending of the plates in the stretching of a lap joint. Left-hand figure—low external force. Right-hand figure—high external force.

Their theory was developed by Goland and Reissner[47] and was tested in detail by Henning[48].

If the plates are appreciably bent, the stress in the adhesive is much greater at the ends of the film than in the centre. Therefore the middle parts of the film carry almost no load and may not be necessary. This conclusion has been confirmed experimentally[49]. When the space between two plates was filled with an adhesive along a 2.5 cm section, the resistance to rupture F was 1.3×10^9 dyn (or 1.3×10^4 newtons). When the middle half of the layer was left unfilled, i.e. the section with a length of 2.5 cm contained 0.625 cm of adhesive + 1.25 cm of void space + 0.625 cm of adhesive, F was still 1.1×10^9 dyn (or 1.1×10^4 newtons). In other words the removal of half the adhesive from the centre reduced F by only 20%. Fig. 13 presents more results[50] of the same kind. Two aluminium plates 25 mm wide and 1.5 mm thick were glued together over a section 20 mm long. The end of this section were in all cases filled with glue but in the centre there remained a void, the length of which was varied from 4 to 16 mm. This length is plotted along the abscissa in Fig. 13, the ordinate representing the stress f sufficient for rupture; it is expressed in bars. The lower curve was calculated disregarding the voids; evidently, when the length of the unfilled slit was 12 mm, i.e. 60% of the total length, f was hardly less than the resistance of a continuous film of adhesive. Calculation of the stress for the filled part of the slit yields the upper curve.

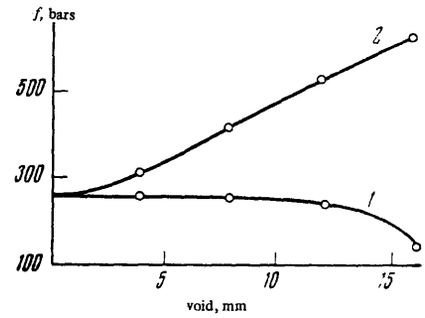

Figure 13. Effect of a cavity in the surface of the adhesive film on the strength of the lap joint. Abscissa—length of the void in millimetres. Ordinate—shear resistance in bars: 1) resistance calculated for the entire length; 2) resistance calculated for the filled section.

The coefficient α, calculated in accordance with one of the previous theories, must be introduced into the general Eqn. (2) in order to obtain some idea of the resistance to shear which may be expected from the given system. For example, α may be found from Eqn. (10), since the geometrical parameters (δ and h_0) of the system and the principal mechanical constants (G_1 and E) of the materials are known. If s_M in Eqn. (3) is low, the transient resistance of the free adhesive film (f_M) is almost equal to the ratio ξ/β. If s is also small in the given adhesive joint, then $f \simeq \xi/\alpha\beta \simeq f_M/\alpha$. For lap joints, $f = F/wL$, where F is the applied force and w and L are the width and length of the adhesive layer (which is of course continuous). We obtain finally

$$F = wLf_M/\alpha \ . \qquad (11)$$

Under favourable conditions F may be predicted, provided that w, L, δ, h_0, G_1, E, and f_M are known. If the most dangerous concentration of stresses is not a result of differential stretching but is a consequence of Eqn. (9) or the flexibility of the plates, other expressions for α must be introduced into Eqn. (2), but the equation itself remains in force; F continues to depend only on f_M and the geometry and mechanical properties of the components of the adhesive joint.

4. Peeling. An adhint subjected to peeling is illustrated in Fig. 1. The horizontal distance ζ between the point of application of the force and the edges of the adhesive "fillet" (at which the arrow from the letter G terminates) greatly influences the peeling resistance but unfortunately so far it has not been possible to calculate it convincingly on the basis of the dimensions and mechanical

constants of the components. In those cases where the flexibility of the ribbon is very high (for example, when a thin metallic foil serves as the adherend), the distance ζ can be virtually neglected. When $\zeta = 0$, there is a simple formula[51] for the minimum force F necessary for peeling:

$$F = kwf_M (E_1/E_1)^{0.25} \delta^{0.75} h_0^{0.25} . \quad (12)$$

In its derivation, it is assumed that the adhesive and the ribbon obey Hooke's law and therefore have unique values (E_1 and E) of the modulus of elasticity. As before, the width and thickness of the ribbon are denoted by the symbols w and δ, the thickness of the layer of adhesive is denoted by h_0, the transient resistance of the molecule by f_M, and the numerical factor $K = 0.38$ when the Poisson factor $\nu = 0$ for both components and $K = 0.76$ when $\nu = 0.33$ in both cases. The rigid adherend is assumed to be completely incapable of being deformed.

The accuracy of Eqn. (12) is of the same order as that of the equation $f = F/wL$ mentioned above, i.e. it disregards both the residual stresses s and the factor α. If, for example, $\alpha = 5$, the values of the force F predicted by Eqn. (12) will be five times higher than the experimental quantities. Inconsistencies of this order of magnitude were observed in the peeling of an aluminium foil glued to glass with purified polyethylene. Probably the maximum value of α is observed at the boundary between air, the adhesive, and the ribbon when the adhesive is brittle and at both ends of the adhesive film along the width w when the maximum relative extension of polyethylene is high. Incidentally, it was easy to show that considerable amounts of polyethylene were present on both rupture surfaces[13].

Equations analogous to Eqn. (12) could be derived also for the simplest cases of non-Hookean materials. Thus Fukuzawa[52] calculated Γ for peeling at an angle of 180° assuming that the adhesive is a viscoelastic substance obeying Maxwell's equation.

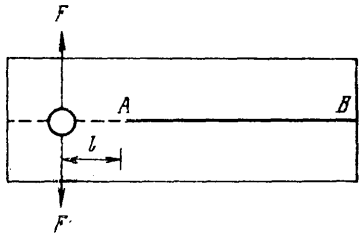

Figure 14. The splitting of two rigid bars glued along the AB plane. F = external force; L = length of crack.

Peeling theory predicts that, although the stress in the adhesive at the "leading" edge of the film (indicated by an arrow in Fig. 14) is a tensile stress, the stress somewhat to the right of the edge (in Fig. 14) changes sign so that there the ribbon is now clamped to the adhesive and compresses it. There is nothing unexpected in this phenomenon: if one end of a lever is pushed downwards, the other end tends to rise. The change in the sign of the deformation of the film was demonstrated by special measurements[53].

The direction of the external force F in Fig. 14 is perpendicular to the plane of the adhesive film. As already mentioned, the peeling angle need not be 90° (or $\pi/2$ radians). When the angle φ is altered, in certain systems [for example in poly(vinyl acetate) reinforced with silk and glued to glass], the force F is inversely proportional to $1 - \cos\varphi$, so that the work formed in peeling, which is $FL(1 - \cos\varphi)$, proves to be independent of φ; l is the length of the peeled section. In other systems the dependence of F on φ will be different for different rates of peeling. For various polyurethanes, the tension Γ for $\varphi = 90°$ was of 1.5 times or twice as high as for $\varphi = 180°$.[54]

When both adherends are rigid bars and are incapable of being bent, splitting is employed instead of peeling, as shown in Fig. 14. The work W which must be performed in the spreading of the crack within the layer of adhesive may be calculated from experiments of this kind. Usually W is proportional to the area S of the crack and the ratio W/S = "γ" is independent of S. For epoxy-resins, this "γ" was in most cases lower only by several per cent than the "γ" measured in the splitting of bars of the same epoxy-resin without any adhesive[55].

VI. DEPENDENCE OF STRENGTH ON EXTERNAL AND INTERNAL CONDITIONS

This section reviews the relations between the breaking stress f and specific resistance to peeling Γ on the one hand and the dimensions of the system, the chemical composition of the adhesive, and other conditions on the other; the results are explained from the standpoint of the author's "rheological" theory and at the same time from the standpoint of the molecular theory clearly presented in a recent review by Kardashev and Vakula[30] and in the book of Berlin and Basin[10].

1. Dependence on the method of measurement. The data in Fig. 7 were obtained for the rupture of butt joints arranged in such a way that the stress concentrations described in section V, 2 were virtually absent. When the adhesive layer was sufficiently thick, the resistance to rupture was almost equal to the tensile strength of the free adhesive in the form of a bar. The same adhesive (purified polyethylene) was employed in the peeling experiments described in section V, 4. The results were lower by a factor of 5 than expected from Eqn. (12); thus one might conclude that in the failure of geometrically different adhesive joints, different quantities are measured. As stated above, this conclusion is unjustified: experimental data do not confirm Eqn. (12) simply because it is valid only for the ideal case which departs widely from reality. So far specimens for peeling tests in which there are no lateral stress concentrations have not been found.

Instructive results were obtained on comparing butt and lap joints and joints subjected to a twisting moment[56]. Aluminium "pins" of different dimensions were attached to one another with commercial adhesives, the tensile strength f_M of which was in the range from 490 to 760 bars (in the free state). Depending on the diameter, the resistance of the adhints to rupture varied between 250 and 620 bars. We may recall that f_M is measured on specimens for which the factor α is identically equal to unity. Probably in the adhints of Winter and Krause the coefficient was about 1.2 — 2.0, i.e. their adhesive joints were designed so skilfully that the concentrations of stresses were lower than calculated in section V, 2. Lap joints in which the thickness of the aluminium plates was 0.1 cm and the length of the overlap 1 cm were ruptured at a stress F/wL = 250 bars. It is not known to what extent the

plates were bent during the measurements, but the "geometrical" concentration of stresses and the differential stretching of the adherends and the adhesive undoubtedly occurred and probably raised α to 490/250 or 760/250, i.e. 2 — 3. When two rings were glued together and a twisting moment was applied to them, the breaking stress was found to be 470 — 660 bars, i.e. α was only slightly higher than unity. The twisting of the rings was recommended many years ago as a rational method for the measurement of adhesive strength[57].

Two short steel cylinders were glued together with polysiloxane rubber and the same adhesive was employed to join two short tubes via their butt ends[58]. The systems with two cylinders were ruptured either by shearing one from the other or by turning one of them about their common axis, while the system of two tubes was ruptured only by means of a twisting moment. The stress f necessary for rupture depended little on the method of breaking employed and the plots of s as a function of the rate of rupture also proved to be almost identical for all three series of experiments. The absolute value of f increased together with the rate from 11 to 20 bars. Unfortunately the tensile strength of the polysiloxane employed was not measured; did it exceed 20 bar?

In all the experiments described in this section proper joints were employed and as far as is known the breaking stress f did not differ appreciably from the breaking stress f_M of the adhesive. The difference between f and f_M can be readily accounted for by the different values of the factors α and β. It is of course possible that the residual stress f in the adhesive layer was also not the same as in a free bar. The question arises if the molecular theory of the strength of adhesive joints can account for these results. Evidently the attractive forces usually quoted in books and papers on adhesion (dispersion forces, hydrogen bonds, etc.) in no way depend on the manner in which the adhint is broken, so that a purely molecular theory is in this case quite useless. The weakness of this theory is so evident that even its supporters had to acknowledge that the measured value of f depends on the stresses in the adhesive and on its strength. How can one estimate in this case the contribution by adhesive forces to the experimental value of f? If the type and number of functional groups on the surface of the adhesive and the adherend and their capacity to interact play a decisive role in adhesion, what part of the stress f of the tension Γ is determined by these parameters? Supporters of the molecular theory have not attempted to answer this question either; the correct answer, is, of course, none.

2. Dependence on the dimensions of the system. The effect of the thickness h_0 of the layer of adhesive on f and Γ has been frequently studied. Curves similar to those in Fig. 7 are typical for butt joints; in practice it was noted long ago that, "the thinner the adhesive layer the stronger the adhesive joint". Apparently Crow[59] obtained the earliest quantitative results. He joined together copper cylinders via their butt ends with the aid of a eutectic solder (tin + lead) and found that the thinnest layers of solder (0.02 cm) were a little less than three times stronger than thick layers (0.5 cm) and that the strength of thick layers was equal to the tensile strength (630 bars) of free rods of the same solder. The dependence of f on h_0 proved to be less pronounced but qualitatively similar for steel cylinders glued together with poly(vinyl acetate)[60] and several other systems.

In the first place it is necessary to show whether this effect of h_0 on f is real. After all, in the extension of adhints at a constant linear rate dh/dt (t is the time and h the variable thickness of the layer of adhesive), the relative deformation, i.e. $(h - h_0)/h_0 = \epsilon$ increases more slowly, the greater h_0; clearly $d\epsilon/dt = (dh/h_0)dt$. It may be that the thicker the adhesive layer, the slower its deformation for dh/dt = const. Since f decreases in many cases when the deformation is slower, the dependence of f on h_0 may be only apparent. Accurate experiments which would make it possible to dispel these doubts once and for all have not apparently been made, but the increase of f with $1/h_0$ is observed in such a wide variety of systems that it is reasonable to regard it as a real phenomenon.

Then the question arises of its causes. One of the causes, which has long been the subject of quantitative tests[61], is described in section V, 1. In those cases where the layer of polymer at the boundary with the adherend has a higher strength than the free polymer[62], one may imagine that two strengthened layers coalesce when h_0 is very low, so that f increases. The hardening and crystallisation of a polymer in thin layers generally speaking lead to a different supermolecular structure and to a different distribution of residual stresses than in thick layers. Thus β and s in Eqn. (2) also vary with h_0.

A change in the thickness h_0 undoubtedly alters also the coefficient α. According to Eqns. (8) and (9), α for ideally plastic adhesive should be inversely proportional to the thickness h_0; however, there are no examples of such a relation in the literature. The effect of h_0 on f for viscoelastic materials (rubbers) should be very remarkable. Rubbers, like gases, offer little resistance to changes in shape but tend to retain a constant volume. If h_0 is small (see Fig. 9), an appreciable increase of h is impossible without a significant increase of the volume V, since the hollows visible at the end of the adhesive film cannot alter V appreciably. If S is the area of the end-face, then $dV \simeq Sdh$. On the other hand, when h_0 is large, the adherends can move far apart without altering V, as shown on the right-hand side of Fig. 9. Therefore one may expect that the increase of f with $1/h_0$ would be particularly pronounced for rubberlike adhesives.

The data for the effect of h_0 on the strength of lap joints are contradictory. The situation is somewhat clearer for the peeling resistance $\Gamma = F/w$. According to Eqn. (12), it is postulated that this resistance increases somewhat with the thickness h_0, i.e. the dependence of Γ on h_0 should be the opposite to that of f on h_0. A qualitative confirmation of this theoretical conclusion can be seen, for example, in the numerous measurements carried out by Gardon[63] on systems consisting of two cellophane ribbons glued together with polyacrylate. Thus, for a rate of rupture of 1 mm s^{-1}, Γ was approximately 100, 250, and 600 kdyn cm^{-1} for thicknesses h_0 of 1.2, 5.1, and 258 μm. According to elementary theory, Γ should have increased by a factor of 3.8 for an increase of h_0 by a factor of 215 (258 : 1.2 = 215); experiments showed that the increase was approximately by a factor of 6.

Since the mathematical theory of peeling and rupture is still very imperfect, one cannot expect a better agreement between theory and experiment. At any rate it is difficult to doubt that the dependence of f and Γ and h_0 has a purely mechanical origin and has nothing in common with molecular adhesion. It is very gratifying to note here that Berlin and Basin[10] essentially agree with this conclusion, which follows from experimental data and from the rheological theory of the strength of adhints.

Nevertheless the increase of the strength f with $1/h_0$ has been sometimes attributed[64] to molecular attraction.

It was suggested that both adherends in the adhesive joints attract one another through the intervening layer of adhesive and that this attraction is stronger the thinner the adhesive layer. This hypothesis was apparently initiated by Smilga and Deryagin[65]. If one nevertheless concludes that f varies with h_0 for mechanical reasons, one has to ask again the supporters of the molecular hypothesis what thickness h_0 corresponds to the equality of the measured strength to A. Some investigators believe that the extrapolation of f to $h_0 = 0$ would yield a value equal or close to A. In reality such extrapolation will affect most the coefficient β, which would then become approximately equal to unity; the experimental value of f will then be almost equal to the ratio $(\xi - s)/\alpha$.

3. The strength of the adhint and the adhesive. According to the rheological theory, the strength f of proper adhints is determined primarily by the strength of the adhesive f_M, since both in the rupture of both the adhint and of a free rod made of the adhesive the crack spreads in the same material. Nevertheless, in the general case f is not equal to f_M for reasons already described in section V. The equality $f = f_M$, can only occur, if it is not fortuitous, when the adhesive joint is made up in such a way that $\alpha = 1$, when the local stress concentrations β are equal in both systems, and when the heat-treatment temperature (and other external conditions) have been chosen so that the stress s_M in the free adhesive differs little from s in the adhint. When all these factors are taken into account in the formation of adhesive joints, the equality of f (for a large thickness of the adhesive layer) and f_M can be demonstrated experimentally, as shown in Fig. 7. In the majority of experiments carried out to compare f with f_M, the values of α, β, and f were not taken into considerations, so that an exact equality of f and f_M cannot be expected. Nevertheless, there is no doubt about a close relation between these two strengths even when the above experiments are considered.

Resistance to rupture f of butt joints and the strength of free adhesive f_M (in bars).

Adhesive	Adherend			f_M	f/f_M
	steel	copper	aluminium		
	f				
Polyamide 6	720	730	660	830	0.84
Polyamide 66	680	750	670	720	0.97
Polyamide 610	530	620	570	480	1.18
Polyamide 11	390	260	410	590	0.60
Polyethylene	170	110	170	300	0.50

The Table compares the values of f and f_M for five adhesives and three adherends; adhesive pin-type butt joints were employed.

The first column indicates the composition of the adhesive, the next three give the values of f, the fifth column lists the f_M, and the sixth gives the ratio of the average values of f and f_M. Polyethylene was not specially purified, since its low f/f_M ratio probably indicates the presence of a weak boundary layer. Nothing is known about the purity of polyamide 11. The f/f_M ratio for other polyamides is so close to unity that there is no doubt about the mechanism of rupture. It is remarkable that f for adhesive joints between two copper "pins" (third column) differed appreciably from the f (was smaller) for other metals only in the case of the two adhesives where the low ratio f/f_M suggests that contaminants may be present in the interfacial layer. It may be that copper accelerates the oxidation of adhesives, as mentioned in section III, 7. In systems for which f was almost equal to f_M, f was independent of the nature of the metal: the average f was 640 bars for steel, 700 bars for copper, and 630 bars for aluminium. From the standpoint of the rheological theory, this result is obvious: since the mechanical properties of different adherends differ, it follows that the coefficients α in their adhints also depend on the nature of the adherend; but when the α nevertheless differ little from unity (as in the systems of Lewis and Tanner), the differences between three similar values of α hardly affect the resistance to stripping. It is difficult to account for the independence of f of the nature of the adherend in terms of the molecular theory; it is difficult to believe that the molecular adhesion of a polymer remains constant whatever the change in the oxide to which the polymer is attached.

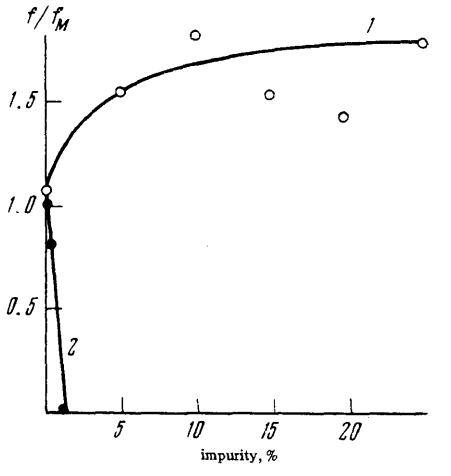

Figure 15. Difference between proper (upper curve) and improper (lower curve) adhints. Abscissa—percentage of contaminant. Ordinate—f/f_M ratio: 1) ethyl palmitate; 2) oleic acid; both in purified polyethylene.

The similarity or even equality of two values of f and f_M, which cannot be accounted for on the basis of the molecular hypothesis, has been noted many times in the literature. Some data have already been presented in section VI, 1 and VI, 2. As early as 1932, Nightingale[67] concluded on the basis of numerous observations that the strength of the soldered joints and the solder differ little however the chemical composition of the solder is varied. The resistance to rupture f in a system of two quartz cylinders with an intervening layer of solid paraffin increased from 3.3 to 14.6 bars when the thickness of the adhesive layer was diminished from 2.5 to 0.003 mm, while the tensile strength of the paraffin was 7.3 bars[68]; it may be that α in the thick adhints was 7.3 : 3.3. The f/f_M ratio varied only in the range 0.62 — 0.70 when four different adhesives consisting of an epoxy-resin cross-linked with diethylenetriamine were ruptured in the form of three bars or in the

form of layers between two aluminium cylinders. The tensile strength of ice between 0° and −10°C usually varies between 10 and 18 bars and butt joints in which copper, steel, and glass adherends were joined by a film of ice broke[69] following the application of a stress of 19 bars.

All these quantitative agreements between f and f_M are observed only because the adhesive joints are of the proper type (see section V). Fig. 15 presents certain data[15] clearly demonstrating the difference between proper and improper adhints. In Fig. 15 the fraction f/f_M is plotted against the weight ratio of the impurity (in purified polyethylene) relative to the overall weight, so that 0.05 on the abscissa axis represents a mixture comprising 0.05 g of the impurity and 0.95 g of polyethylene. The adherends consisted of stainless steel and the shape was such that α in the system was only slightly higher than unity. Curve *1* refers to mixtures of purified polyethylene and ethyl palmitate. Evidently f exceeded f_M at all impurity concentrations; one must suppose that this phenomenon was due to the factor β: on addition of palmitate, polyethylene became softened to such an extent that it was difficult to prepare from it well-formed bars for the measurement f_M. Curve *2* has been plotted for mixtures of purified polyethylene and oleic acid; here f/f_M decreases almost to zero when the concentration of the impurity is only 1%. The difference between the two curves is striking; it corresponds to a profound difference between proper (ethyl palmitate) and improper (oleic acid) adhints. The resistance to rupture of improper adhints has nothing in common with the strength of the adhesive and is much lower than the latter, since rupture does not occur in the adhesive but in a weak boundary layer.

4. The strength of adhints and the composition of the adhesive. The difference between the rheological and molecular theories of strength is shown perhaps most clearly in an examination of the dependence of strength on the molecular composition and structure of the adhesive. Unfortunately this difference remains qualitative in principle because the predictions of the molecular hypothesis are so nebulous that no quantitative or even semiquantitative conclusions can be derived from it. After repeated attempts to provide the molecular hypothesis with flesh and bones, one must conclude that essentially this theory does not exist; there are only feelings, emotions, and guesses.

What sort of theory could it be? It could relate f, for example, to the densities of cohesion energy ($\lambda\rho$) or to solubility parameters ($\sqrt{\lambda\rho}$); λ denotes the latent heat of evaporation per gramme and ρ the density (g cm^{-3}); the dimensions of the product $\lambda\rho$ are g cm^{-1} s^{-2}, i.e. the same as those of the stress. We shall designate the adhesive by the numeral 1 and the adherend by 2; then one of the possible rules of the molecular theory would be represented by the expression $f = \lambda_1\rho_1 - k(\lambda_2\rho_2 - \lambda_1\rho_1)$, where k is an unknown constant. According to this formula, when the adherend and the adhesive are very similar, $f = \lambda_1\rho_1$ and f is smaller the smaller the difference between $\lambda_1\rho_1$ and $\lambda_2\rho_2$. This rule resembles the empirical rules for the miscibility of liquids. Or f might obey the "rule of polarities": $f = a - b|n_2\mu_2 - n_1\mu_1|$, where a and b are two unknown constants, n_1 and n_2 are the numbers of dipoles per unit volume of the adhesive and the adherend, and μ_1 and μ_2 are their molecular dipole moments. When $n_2\mu_2 \simeq n_1\mu_1$, i.e. the adhesive and the adherend are both polar or both non-polar, f reaches the maximum possible value (a); if the difference $|n_2\mu_2 - n_1\mu_1|$ is large, f is much lower than a.

No rule of this kind appears to be quoted in the literature. In the formulation of the "rule of polarities" no one has even explained what meaning should be assigned to polarity: the dipole moment of the chemical bond (for example C—H), or the permanent dipole moment μ of an individual molecule (according to this criterion, even toluene is polar), or the product $n\mu$ just employed, or some other quantity. Incidentally, one cannot avoid a conflict between the "rule of polarities", however defined, and facts: non-polar polyethylene can be very effectively glued to glass and metals, while ethyl palmitate and oleic acid (the dipole moments of which are identical) have different effects on f for polyethylene adhints.

According to the rheological theory, which alone can claim to have a general significance and which alone is capable of quantitative predictions, the composition and structure of the adhesive influence the strength of the adhint via two completely different mechanisms depending on whether the proper adhint ⇌ improper adhint transition is observed. As already stated, the mechanisms of the formation of weak boundary layers are extremely varied and a change in the composition of the adhesive can readily include or exclude one of these mechanisms.

For example, we shall suppose that the chemical composition of the adhesive varies systematically in such a way that the surface tension γ of the liquid adhesive increases continuously. Since the contact angle θ usually increases with γ, at some point in the series, i.e. for a particular composition of the adhesive, the wetting will become insufficient and it will be impossible to remove air bubbles from the surface of the adherend with the liquid adhesive. In this series all the initial members (for which γ is low) will give rise to proper adhints (with high values of f), while the adhints formed by all subsequent members will break on application of weak stresses f in a weak boundary layer of the first kind.

A change in the chemical nature of the adhesive can lead to weak boundary layers of the first group, which are independent of contact angles. We shall examine a series of polymers with similar structures but with a gradually increasing molecular weight M. In many cases, when M increases, the melting point and the viscosity of the melt also increase. If the conditions governing the formation of the adhint are maintained strictly constant, for example, when the system is heated for a specific time at a specific temperature, the duration of heating may be sufficient for the removal of air bubbles when M of the liquid is low but may be too short for very viscous liquids with high molecular weights. Possibly, this is the cause (or one of the causes) of the observation that the strength of adhesive joints is sometimes a maximum for a moderate value of M of the adhesive; for example, epoxy-resins cross-linked with triethanolammonium titanate gives rise to the maximum f (shear resistance) for M = 800.

It would be easy to test this explanation. It would be necessary to measure the tensile strength f_M of the same polymers in the form of free rods and compare it with f. If f is similar to f_M for all $M < 800$ and much lower than f_M for $M > 800$, then the presence of a weak boundary layer in the second group of specimens would be very probable. Unfortunately f_M has not been measured and compared with f. This is an example of an extremely common error, which frequently lowers the level of experiments from scientific to empirical. Those who wish to understand the mechanism of the phenomenon, find the measurement of the tensile strength of adhesive joints almost useless if they are not supplemented at least by data concerning the dimensions of the specimen and the

measurements of f_M and of the thickness of the residual adhesive on the adherend. Well-founded conclusions concerning the mechanism can be reached only if the geometry of the system, the location of rupture, and the degree of similarity between f and f_M are known.

By altering the chemical nature of the adhesive, it is possible to pass from proper to improper adhints of the second group, described in section III, 2. If a liquid X is soluble in a solid adhesive A up to a concentration c_0(%), then the adhesive joints in which the adhesive has the composition $(100 - c)A + cX$ have a high strength f as long as $c < c_0$ but disintegrate readily exactly along the interface when $c > c_0$. As already stated, transitions of this kind were observed on dissolution of oleic acid in purified polyethylene. Probably they occurred also in a system comprising an epoxy-resin and tetraethylenepentamine (TEPA).[70] Butt joints between copper "pins" had a tensile strength of about 700 bars when c of the amine was 5 — 9%. When the TEPA concentration was raised to 17%, f fell approximately to 80 bars; at the same time the location of rupture migrated from the bulk of the adhesive to the interface. The strength f_M of free films of the same polymer was somewhat less than 600 bars for a ratio TEPA: epoxy-resin = 0.08 and depended little on it following further cross-linking; thus the ratio of the two strengths f/f_M was approximately 1.2 for c = 7%, 0.17 for c = 17%, and 0.07 for c = 0.33%. The curve obtained at high concentrations resembles the f/f_M curve for mixtures of polyethylene and oleic acid illustrated in Fig. 15. Probably the excess tetraethylenepentamine formed a weak boundary layer in which rupture in fact occurred. It is noteworthy that in the above investigation measurements were made of f_M and the location of rupture was determined at least qualitatively; therefore the mechanism of failure can be actually inferred and not merely discussed.

In other cases one must employ as a basis only the values of the strength and not the author's impression that the rupture was cohesional or adhesional. Films of synthetic and natural rubber were peeled from cellophane freed from glycerol[71]. The peeling resistance Γ was on average 1400 kdyn cm^{-1} for synthetic rubber and only 18 kdyn cm^{-1} for natural rubber. This difference cannot be reduced to a difference between the mechanical properties of the polymers; natural rubber, the peeling of which was "adhesional", undoubtedly formed a weak boundary layer at the junction with cellophane and probably also at the junction with other polymers[72]. Unfortunately it was impossible to find any data concerning the nature of this layer. Only on peeling natural rubber from polyisobutylene, did Γ exceed 300 kdyn cm^{-1}; one must suppose that the material of the weak boundary layer formed by natural rubber dissolved in polyisobutylene, which is very similar chemically to natural rubber. Γ for polymeric coatings on ordinary polyethylene was also very low with the exception of two butadiene rubbers; is it possible that neutral impurities present in polyethylene are soluble in polybutadienes?

Weak boundary layers of the fixed kind, formed in chemical reactions between an adhesive and an adherend, can also arise and disappear as the composition of the adhesive is varied systematically. In Berlin and Basin's book[10], where the molecular hypothesis of strength is defended, it is mentioned that the introduction of maleic acid into copolymers of vinyl chloride and vinyl acetate increases their "adhesion to metals" (i.e. f), but at the same time it accelerates corrosion and is therefore impractical. It is indeed remarkable how truth driven out of the door returns through the window; where else would one expect to find strong adhesion if not between an acid and a metal!

Possibly the TEPA — epoxy-resin system mentioned above is an example of improper adhints of the sixth and not the second kind. The point is that f for adhesive joints between titanium "pins" did not fall below 500 bar even when the ratio TEPA : resins was 0.25. One must suppose that the excess TEPA did not form weak boundary layers by itself but together with copper, which readily enters into complexes with amines. Additional examples are presented in section III, 6.

In those very numerous systems where no proper adhints $\rightleftharpoons$ improper adhints transitions occur and all the adhesive joints may be regarded as proper, the effect of composition on f and Γ may be elucidated on the basis of Eqns. (2) and (12).

According to Eqn. (12), Γ is proportional to the strength f_M. In Eqn. (2), the ratio ξ/β is close to f_M although the coefficient β is usually smaller in a thin "fillet" of adhesive than in a large bar employed for the measurement of f_M. Perhaps one may expect that both f and Γ will increase with the strength f_M of the free adhesive. This prediction of the rheological theory is fairly frequently confirmed. The variation of f and Γ with f_M is so evident that it cannot fail to be noted even by convinced supporters of the molecular hypothesis; thus one group of investigators[73] admit that the "problem of adhesional strength is inseparable... from the problem of cohesional strength"; and others[30] attribute the impairment of the "adhesive capacity" of polymeric esters (on increasing the length of the alkyl group) to the "decrease of the cohesional strength of polymers". Thus the chemical composition of a solid determines to a large extent the value of f_M and to a somewhat lesser extent also f and Γ. To a lesser extent partly because β in the adhesive layer can differ markedly from β_M in a free adhesive specimen. It is quite likely that the evaporation of the solvent from the free specimen will take place without hindrance, while evaporation from a film between two adherends will be so difficult that β_M will prove to be several times smaller than β. Since the strength of solids is equal to the strength of their weakest section, it is insufficient to state (and to note) that a substance A served as the adhesive. How was it prepared? What kind of defects remained in it? In order to understand the results of experiments on adhesive joints, it is almost necessary to have bacteriological information about them. Just as to the bacteriologist a gel containing one part by weight of tubercle bacilli per 10^{12} parts of agar is quite unlike the gel from which Koch bacilli are absent, to the investigator of strength a cubic centimetre of a solid in which a cubic micron contains a sharp crack differs decisively from another cubic centimetre in which such cracks are absent.

The composition of the adhesive can have different effects on the stripping resistance f and on f_M also because the coefficient α varies with composition. Generally speaking, α is higher the greater the difference $E - E_1$ or the ratio E/E_1; we may recall that E is the modulus of elasticity of the adherend and E_1 that of the adhesive. By varying the chemical nature of the adhesive, we also alter its E_1. Certain strength curves with a maximum may be obtained because $E = E_1$ and $\alpha = 1$ when the composition corresponds to the maximum. For example, we may suppose that two rubber "pins" are glued together with a rubber adhesive and that the composition of the adhesive is varied systematically by the introduction of increasing amounts of chlorine into the rubber. The stripping resistance f in this system may initially increase because E_1

increases with the amount of chlorine and $E - E_1$ decreases; at a certain chlorine concentration, $E_1 = E$ and f reaches its maximum value; on further introduction of chlorine, E_1 becomes greater than E, α again increases, and f again diminishes. This explanation too could be easily tested; it would be sufficient to replace rubber adherends by glass or steel adherends for which E would remain in all cases much higher than E_1; in such systems a maximum would not be observed. As a result of an incorrect hypothesis, such comparison has not been made.

The difference between the residual stresses s has already been resorted to frequently for the explanation of the incomplete agreement between the effect of composition on f and f_M. The relaxation of stresses in a free bar of adhesive takes place in many cases more readily and more completely than in a "fillet" clamped between two rigid adherends; consequently the quantity $\zeta/\beta - s$ in the bar is frequently higher than in the layer of adhesive.

In an examination of butt joints, it is usually permissible to assume that the adherends are completely undeformed during the rupture process. Such an assumption is rarely justified for lap joints and never for peeling and rupture. In such systems the values of f and Γ have no physical significance if the reader is not informed about the dimensions and the mechanical properties of the adherends or if the experimenter did not pay attention to these factors.

The foregoing can be elucidated by the example quoted in the paper of Kardashev and Vakula[30]. A hydroxylated polyester was condensed with a mixture of tri-(*p*-isocyanatophenyl)methane (TIPM) $(OCN.C_6H_4)_3CH$ and hexamethylene di-isocyanate (HMDI) $[OCN(CH_2)_6NCO]$; the greater was the amount of TIPM in the mixture, the denser was the cross-linking between the chains formed by the polyester and HMDI and, one must suppose, the higher was the modulus E_1 of the polymer. This polymer has been used as an adhesive between two unknown adherends forming a lap joint. It was found that the shear resistance decreased monotonically with increase of the relative content of TIPM in the mixture. If the adherend consisted of plates, they were bent as shown in Fig. 12; it may be that peeling and not shear occurred. The peeling resistance is generally speaking lower the more rigid the adhesive; it is evident even from Eqn. (12), which under-estimates the influence of rigidity; Γ diminishes when E_1 increases. Consequently the effect of the concentration of TIPM on strength can be understood as follows: the greater the amount of TIPM, the higher E_1; the higher E_1, the lower Γ; and the quantity Γ and not the true shear resistance determined the strength of the lap joints. Again this explanation would not be difficult to test using massive bars instead of plates but the idea of such a test apparently did not occur to the authors.

All hypotheses relating the chemical structure of the adhesive directly to the values of f or Γ are incorrect, since they do not take into account the necessary values of α, β, s, f_M, etc. let alone the possibility of the proper adhint $\rightleftharpoons$ improper adhint transition. Moreover, they are arbitrary, since they are based on an arbitrary choice of certain chemical units and the neglect of all others. We may point to the simplest example taken from the paper of Kardashev and Vakula[30]. Adhesives containing RCH_3, RCH_2Cl and RCH_2Br molecules were compared. The conclusion arrived at as a result of the observations was that the "difference between the adhesive properties of halogen-containing polymers may be accounted for by the presence of bromine and chlorine atoms". How this can be explained is not unfortunately stated. Nor is it shown that the individual properties of the halogens are significant (for example, the structure of their electronic shells); it may be that the peeling resistance depended only on the molecular weight M of the adhesive and varied in the series RCH_3, RCH_2Cl, RCH_2Br exclusively because M also varied in this series.

A more complex example may be found in the paper by De Bruyne[74]. Lap joints were formed between aluminium plates with the aid of adhesives containing epoxy-resins and phthalic anhydride. All the polymers contained 0.85 of the molecule of the anhydride per epoxy-group but also present were n groups $[-OC_6H_4C(CH_3)_2-C_6H_4OCH_2CHOH.CH_2-]$, n being varied systematically from 0.05 to 5. The shear resistance was much greater for $n > 1.5$ than for $n < 0.5$. Since the tensile strength f_M of the free polymers (bars, films, etc.) usually increases with n, this observation can be most simply accounted for by the usual similarity between f and f_M. The author preferred to point out that with increase of n there is an increase in the number of hydroxy-groups in the adhesive and that therefore f is large when the concentration of hydroxyls is high. Evidently other conclusions just as valid are possible. The shear resistance f increases with the number of benzene rings; perhaps these rings are the cause of "adhesion". The presence of isopropylidene groups $(CH_3)_2C$: also increases f; it may be that "adhesion" is caused by them. The higher the value of n, the smaller the number of carboxy-groups (from phthalic anhydride); the carboxy-groups may suppress "adhesion". This last conclusion is particularly remarkable since supporters of the molecular hypothesis of strength usually assert that carboxy-groups promote "adhesion".

The word adhesion is not placed in quotes by the above investigators but in this review the quotes are necessary in order to remind the reader that the true molecular adhesion A has nothing in common with the resistance to stripping, shear, peeling, etc. Adhesion is not the only term employed improperly (see the remarks by Raevskii and Pritykin on this matter[75]). The terms "adhesive capacity" and "adhesive properties" are used. These properties do not exist. Any substance which can exist in the liquid or plastic state so that it can fill hollows on the surface of the adherend and is capable of solidification in contact with the adherend can serve as an adhesive.

There would be no need to quarrel about words, but the danger is that the expressions "adhesion of substance A to substance B" or the "adhesive capacity of A" lead the reader to the error according to which the resistance to rupture of a single arbitrary adhint is adopted as a constant and characteristic property of the substance. Thus the resistance to rupture of films of a polyethylene and of P-118 polyisobutylene was found to be 95 kdyn cm^{-1} when the films had a particular thickness, a particular width, contained particular impurities, etc.; this resistance would be different if the amounts and nature of the impurities, the width, the thickness, etc. were altered; therefore the assertion that the "adhesion" of polybutylene to polyethylene is 95 kdyn cm^{-1} is illogical.

The main reason for the popularity of erroneous views is that organic chemists, who, of course, synthesise polymeric adhesives, continue to work on them in the field of tests and applications. Specialists in the measurement of strength and other mechanical properties of materials must be induced to undertake critical tests of the strength of adhesive joints. Since generally speaking organic chemists are unfamiliar with the science of the resistance of materials, the theory of elasticity, etc., they do not

find the evidence based on these sciences to be convincing. It is very remarkable that Berlin and Basin[10] mention the work on polyethylene briefly described in section III, 2 of the present review in a section devoted to the "morphology of the solid surface" (Ref. 10, p. 56) although polyethylene is an adhesive and not an adherend; in the description of the use of polyethylene as an adhesive on pages 196 and 197 of Ref. 10, it is written that "evidently the appearance of oxygen-containing groups in polyethylene... is the main cause" of the increase of the strength polyethylene adhints when polyethylenes are subjected to a special treatment. As mentioned in section III, 2 (and of course in the papers describing the original experiments), all the adhesive joints were formed in an atmosphere of nitrogen and the purified polyethylene contained less oxygen than the initial material.

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Metallopolymers

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The formation of highly disperse metal particles in a polymer medium is accompanied by the chemisorption interaction of their freshly formed surfaces with the polymer macromolecules. Such systems have several advantages over ordinary filled polymers, and have been termed "metallopolymers". Several methods of obtaining such systems—electrolytic, electroflotation, thermal, and mechanochemical—are surveyed. The nature and the mechanism of interaction between the surfaces of various metals and organic (also organosilicon) polymers are described in detail. The physicochemical properties of metallopolymers and possible fields of their application are discussed. A list of 175 references is included.

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I. INTRODUCTION

The development of new technology presents the chemistry of macromolecular compounds with the task of producing polymeric materials possessing several specific new properties. It has become necessary to combine the advantages inherent in polymers (low specific gravity, high elasticity and durability) with the electrical conductivity and magnetic, antifriction, catalytic, and other properties typical of metals and inorganic compounds.

Such polymeric materials can in principle be obtained in two ways: new polymers can be synthesised with several of the specified properties; and filled polymers, combining the valuable properties of their components, can be produced. Both lines of scientific research are being vigorously pursued at the present time [1-4], but polymeric materials containing various kinds of filler have already found wide practical application. The filling of polymers not only enables materials to be obtained with novel properties but also permits their physical, mechanical, and physicochemical characteristics to be varied in a controlled manner, with enhancement of the appearance and reduction in the price of goods made of plastics.

Several reviews [5-7] and monographs [8-10] have been published on the production, structure, and properties of polymeric materials containing various mineral fillers. Considerably fewer publications have appeared on the preparation and properties of polymers filled with metals of different kinds and degrees of dispersion [11]. Polymers filled with metals possess several quite specific properties (electrical, magnetic, catalytic) in addition to the above advantages inherent in polymers containing mineral fillers [12-14]. Furthermore, these two groups of filled polymers differ in the nature and the mechanism of the interaction at the solid–polymer interface [15,16].

Coarse powders, mixed mechanically with the polymer, are generally used as fillers, the particles of which form aggregates distributed non-uniformly through the polymer. During recent years systematic investigations have been made on new methods for obtaining metal-filled polymers and on the properties of the systems [17-20]. These methods consist essentially in forming highly disperse metal particles within the polymer, instead of introducing them ready made. The metal particles, having active centres on their surfaces at the instant of formation, enter into chemisorption interaction with macromolecules of the polymer within which they are formed. This leads to the production of two-phase systems having the most uniform distribution of highly disperse metal particles in the bulk of the polymer and in a stable state of aggregation. Such systems have been termed "metallopolymers". [18] Investigation of the physicochemical and mechanical properties of these systems has revealed considerable differences between metallopolymers and ordinary polymers filled with metals [21], these differences being due to the methods of preparation. The experimental results which have accumulated enable certain generalisations to be made concerning the methods of preparation, the mechanism of formation, and the properties of metallopolymers.

II. METHODS FOR THE PREPARATION OF METALLOPOLYMERS

Metallopolymers can be obtained by various methods provided that a fundamental condition is observed: highly disperse metal particles should be formed in the presence of polymers, with the appearance of chemisorption bonding between the macromolecules and the surface of the metal particles. At the present time the following methods—electrolytic, electroflotation, thermal, and mechanochemical—have been developed for the production of metallopolymers.

1. Electrolytic Method

Cathodic deposits obtained in the presence of suitable surface-active agents can be dispersed in hydrocarbon media to form stable concentrated sols.

The stability of such metal organosols is governed mainly by the degree of solvation of the metal particles by the surface-active agents. The latter compounds usually interact with the surface of colloidal metal particles, with the formation of chemically bound adsorbed films which are strongly solvated by the dispersion medium. The interaction between surface-active agents and metal particles should be limited to the formation of surface compounds firmly bound with the main mass of the metal particles. If chemical compounds of exactly stoichiometric composition are formed on the surface, and are soluble in the organic medium, the adsorbed films are unstable.

The stabilising films must be formed on the surface of the colloidal metal particles at the instant at which the latter are produced. Otherwise, the particles have time to coagulate, with the formation of coarse aggregates, which are not peptised on the subsequent addition of surface-active agents.

The above mechanism of formation of metal organosols operates also when the surface-active agents used are compounds of high molecular weight, whose macromolecules contain polar functional groups.

Examination of the structural–mechanical properties of polymer solutions showed[24] that even small additions of an active filler constitute centres for the formation of a continuous three-dimensional network, which arises from the adsorption and orientation of polymer molecules under the influence of the force field due to the filler particles. The ability of macromolecular compounds to form structures in solution and the cross-linking of a polymer on the introduction of a metal sol, together with the stability of these structures and their tendency to re-form after destruction, are the deciding factors responsible for the stability of a metal organosol.

The nature of the interaction between metal particles and macromolecules is also of substantial importance in determining the stability of the structural network of polymers in solution. Structure formation is most effective in the case of the irreversible adsorption of a polymer due to chemical interaction between the surface of the metal particle and the macromolecules.

An electrolytic method for obtaining metallopolymers in a double-layer bath with a rotating cathode[17] developed from the above investigations of the stability of concentrated metal organosols and ideas on the structural–mechanical properties of polymer solutions in the presence of fillers.

The essence of the electrolytic method is that, when aqueous solutions of appropriate salts (the lower layer of the bath) are electrolysed, metal particles deposited on a disc cathode rotating horizontally are transported to the upper, organic layer of the bath containing the polymer solution. This involves interaction between the metal particles and the polymer macromolecules. Polymer adsorbed on the cathode surface partly shields the latter, and electrolysis occurs only at active centres free from adsorbed molecules. Two processes—passivation and metal electrodeposition—take place. Passivation of the cathode increases its polarisation, which is a measure of the energy requirement for growth of the metal crystals and the formation of new centres of crystallisation[25,26]. Low cathodic polarisations correspond mainly to the activation energy for the transfer of metal ions from solution into the crystal lattice of the metal, i.e. crystal growth of the metal. Very often this energy is insufficient for the formation of new crystal nuclei, so that at low cathodic polarisations metals separate predominantly as coarsely crystalline deposits.

Adsorption of a polymer on the original cathode surface and also on the small metal crystals that are formed, together with the associated increase in cathodic polarisation, favours the formation of highly disperse metal particles, which become lyophilic with respect to the organic dispersion medium.

Rapid transfer of the metal particles creates favourable conditions for interaction between the polymer and the active centres arising on the freshly formed metal surfaces. The nature of the macromolecules has a substantial effect on the transfer of highly disperse metal particles to the upper layer of the bath. Thus with natural rubber of polyisobutylene highly disperse metal particles do not pass into the organic layer, but are concentrated at the interface between upper and lower layers; transfer to the organic layer becomes possible only as a result of inversion of the selective wetting by the addition of small amounts of simple surface-active agents, e.g. oleic acid[19].

If polymers having polar functional groups are present in the organic layer during electrolysis, the metal particles formed pass into the organic layer even in the absence of simple surface-active agents. The polar macromolecules are adsorbed irreversibly on the surface of the metal particles with formation of the corresponding surface chemical compounds[17]. Stable concentrated sols of metallopolymers can be obtained in this way. With a small content of highly disperse metal particles in the organosol, removal of the solvent yields solid or rubber-like products; with high (above 50%†) metal concentrations powders are obtained which can easily be processed.

A series of investigations[27–30] has been made on the effect of various factors—cathodic current density, temperature, electrolyte and polymer concentrations, nature of electrolyte and of polymer, pH of medium—on the current efficiency and the degree of dispersion of the metal particles formed at the cathode. All these relations are extremal in character. Optimum conditions for obtaining metallopolymers by the electrolytic method can be found experimentally for each metal–polymer system. The nature of the polymer has a decisive effect not only on the dispersion and yield of metal but also on its particle shape. Particles formed at the cathode usually have a strongly developed surface owing to their production as dendrites and other complicated forms with strong dimensional anisotropy[29–32].

2. Electroflotation Method

During electrolysis a solution of a surface-active agent of low or high molecular weight in an organic solvent is fed continuously through the pores of a stationary cylindrical cathode in a vertical position, and is sorbed at the electrolyte surface. The metal particles deposited on the strongly passivated cathode surface adsorb the surface-active substances from the organic medium, so that their surface becomes hydrophobic. The sorption of polymer molecules on the fresh particle surfaces favours their detachment from the cathode surface and flotation into the upper layer of the bath[33,34]. Flotation is promoted by a stream of nitrogen along the walls of the cathode during electrolysis. At the same time the nitrogen protects the highly disperse metal particles from oxidation.

The electroflotation method is more suitable than the electrolytic method for industrial use. On an industrial scale the latter method of obtaining metallopolymers in a two-layer bath with a rotating cathode encounters certain difficulties, caused by the need to design electrolytic cells with a rotating shaft and cathode, as well as current leads with a special device to prevent sparking. Moreover, the continuous production of metallopolymers is impossible in this case. The electroflotation method is free from these defects, and permits easy control of the degree of dispersion and the morphology of the metal particles formed at the cathode.

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†Percentages by weight are indicated here and subsequently.

3. Thermal Method

Several organic and inorganic compounds of metals, when heated in a reducing atmosphere or in a vacuum to a certain temperature, decompose with the separation of finely divided metal particles[35,36]. Decomposition of such compounds in an organic medium (oils, high-boiling solvents) may yield concentrated, highly disperse metal organosols[17,37].

Among compounds which decompose readily at comparatively low temperatures are certain salts of formic acid: when heated, they break down with the formation of disperse particles of the corresponding metal and volatile products (carbon dioxide, carbon monoxide, hydrogen)[36]. Silver, copper, nickel, cobalt, iron, and lead formates decompose in this way at temperatures not exceeding 250°C.[38,39] Differential thermal analysis has shown[40] that iron, nickel, and cobalt formates lose uncombined water at 102–103° and water of crystallisation at 115–137°C. The intense endothermic processes at 216°, 192°, and 203°C on the thermograms of these salts have been related to the corresponding decomposition points and the formation of finely divided particles of the metals. Chemical analysis of the metal powders showed them to contain on the average ~96.3% of the pure metal. Silver formate decomposes vigorously even at 64–67°C,[41] whereas copper formate begins to break down at 186°C.[42]

Freidlina and Bulanova established[36] that lead formate decomposes above 200°C with the separation of gaseous products, volatile liquids, metallic lead, and lead oxide. The thermograms show an intense double endothermic process at 240–260°C, ascribed to decomposition of the salt to metallic lead[43,44].

The conditions and the kinetics of the decomposition of metal oxalates, which also break down to yield the pure metals[45,46], have been considerably less investigated.

Among inorganic metal salts which decompose at relatively low temperatures with formation of a metal phase we mention the iron hexacyanoferrates. Mittasch[47,48] and Eisenhut[49], while examining the possibility of using decomposition products from iron ferrocyanides as catalysts for the synthesis of ammonia, showed that particles of α-iron are formed in a mixture of nitrogen and hydrogen above 300°C. Differential thermal analysis has established that all the following iron hexacyanoferrates—$Fe_2[Fe(CN)_6]$, $Fe_4[Fe(CN)_6]_3$, $Fe_3^{II}Fe_2^{III}[Fe(CN)_6]_3$, $Fe_3[Fe(CN)_6]_2$, $Fe[Fe(CN)_6]$, and $Fe_3^{II}Fe_4^{III}[Fe(CN)_6]_6$—decompose between 180° and 240°C.[50] Chemical analysis showed that the solid decomposition products of these salts contained 30–80% of highly disperse metallic iron with some iron carbide, the bulk of the metal being deposited during the first hour of reaction.

Thermoplastic polymers have been successfully used as the organic medium in the decomposition of such salts. The presence of the highly developed free surface of the metal particles at the instant of their formation in a polymer medium favours interaction of the surface metal atoms with functional groups and multiple bonds of the polymer, as well as with radicals formed by the partial thermal degradation of the macromolecules.

On this basis a thermal method was developed for obtaining metallopolymers[51,52], which consisted essentially in introducing easily decomposable metal salts into concentrated solutions of the polymers in a highly disperse state and precipitating the polymers with vigorous stirring. The washed and dried polymer containing particles of the salt was placed in a special apparatus[52], where it was kept in a vacuum at the optimum temperature for decomposition of the salt and formation of the metallopolymer. The time required for complete decomposition of metal salts in polymeric media is considerably longer than for the pure salts, owing to the poor thermal conductivity of polymers.

In contrast to ordinary mechanical mixtures of finely divided metals with polymers, metallopolymers obtained by the thermal method have a high degree of dispersion (1–5 μm) and a uniform distribution of metal particles in the bulk of the polymer, together with considerable irreversible adsorption of macromolecules on the surface of the metal particles at the instant of their formation. The quantity of irreversibly bound polymer is proportional to the metal content of the polymer and the duration of heating, and depends on the nature both of the polymer and of the metal[53]. The above differences between metallopolymers and ordinary mixtures have a favourable effect on the physicochemical, mechanical, and other properties characteristic of metal-filled polymeric systems[21,44,54–59].

The thermal method of obtaining metallopolymers is of especial interest in cases in which electrolytic methods are unsuitable owing to the sparing solubility of the polymer or the difficulty of depositing a highly disperse metal on the cathode. Another advantage of the thermal method is that solvent does not have to be removed before the metallopolymer is processed into articles.

4. Mechanochemical Method

The properties of polymers filled with coarsely divided metals are largely determined by the nature of the metal surface and the adhesive forces between the polymers and various metals[60]. The affinity of metal particles for a polymer can be increased by preliminary modification of their surface with substances of low molecular weight having a similar nature to the polymer[17,61,62], monomers capable of polymerisation on the solid surface[63–65], or directly by molecules of the polymer itself by means of mechanical, radiation, or other treatment of the coarse metal–polymer system[66]. Such treatment—in particular mechanical ones—produce cleavage of the polymer molecules with the appearance of free macroradicals, which may interact with the metal surface to form stable metal–polymer chemisorption bonds.

A mechanochemical method for obtaining metallopolymers has been based on these concepts. There are several varieties of this method—(*a*) the polymerisation of monomers on the freshly formed surface of the metal particles, initiated by active centres in this surface produced by the dispersion of metals in the monomers[65]; (*b*) the polymerisation of monomers on the surface of metal particles previously dispersed in a high vacuum (in an inert atmosphere or in the presence of substances which protect the metal surface from intense oxidation)[63,67]; (*c*) preliminary dispersion of metals in surface-active agents of low molecular weight, followed by the introduction of polymers containing active functional groups or multiple bonds, which promote chemisorption of the polymer on the surface of the metal particles[62,68]; (*d*) mechanical dispersion of metals in polymers[69,70]; and (*e*) simultaneous vaporisation of metal and monomer (polymer) in a vacuum, leading to the formation of highly disperse metal particles with macromolecules of the polymer chemisorbed on their surface[71,72].

Kargin, Plate, and their coworkers[73,74] investigated the processes of polymerisation occurring when metals, salts,

and oxides were subjected to vibrational milling in vinyl monomers. As a consequence of the exposure of energetically active faces the surface formed by grinding possesses considerable reactivity, which is apparent in a sharp increase in the adsorptive and chemisorption power. If monomers are present at the instant of formation of such a surface, the active centres in it of ionic or radical type interact with the monomer molecules to form a growing macroradical.

These workers investigated the polymerisation of styrene, methyl methacrylate, α-methylstyrene, acrylonitrile, and vinyl acetate on the surfaces of iron, nickel, chromium, and titanium during grinding, and proved by direct methods the formation of polymers grafted chemically to dispersed substances. The degree of conversion of the monomers increased with the duration of milling, the yield of polymer being small initially, after which it increased sharply. The degree of conversion at a constant time of dispersion depended on the proportions of the components: the highest yield of polymer was reached with small quantities of the monomer, this being associated with the better conditions for grinding.

The relatively coarse grinding of small quantities of iron with a phenol–formaldehyde resin [13,66,75] gave materials in which hardening of the resin was accelerated and its thermomechanical characteristics were improved. This can be explained by chemisorption interaction between active groups of the polymer [76] (phenolic hydroxyls, oxydimethylene groups) and the disperse metal particles.

With polyethylene and polystyrene [66] no appreciable change in properties was observed even on the introduction of considerable quantities of disperse iron. Only when concentrated solutions of these polymers were ground mechanically with the metal powder did interaction occur between the resulting macroradicals and active centres in the metal, as a consequence of mechanical degradation of the polymer macromolecules and "renewal" of the surfaces of the metal particles. The thermomechanical and mechanical characteristics of these systems varied not only with the conditions of mechanochemical treatment but also with the particulate form of the iron [77]: powders containing dendritic particles were more effective as fillers for polymers.

An optimum time of grinding was established [66] for the metal–polymer composition, since prolonged mechanical action on the system produces considerable degradation of the polymer.

Although the above papers give no direct proof of the occurrence of chemisorption interaction between polymers and metal particles when ground together, the effective improvement in several physicomechanical characteristics of these systems can be explained by the formation of surface compounds between polymers and metal, i.e. by the formation of metallopolymers.

Processes occurring at an interface between a metal and a polymer in dynamic contact have been surveyed [78]. The presence of the polymer was shown to promote finer subdivision of the metal (e.g. iron) in a ball mill. The explanation is that the polymeric molecules are activated chemically during loading, and interact with the exposed crystalline surfaces of the metal particles, diminishing their free energy, which leads to intense dispersion of the metal. Surface-active substances of high molecular weight, e.g. poly(methyl methacrylate), were considerably more effective than simple compounds, e.g. oleic acid.

The dispersion of metal powders in the presence of surface-active agents of amine type creates favourable conditions for the formation of chemically fixed adsorbed layers, consisting mainly of compounds of the type M–NH_2 or M–NH–M. [68] This makes interaction between metal particles and polymer macromolecules substantially easier, and promotes a uniform distribution of the particles in the polymer.

The introduction of highly disperse metal powders into polar rubbers (SKN-26, Nairit chloroprene rubber) improves their stability and also accelerates vulcanisation, as a consequence of interaction between the surface of the metal particles [79–81] and the polymer molecules at the instant of opening of the double bonds.

The above applications of the mechanochemical method of obtaining metallopolymers require only simple equipment, and will undoubtedly find wide use in industry in the very near future.

III. MECHANISM OF INTERACTION BETWEEN POLYMERS AND COLLOIDAL METAL PARTICLES DURING FORMATION

Several factors—nature of polymer and metal, chemical state of metal surface, conditions of contact between polymer and metal—govern the character of the interaction between polymer macromolecules and the surface of the metal particles. The present Section discusses various mechanisms of interaction at the interface between metal particles obtained by the above methods and the macromolecules of various polymers, leading to the formation of metallopolymers. In this connection it is necessary to consider also the changes occurring in the mechanism and the kinetics of polymerisation and polycondensation in the presence of highly disperse metals.

1. Metallopolymers based on Macromolecular Organic Compounds

Investigations of chemisorption interaction in the formation of metallopolymers have been made mainly on systems containing polymers having functional groups which are reactive towards metals and their oxides.

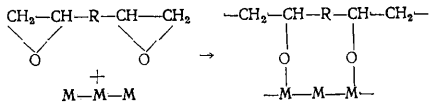
Epoxide–dian resins‡

During investigation of electrolysis in the presence of various polymers it was noted that the epoxide resin ED-5, in contrast to polymers not containing functional groups (polyisoprene, natural rubber), promotes migration of metal particles from the cathode into the organic layer with formation of a stable concentrated metal organosol [18,29,82]. In this case the metal particles are easily made lyophilic with respect to the organic dispersion medium.

Infrared-spectroscopic examination of the products of interaction of ED-5 resin with the metal (iron, lead, etc.) particles at the instant of their formation at the cathode showed a considerable diminution in intensity of the 915 cm^{-1} absorption band corresponding to bending vibrations of epoxy-groups [18], with an inverse relation between the concentration of metal in the polymer and the intensity of this band [18,27,83]. This undoubtedly proves that, at the instant of formation, the highly disperse metal particles

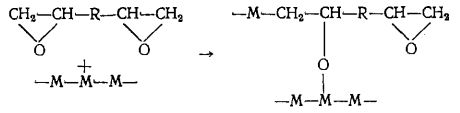
‡Dian = 1,3-diphenylpropane-*pp'*-diol (Ed. of Translation).

react chemically with macromolecules of the epoxide–dian resins. This evidently involves opening of the epoxy-rings:



Such a mechanism should yield three-dimensional structures, in which the highly disperse metal particles act as junction points. In fact ED-5 resin containing 12% of electrolytic lead but without the introduction of any hardening agent was completely hardened at 210°C in 90 min [83]; the pure resin had not hardened at this temperature after 10 h had elapsed.

Investigation of the mechanism of formation of metallopolymers from an epoxide resin and highly disperse palladium obtained by the electrolytic method yielded similar results [84,85]. Palladium metallopolymers exhibited new infrared absorption bands in the region of 440 and 420 cm^{-1}, whose intensity increased with the metal content of the polymer [86]. The appearance of these bands is obviously due to the formation of chemisorption bonds, not only of the C–O–M but also of the C–M type, during hardening [87]:



Differential thermal analysis shows that considerable thermal effects accompany the interaction of epoxide resins with highly disperse metals: they occur in the region of 190°C in the case of copper [42,88], 280–300°C with lead [89], at 293°, 322°, and 380°C with palladium [86], at 196–223°C with iron and cobalt [53], and at 186–198°C with nickel [53]. The intensity of these effects generally increases with increased metal content of the metallopolymer, while they move to lower temperatures on the differential thermal analysis curve.

The appearance of free radicals has been recorded [42,86,88] even at 200–210°C in the metallopolymers on the introduction of highly disperse copper, palladium, or lead into ED-5 epoxide resin, the majority of them being formed during the first 30–60 min of heating. The intensity of the electron spin resonance signal increased with rise in temperature, while the band width remained constant at 10.6–10.9 G. The appearance of this band can be attributed to the generation of macroradicals of the epoxide–dian resin accompanying formation of the metallopolymers. It is noteworthy that heating the pure resin to 260°C does not result in the appearance of radicals.

The radicals produced in metallopolymers based on an epoxide resin are extremely stable (their lifetime at room temperature is of the order of several months), which is obviously due to the formation of a rigid three-dimensional polymer structure. The lower temperature at which macroradicals appear in metallopolymers, in comparison with the pure resin, indicates not only polymerlike transitions in the polymer chains but also acceleration by the highly disperse metals of the thermal degradation of the polymers.

Kinetic investigation of the hardening of an epoxide resin by various highly disperse metals leads to the conclusion that the quantity of bound resin depends not only on the concentration of the metal and the time of heating at a given temperature but also on the nature of the metal (Table 1). Such substantial differences in the quantity of resin bound by different metals at a given hardening temperature and metal concentration in the resin are obviously associated with the electronic structure of the metal atoms. According to Trapnell [90] chemisorption on metals involves the formation of surface compounds with *d*-electrons of the metal atoms. Table 1 [27,29,42,82–89] shows that, during the chemisorption of the epoxide resin, the activity of the metals diminishes as the *d*-shells of the metal atoms become filled.

Table 1.

Metal	Metal in metallopolymer, wt.%	Hardening temp., °C	Bound resin, wt.%, after 2 h	6 h	12 h
Iron[a]	10		98.27	98.84	99.40
	20	230	98.32	93.03	99.48
	30		98.30	99.08	99.49
Nickel	10		75.80	96.39	98.30
	20	230	94.00	97.40	98.60
	30		94.40	97.88	98.88
Palladium	11		8.8[b]	74[e]	
	21.9	225	27.5[c]	92.7[b]	
	26		79.3	94.0	
Lead	12	240	92.0[d]		
Cadmium	10	220	21.0		
Copper	10	240	57.0		
	10		30.5		
	20	210			
	30		60.12		

[a]Identical results obtained for cobalt.
[b–e]Heated for 1, $1\frac{1}{2}$, $2\frac{1}{2}$, and 4 h respectively.

Cadmium and palladium possess comparatively low chemisorption activity, although the latter is a metal of variable valency. The high activity of lead in comparison with the other metals cited here is obviously due to its tendency to form covalent compounds, for the surface compounds formed by an epoxide resin with metals are of this type [16].

The suggested mechanism of the formation of metallopolymers is supported by a comparative study of the conditions under which the pure epoxide–dian resin and metallopolymers formed from it are hardened when exposed to γ-rays [91,92]. Whereas in the radiation hardening of the pure resin a decrease in the concentration of epoxy-rings is accompanied by an increase in the concentration of carboxyl and hydroxyl groups, the carboxyl content remains constant during irradiation of the lead metallopolymers, while the concentration of hydroxyl and epoxide groups decreases sharply. This is obviously due to the accelerating action of γ-rays on the chemisorption of the resin on the surface of the highly disperse metal particles.

X-Ray examination of the γ-irradiated pure resin and metallopolymers based on it indicates that increase in the duration of exposure produces increased ordering of the epoxide–dian resin molecules with the appearance of a quasi-crystalline structure [93]. The introduction of highly disperse copper into the resin promotes a considerable increase in the ordering of the macromolecules after irradiation, but this is not observed in the presence of lead.

Poly(vinyl acetate)

Several studies have been made [31,94–97] of the formation of metallopolymers of poly(vinyl acetate) $[CH_2.CH(OCOCH_3)]_n$ with highly disperse lead and palladium.

Investigation of the effect of the molecular weight of this polymer in the range 117 000–4000 showed that a decrease to ~ 13 000 was accompanied by an increase in the activity of the polymer during electrolysis. A decrease in molecular weight favours a diminution in the blocks of the mosaic of metal particles and also a decrease in size of the particles themselves. These phenomena are probably associated with the adsorption activity of poly(vinyl acetate) [98].

Study of the nature of the bond formed when a polymer is adsorbed on the surface of disperse metal particles indicates ion–dipole interaction between carbonyl groups of the poly(vinyl acetate) and the metal surface. Further evidence of this is the shift in the 1734 cm^{-1} infrared band to 1711–1706 cm^{-1} in the spectrum of the metallopolymer (at a palladium content of 5–10%).

Heating poly(vinyl acetate) metallopolymers produces marked cross-linking of the system [99,100], as a consequence of the detachment of acetate groups from the polymer and interaction of the resulting radicals with the metal surface to form an M–C chemisorption bond [86].

Increase in the concentration of metal, in particular palladium, in the polymer is accompanied by a considerable increase in the concentration of free radicals and a lowering of the temperature at which they are detected. The appearance of free radicals at extremely low temperatures (Table 2) [86] is evidence of chemisorption interaction of the highly disperse palladium particles with macromolecules of poly(vinyl acetate) in the formation of metallopolymers.

Table 2.

Pd in metallopolymer, %	Free radicals in metallopolymer, spins g^{-1}	Radicals detected at, °C
22.45	$4.75 \cdot 10^{17}$	180
47.25	$2.19 \cdot 10^{18}$	100
80.0	$3.40 \cdot 10^{18}$	30

Rubbers

The early publications showed [18–20,101,102] that polyisobutylene and natural rubber, possessing neither functional nor other active groups, do not interact directly with the surface of metal particles at the instant of their deposition on the cathode. A metal organosol is formed only in an oleic-acid solution of the polymer. In neither case did infrared spectroscopy detect a metal–rubber macromolecule chemisorption bond. However, investigation of the swelling and desorption of metallopolymers obtained in this way has established that irreversible adsorption of the polymer on the metal surface nevertheless takes place. In this case interaction between rubber macromolecules and the surface of the metal particles is evidently accomplished through an adsorbed layer of oleic-acid molecules [20].

Electrolysis in the presence of a carboxylate or other polar rubber produces direct chemisorption interaction between rubber macromolecules and particles of various metals [18,28,69]. The swelling and the desorption of such rubbers show this process to be irreversible, and infrared spectroscopy has established ion–dipole interaction between the metal and functional groups of the polymer. The band at 1720 cm^{-1} in the infrared spectra of the metallopolymer, corresponding to vibrations of the C=O group, shifts and diminishes in integral intensity with increase in the concentration of metal in the rubber and rise in temperature, which confirms a chemisorption mechanism of interaction between polar rubbers and metal particles. In this case the latter act as hardener, and promote the formation of a three-dimensional structure in the metallopolymer.

The hypothesis was put forward [74,103] that, when iron is ground in the presence of polyisoprene, the rubber macromolecules initially undergo rupture at the tertiary carbon atom as the weakest point in the chain, and the resulting macroradicals then interact with the metal surface. Investigation of the semiconductor properties of mechanical mixtures of polyisoprene with iron and of compositions where chemisorption interaction between polymer and metal takes place as a consequence of mechanochemical processes, and of the polymerisation of isoprene on freshly formed faces of particles of the metal, shows that chemisorption interaction between the components determines the type of conduction of the resulting systems.

Polystyrene

Metallopolymers have been prepared from polystyrene and highly disperse lead, copper [58], and silver [41] by the thermal method; bismuth and manganese [104] have been introduced by a mechanochemical method. The accompanying chemisorption interaction at the metal–polymer interface results in the formation of a stable three-dimensional structure in the polymer. Furthermore, heat-treatment of the polystyrene–metal system produces significant rises in the glass and flow points of the polymer even in the presence of small amounts of the metal. As in the case of an epoxide resin, the nature of the metal influences the bonding of the polymer and the change in its thermomechanical properties. Metallopolymers based on polystyrene and highly disperse metals are not formed by the electrolytic method, as in the case of non-polar rubbers.

The cathodic deposition of lead [43] and cadmium [104] in the presence of polystyrene and oleic acid in the upper layer of the bath is accompanied by interaction between polymer and metal particles only at the level of van der Waals forces, as was to be expected. The equilibrium swelling for such systems is independent of the content of highly disperse metal in the polymer, but the rate of swelling of filled specimens is even higher than that of pure polystyrene. The introduction of a highly disperse metal into polystyrene, in the absence of chemisorption interaction between them, obviously causes the formation of loose layers of polymer at its interface with the metal, which facilitates penetration of the solvent into the polymer and swelling of the latter [8].

Study of the polymerisation of styrene in the presence of highly disperse metals obtained by various methods is of interest in connection both with the mechanism of the formation of metallopolymers and with the polymerisation of monomers on a solid surface. The rate of polymerisation of styrene in the presence of highly disperse iron, chromium, bismuth, and manganese [106,107] increased, especially during the early stages, if the concentration of these metals did not exceed 1.5%. The yield of polymer also increased, but the variation in the molecular weight was extremal. The increases in the rate of polymerisation and in the yield of polymer are obviously explained by the catalytic action of highly disperse metals on the decomposition of a peroxide initiator of polymerisation. At the

same time, the high rate of formation of growing macroradicals leads to a decrease in the mean molecular weight of the polymer. This process was so intense that the softening point of the metallopolymer fell with increase in the concentration of metal in it [67].

The polymerisation of styrene in the presence of chloride salts is accelerated [108] by additions of colloidal palladium and gold. It is suggested [108] that the polymerisation of styrene, on the freshly generated surface of the colloidal metal particles, is initiated by the formation of π-complexes involving *d*-orbitals of metals with variable valency and vinyl groups of the monomer. It is supposed that the metal particles are not regenerated, but are bound similarly to fragments of an ordinary initiator: i.e. chemical grafting of the polymer on to the surface of the metal particles is assumed.

A Japanese study [109] of the polymerisation of styrene on combined catalysts of the activated metal–organic halide type confirms that polymerisation is most active with metals having a freshly formed surface.

Thus the introduction of highly disperse metals having an active surface into styrene undergoing polymerisation creates favourable conditions for chemisorption interaction between metal and polymer, which should have a significant effect on the physicochemical properties of the resulting polymers, despite the small amounts of metal introduced. The addition of 1.5% of manganese or bismuth to styrene undergoing polymerisation [55] raises the temperature at the start of thermo-oxidative degradation of the polymer from 280° to 337°C.

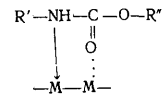
Nitrogen-containing Polymers (polyurethanes, polyamides)

The presence of tervalent nitrogen atoms of well defined π-donating character in a polymer chain should have a significant influence on the adsorption of these polymers on metal particles. In any case, hydrogen bonding may be expected between a hydrated or oxidised metal surface and amide groups in the polymer. However, Bills [110], in an investigation of the swelling of polyurethane–polyisobutylene filled with glass, salts, and also disperse aluminium and tin, did not observe any significant interaction between the polymer and the fillers. This was obviously due to the conditions of filling, which did not guarantee adequate and reliable contact between polymer macromolecules and the filler surface.

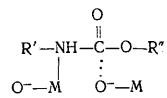
Examination of metallopolymers obtained from polyurethane rubbers and highly disperse cathodically deposited iron particles [111] support Trapnell's view [90] that coordinate interaction occurs at the interface between nitrogen-containing polymer and metal. The infrared spectra of these metallopolymers exhibit a shift to lower frequencies of the 1727 cm^{-1} band representing stretching vibrations of the C=O groups of polyurethane, the displacement being larger the higher the concentration of metal in the metallopolymer. Furthermore, the band in the region of 700 cm^{-1}, due to deformation vibrations of NH groups in the pure polymer, disappears, which may indicate that this bond is partly ionic in the metallopolymer.

Especially large differences in the spectra are observed in the range 600–400 cm^{-1}. Polyurethane exhibits several absorption bands, with maxima at 560, 518, and 495 cm^{-1}, these being due to deformation and out-of-plane vibrations of C–N bonds. The 560 cm^{-1} band is much weaker in the spectrum of the metallopolymer, and has shifted to the range 630–620 cm^{-1}. A new band appears in the region of 507 cm^{-1}, whose intensity increases with the metal content of the polymer; this band is due to stretching vibrations of the M–N bond.

Similar results have been obtained for metallopolymers based on capron [Soviet polyamide-6] and copper [112], iron, nickel, and cobalt [113,114]. These experimental results are consistent with the views of Rutzler [16] and Trapnell [90] on the nature of the adhesive bond between a nitrogen-containing polymer (nylon) and steel, according to which the interaction between metal and polymer involves the formation of surface coordination compounds—(1) with an unoxidised metal surface



or (2) with an oxidised metal surface



Chelate polymers

Chelate (coordination) polymers are similar to nitrogen-containing metallopolymers in the character of their interaction with metals.

Many chelate polymers containing conjugated bonds in their chain possess semiconductor properties [115]. The introduction of highly disperse metals, forming coordinate bonds with the polymer macromolecules, has a substantial effect on the type of conduction and the conductance parameters of these materials. Berlin et al. [115,116] worked out methods for obtaining, and investigated the electrophysical properties of, compositions consisting of disperse metals and chelate polymers. They used tetracyanoethylene as monomer [117], capable on polymerisation of interacting with metal surfaces to form polymeric chelate compounds.

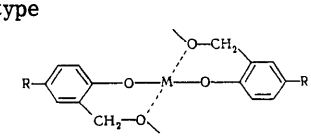
Information has been published also on the polymerisation of phthalocyanines [118], and the synthesis of polymeric Schiff bases and polyazaporphyrins [119] in the presence of powdered metals, accompanied by the formation of coordinate bonds between the surface of the metals and the polymeric molecules.

Since these polymers themselves possess several interesting semiconducting, electrical, and catalytic properties, the further addition of highly disperse metals should obviously intensify these properties in several cases or change their character.

Other organic polymers

The nature of the interaction between polyethylene glycol maleate phthalate, a polyester containing polar ester groups and unsaturated bonds, and the surface of cathodically deposited highly disperse iron has been investigated by infrared spectroscopy, which has established that double bonds are opened with the formation of a chemisorption C–Fe bond [120].

Interesting investigations have been made [121] on the mechanism of the interaction of metals with phenol–formaldehyde resins, which are able to form chelate bonds [76] of the type



with an oxide film on a metal.

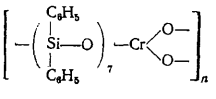
The possibility of forming chemisorption bonds with metals is not confined to polymers containing functional groups or unsaturated bonds. The thermo-oxidative degradation of polyethylene containing disperse iron is sharply accelerated at 240°C, with the formation of chemisorption compounds between macroradicals of the degraded polyethylene and iron.

2. Metallopolymers based on Organometallic Siloxane Polymers and Polyorganosiloxanes

Metallopolymers based on organoelementary siloxane polymers and polysiloxanes are of considerable interest because of the great thermal stability of the initial polymers, which can be still further improved by the introduction of highly disperse metals. Investigation of the mechanism of the formation of these metallopolymers is thus closely connected with problems of the thermal stability, thermal degradation, and stabilisation of the above polymers filled with highly disperse metals [124].

Polydiphenylsiloxanoxychromium

Polydiphenylsiloxanoxychromium has the cyclolinear structure



and possesses excellent thermal stability [125,126]. Metallopolymers have been obtained from it by a thermal method. The decomposition of lead formate in the polymer [127] at 240°C for 6 h yields a metallopolymer, whose structural forms differ considerably, according to differential thermal analysis data, from those described for the pure polymer [126].

Atkins et al. [128], who studied the thermal stabilisation of polydimethylsiloxane rubbers by metals, including lead, suggested that at high temperatures lead oxides rupture the chain of the siloxane polymer, and then react with the macroradicals thus produced, forming a new polymer containing lead in the main chain. Andrianov [129], in work on the stabilisation of cyclolinear polymethylphenylsiloxanes by metal oxides, showed that chrome yellow may cause rupture of silicon–carbon bonds and also the cleavage of rings in the polymer. Analogous changes obviously occur in the structure of polydiphenylsiloxanoxychromium on the formation of metallopolymers containing lead.

The infrared spectra of these metallopolymers reveal a direct dependence, on the concentration of lead in the polymer, of the decrease in integral intensity of absorption bands at 1050 and 1010 cm^{-1}, due to silicon–oxygen stretching vibrations in small rings, and a considerable strengthening of bands at 1090–1080 cm^{-1}, due to silicon–oxygen stretching vibrations in linear polymer chains [130]. Thus the spectroscopic results provide experimental evidence of ring-opening in polydiphenylsiloxanoxychromium under the influence of highly disperse lead. Furthermore, the infrared spectra of the metallopolymers contain a new band at 620 cm^{-1}, whose intensity increases with increased concentration of lead in the polymer. This band is obviously due to vibrations of the chemisorption SiO–Pb bond, formed by interaction between polymer radicals and the surface of the lead particles.

Both infrared spectroscopy and differential thermal analysis suggest that, when a mixture of polydiphenylsiloxanoxychromium and lead formate is heated at 240°C, polymer molecules are adsorbed on the freshly formed surface of the deposited lead particles, which catalyse ring-opening and obviously the detachment of phenyl radicals. The resulting macroradicals undergo chemisorption interaction with the surface of the lead particles, to form linear, branched, and perhaps cross-linked polymer macromolecules containing lead atoms as well as chromium.

Similar results have been obtained for metallopolymers based on polydiphenylsiloxanoxychromium and highly disperse iron formed by the thermal decomposition of iron ferrocyanide in the polymer [131].

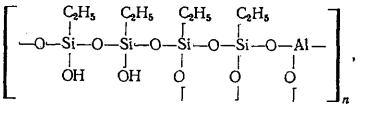
Investigations of the thermomechanical properties of these metallopolymers [132] have revealed no simple relation between softening temperature and concentration of metal in the polymer, such as occurs with linear organic polymers. At low metal concentrations (up to 4%) the softening point of the metallopolymers rises, as a consequence of the increased number of sorbed macromolecules on the solid surface. However, further increase in concentration (5–10%) is accompanied in all cases by a fall in the softening point. At higher metal concentrations the softening temperature either rises slightly or else remains unchanged.

The lowering of the softening point at metal concentrations of 4–10% is obviously due to intense decyclisation of the polymer under the catalytic influence of the highly disperse metals, with the formation of linear polymer molecules, which are more mobile than cyclolinear molecules. This process probably occurs to a considerable extent only when the metal concentration reaches 4%. It continues at concentrations above 10%, but is accompanied by intensified cross-linking of the polymer, so that only a slight rise in softening temperature of the metallopolymers is observed. This type of dependence of the softening temperature on the metal content in the polymer has been found with all metallopolymer systems based on cyclic and cyclolinear organometallic siloxane polymers [133].

Highly disperse metals are efficient catalysts of ring-opening in organometallic siloxane polymers. This is evident with polydiphenylsiloxanoxychromium in particular in the fact that the introduction of a small quantity of highly disperse metal (by the thermal decomposition of suitable salts in the polymer) makes the polymer capable of softening.

Polyethylsiloxanoxyaluminium and oligomeric αω-dihydroxypolydimethylsiloxane

Polymethylphenylsiloxane contains no active functional groups, and is therefore neutral in the electrochemical crystallisation of highly disperse iron [134]. Polyethylsiloxanoxyaluminium



which is a cyclolinear polymer, contains a sufficient number of hydroxy-groups [135] for metallopolymers to be obtained [30] by the electrolytic method. The electrochemical crystallisation of highly disperse cadmium in the presence of this polymer and the transport of metal to the

upper, organic layer of the bath are ensured by interaction between polymer hydroxyls and the surface of the cadmium particles deposited on the cathode.

Differential thermal analysis and infrared spectroscopy show that, when metallopolymers based on polyethylsiloxanoxyaluminium and cadmium are heated at 200°C, the radicals formed by the detachment of hydroxyls interact with highly disperse cadmium particles[30].

Investigation of the electrochemical crystallisation of highly disperse cadmium in the presence of $\alpha\omega$-dihydroxypolydimethylsiloxane—a reactive organosilicon oligomer—in the upper, organic layer of the bath[32] has shown that here also the metal particles interact with hydroxyls of the oligomer to form a chemisorption bond. This is accompanied by polycondensation of the oligomer under the catalytic influence of the metal particles formed at the cathode.

Polydiphenylsiloxane

Metallopolymers of the type described above have been obtained both from the ready made organometallic polymers and oligomers containing hydroxy-groups and by the polycondensation of hydroxylated organosilicon monomers (e.g. diphenylsilanediol) in the presence of highly disperse metals.

At temperatures above 200°C diphenylsilanediol undergoes condensation[136] with the liberation of water and benzene, owing to the occurrence of two reactions—(1) interaction of the monomer hydroxyls with elimination of water and formation of a siloxane bond, and (2) interaction between hydroxyls and phenyl radicals with elimination of benzene and formation of a siloxane bond.

In the polycondensation of diphenylsilanediol in the presence of highly disperse lead[137] and iron[50] obtained by thermal decomposition of lead formate and iron ferrocyanide in the monomer, reaction (1) predominates with increase in the content of these salts. This may be due to the action either of the liberated metals or of the salts themselves and their volatile decomposition products (formic acid, cyanogen), which are acidic in character.

Acids catalyse the condensation of this monomer with the formation of a cyclic trimer—hexaphenylcyclotrisiloxane—and the elimination of water.

The polycondensation of pure diphenylsilanediol at 240°C is a rapid process, complete within 15–20 min. This excludes any effect of the highly disperse metal on the process, since appreciable quantities of the metal are formed only on more prolonged heating. The kinetics of the condensation of the monomer and of the decomposition of the metal salts indicate that the salts catalyse condensation of the monomer with elimination of water and formation of the cyclic trimer. However, the infrared spectra of the final condensation products containing highly disperse lead or iron indicate the formation of linear products, the quantity of which increases with the concentration of metal in the polymer. This apparent contradiction between kinetic and spectroscopic results disappears if the cyclic trimers formed in the initial period of condensation open up under the influence of highly disperse metals in the second stage with the formation of linear macromolecules. The occurrence of two stages in the formation of metallopolymers from diphenylsilanediol is also confirmed indirectly by the dependence of the softening point of the metallopolymers on the concentration of metal, which is similar in character to that found with polydiphenylsiloxanoxychromium.

Since the salts and their volatile decomposition products affect the mechanism of the polycondensation of diphenylsilanediol, it was desirable to investigate its polycondensation in the presence of a highly disperse metal already introduced into it by the electrolytic method. The infrared spectra of diphenylsilanediol containing electrodeposited lead[139], in comparison with the spectrum of the pure monomer, show a considerable shift to higher frequencies (940–920 cm^{-1}) of the 890–845 cm^{-1} doublet, corresponding to deformation vibrations of the hydroxyl in the Si–OH bond[130]. The broad absorption band at 3200 cm^{-1}, due to hydroxy-stretching vibrations in the solid monomer[130], is also displaced to shorter wavelengths (3400 cm^{-1}). Such a considerable shift in these bands is obviously due to chemisorption of the monomer on the surface of the lead particles at the instant of their deposition on the cathode.

The energy of interaction of hydroxyls with the metal surface calculated from the shift[140] is ~7 kcal $mole^{-1}$, which corresponds in magnitude with the energy of a hydrogen bond. Chemisorption on a freshly formed lead surface diminishes the mobility of the monomer molecules and causes a redistribution of the electron density of all the bonds, which should affect the reactivity of individual groups in the molecules and the mechanism of condensation of diphenylsilanediol as a whole. The thermal condensation of diphenylsilanediol containing electrolytic lead, unlike its condensation in the presence of lead formate decomposing to the metal, takes place only by reaction (2)—with the elimination of benzene.

The above results suggest a mechanism for the polycondensation of diphenylsilanediol in the presence of highly disperse electrodeposited lead in which, at the instant of deposition of the lead particles, monomer molecules are adsorbed by one hydroxyl on the freshly formed metal surface. When the monomer is heated phenyl radicals, unhindered by adsorption, interact readily with the hydrogen atom of a hydroxy-group in an adjacent molecule, benzene being eliminated. This should yield mainly a linear polymer adsorbed by hydroxyls on to the metal. Under these conditions there is little likelihood of the formation of cyclic trimers, owing to the rigidity of the growing macromolecule adsorbed at one end. These conclusions are supported by infrared-spectroscopic examination of the metallopolymers.

Although the dependence of the softening point of the metallopolymers on the metal concentration is the same in character as that for cyclolinear and cyclic polymers, the fall in softening temperature in the concentration range 4–10% is considerably less pronounced, obviously owing to the formation of small amounts of cyclic molecules. It should also be noted that, for the same lead content, the absolute softening points of metallopolymers obtained by the electrolytic method are higher than those of specimens obtained by a thermal method. The probable reason is more effective interaction in the former case between the monomer—later also the polymer—and the highly disperse metal.

Briefly summarising the investigations on the mechanism of the formation of metallopolymers based on organo-elementary polysiloxanes and polyorganosiloxanes, we note that all cyclic and cyclolinear polymers undergo ring-opening under the influence of highly disperse metals[133]. This may be accompanied by the formation of chemisorption bonds of the type Si–O–M between the macroradicals and the metal surface. Among the metals examined, highly disperse lead was the most active[50]. Linear polyorganosiloxanes containing functional groups react with highly disperse metals under ordinary conditions;

on heating such interaction involves chain breakage and incorporation of the heteroatom into the polymer chain [128].

IV. PHYSICOCHEMICAL PROPERTIES AND APPLICATIONS OF METALLOPOLYMERS

Chemisorption interaction with a highly disperse metal affects also the boundary layers of a polymer to a certain depth, appreciably changing its properties in compositions. The physicochemical properties and the applications of metallopolymers pose vast and many-sided problems, a full consideration of which could form the subject of a separate review.

Electrical Properties

The electrical properties of metallopolymers are determined by the nature and the concentration of the metal, the method of its introduction, and also the character of the interaction [150] between metal and polymer.

With metallopolymers based on rubbers (natural rubber and polyisobutylene) and highly disperse iron [19] cobalt, and nickel [20] obtained electrolytically, the conductivity increases only slightly as long as the metal concentration does not exceed 20–40%. The explanation is that, under the influence of the metal particles, the rubbers acquire an ordered network structure.

At higher metal concentrations the particles form chain structures and are in contact with one another; the conductance shows an avalanche-like increase. As the metal concentration increases to 80%, the systems become almost as highly conducting as metals, their conductance falling with rise in temperature. A similar type of conductivity has been found for the polystyrene–silver system [41] and for those formed by an epoxide resin with copper [57] and with iron [141].

The explanation of the sudden increase in conductance at metal concentrations exceeding 40% is that, in metallopolymers having low metal contents, the metal particles are mostly separated by distances exceeding their mean diameter, and the probability that particles will be incorporated into a chain of a certain length is small. At metal concentrations above 40% the distances between the particles become comparable with their diameter, so that the further addition even of small quantities of metal will lock a series of adjacent particles, and this is responsible for the sharp increase in conductance at these concentrations.

The conductance of metallopolymers is due not only to metal chain structures but also to the tunnel effect [57]. At energies corresponding to a particular voltage the current carriers are able to overcome the potential barrier of the polymer shell, when the number of carriers in the system will increase exponentially.

Several researches have shown that the mode of preparation of the specimens has a great effect on the conductance of metal-containing polymer systems. Thus raising the temperature and the pressure at which the samples were prepared leads to a considerable increase in the conductivity [151]. This effect is especially strongly developed in the region of plastic deformations of the systems.

If a magnetic field is applied during the formation of metallopolymers, which gives a directed orientation of metal particles in the polymer, anisotropy of the conductance is observed [152].

Levina et al. discovered [74,103] that the vibrational milling of iron in isoprene, which polymerises on the fresh faces of the metal particles, yields a semiconductor material having electronic conduction; if the vibrational milling is conducted in ready made polyisoprene, material having positive-hole conduction is formed. The character of the interaction between polymer macromolecules and iron particles must obviously be taken as responsible for the type of conduction.

Dielectric Constant

Experimental values of the dielectric constant and the loss angle for the metallopolymers formed by an epoxide resin with copper [57] and with palladium [153] differ from the theoretical values, which is explained by the presence of radicals fixed on the surface of the metal particles. The dielectric constant of the metallopolymers is diminished by chemisorption interaction and cross-linking of the epoxide resin on the metal surface, which leads to bonding of the epoxy-groups.

Formation of radicals is intensified during hardening, and the dielectric constant of the system increases. When the system is completely hardened, with formation of a dense three-dimensional structure, the kinetic mobility of the remaining free radicals diminishes, as also the dielectric constant and the tangent of the loss angle.

Catalytic Properties

The use of polymers as stabilisers and carriers of the active phase in hydrogenation catalysts has for a long time attracted the attention of many investigators [154–158].

During recent years Sokol'skii and his coworkers have made extensive investigations [159–167] on the hydrogenation of organic compounds, containing double and triple bonds, over platinum-group catalysts deposited as finely divided reduced metal powders on a polymeric carrier—polyacrylonitrile, polyvinyl alcohol, anid, poly(ethylene terephthalate). The selectivity and the activity of these catalysts are determined in considerable measure by the nature of the polymer [168]. This is evidently related to the deformation of the electron shells of atoms of the disperse metal adsorbed on polar groups of the polymer, and to the orientation of molecules of the unsaturated compound as it approaches the catalyst surface along the polymer chain, with the unsaturated groups located on the active centres of the metal [168].

Metallopolymers based on polydimethylphenylsiloxane and highly disperse electrolytic iron have been studied [169–172] as catalysts for the synthesis of ammonia. Thermostable polysiloxanes proved to be resistant stabilisers of the surface of the active phase (100–120 $m^2 g^{-1}$), and provided reliable protection against sintering of the metal particles. The above metallopolymers were comparable in efficiency with an industrial iron catalyst.

The great catalytic activity of metallopolymers based on an epoxide resin, poly(vinyl acetate), and highly disperse electrolytic palladium for the hydrogenation of unsaturated organic compounds remains almost unchanged on prolonged storage of the catalyst under ordinary conditions [86].

Investigation of the catalytic properties of metallopolymers requires further development both in the search for new systems suitable for definite catalytic reactions

and in the establishment of the interrelation between the semiconductor and the catalytic properties of metallopolymers [173].

Metallopolymers are used also in the purification of petroleum products from organosulphur compounds at normal pressures and temperatures [174,175].

Antifriction Properties

Metallopolymers find application as antifriction materials [56]. The combination of polymers, which possess low coefficients of friction or abrasion, with the highly disperse metals traditionally employed in friction joints (copper, lead, etc.) yields antifriction materials having low coefficients of friction and, what is very important, high thermal conductivity and good mechanical properties [60].

Thermomechanical Properties

Chemisorption interaction between polymers and metals greatly restricts the mobility of individual macromolecules and supermolecular structures [8] in contact with the surface of the metal particles, so that the softening and glass points of metallopolymers are particularly high [21] compared with those of ordinary filled polymers. The thermomechanical properties of a polymer are affected significantly not only by the type of interaction between polymer and metal but also by the concentration, degree of dispersion [66], particle shape [77], and nature of the surface of the filler. The high degree of dispersion and uniformity of distribution of metal particles introduced into polymers by the methods described above are already sufficient to ensure considerable differences in thermomechanical properties between metallopolymers [41] and ordinary filled systems.

The effect of the character of interaction between polymer and metal on the thermomechanical properties of the compositions can be clearly traced from the variation in the softening points of metallopolymers based on polystyrene [41,58,67], where interaction between polymer and metal surface is weak, and in those based on an epoxide–dian resin [21,84,85,141], poly(vinyl acetate) [99], and capron [112–114], where chemisorption interaction between macromolecules and metal surface has been established. At the same concentrations of different metals the softening temperatures of the second group of metallopolymers are always far higher. Furthermore, whereas the first group of metallopolymers exhibit an almost linear dependence of softening point on metal concentration, metallopolymers based on the epoxide–dian resin with copper [21] and especially iron [141] already exhibit a sharp rise in softening temperature at comparatively low metal concentrations, and then loss of deformability, which is associated with complete hardening of the resin by the metal.

Raising the temperature [99] and increasing the duration [84,85] of preliminary heat-treatment with the second group of metallopolymers will raise the glass and softening points for a given concentration of metal in them.

Mechanical Properties

Study of the thermomechanical properties of filled polymers provides a clearer idea of the processes that occur when a polymer interacts with metal particles and of their effect on the mechanical properties of metallopolymers.

The introduction of lead by the thermal method into an epoxide–dian resin [89] increases the breaking strength and the elongation (up to a certain concentration of the metal), as well as the modulus of elasticity of the specimens, lead serving in this case as hardener. Raising the lead concentration above an optimum value leads to the formation of a more brittle and rigid system, which sharply lowers the strength characteristics of the metallopolymer.

The particle shape of the metal also affects the mechanical characteristics of the compositions. Powders comprising dendritic particles are most effective in improving the mechanical properties of filled polymers [77]. The introduction of highly disperse aluminium, manganese, iron, and silicon powders [67], made lyophilic towards rubber, has a vulcanising and reinforcing action on compositions of chloroprene and butadiene–nitrile rubbers. The improvement of the mechanical properties of rubber [68,90,81] in the presence of highly disperse metals is obviously due to the formation of stable rubber–metal bonds.

Swelling

The introduction of a filler into polymer systems may form additional cross-link in the three-dimensional network, but may also decrease its density. These additional cross-links are usually broken by swelling, with a considerable increase in the apparent degree of swelling of the polymer [142]. Swelling of this character is found with metallopolymers based on polystyrene and lead [43,104], where only weak van der Waals interactions link polystyrene macromolecules and metal particles.

However, in the thermal preparation of metallopolymers from polystyrene and a more active metal, silver [41], when a stable three-dimensional structure can be formed by thermal degradation of the polymer macromolecules followed by chemical interaction between the macroradicals and the surface of the silver particles, the ability of the metallopolymer to swell diminishes with increase in the metal content. Chemisorption interaction of polymers with the surface of metal particles leads to a sharp restriction of the mobility of the polymer chains, owing to the formation of additional chemical cross-links in the polymer network.

The introduction of highly disperse iron into non-polar rubbers (natural rubber, polyisobutylene) produces a considerable decrease in their swelling, and specimens containing 80% of the metal hardly swell at all [19]. A similar pattern is observed with these polymers on the electrolytic introduction of nickel and cobalt [20]. When the same quantities of these metals are added to a rubber, the decrease in the equilibrium degree of swelling depends on the nature of the metal. Furthermore, equilibrium swelling is reached more rapidly with metallopolymers than with the corresponding pure polymers, owing to the loose packing of surface layers of the polymer in the former case [8].

Metallopolymers based on an epoxide resin and copper, prepared by a thermal method, also show a decrease in swelling with increase in the copper content from 1% to 40%. [52] The character of the swelling changes sharply at copper concentrations above 40%. Samples containing 50–60% of copper hardly swell at all in 180 min. The swelling of specimens containing 60% of copper is one-tenth of that observed with 40% of copper.

Theoretical values of the degree of swelling of metallopolymers based on poly(vinyl acetate) and palladium [99], calculated by means of the Flory–Rehner equation [142], exceed the experimental values, the difference being larger the higher the palladium content.

All this indicates that bonds formed between metal surface and polymer in the preparation of metallopolymers are not broken during swelling.

Thermal and Thermo-oxidative Degradation

The influence of highly disperse metals on the thermal and thermo-oxidative degradation of metallopolymers has been by no means fully investigated, although it is of great interest. The introduction of up to 33% of highly disperse iron into an epoxide resin somewhat increases the rate of thermal degradation of the latter, but aluminium has no appreciable effect on this process [143,144]. Polyethylene also undergoes considerably more vigorous thermo-oxidative degradation when filled with disperse iron [122].

Differential thermal analysis has been used to examine the effect of the concentration of various metals on the thermo-oxidative degradation of metallopolymers, in particular those based on the epoxide–dian resin with copper [21] and on polystyrene with bismuth, manganese, and lead [54,55]. In all cases an appreciable rise in the temperature at which degradation began was observed only at low metal concentrations (up to 1.5%). The same method has shown that the optimum temperatures for the start of the thermo-oxidative degradation of metallopolymers based on an epoxide resin were reached at contents of 40–80% of copper [21] and of iron [141]. Similar results have been obtained for systems based on natural rubber and various metals [145].

However, the use of differential thermal analysis will not give a complete understanding of the role of metals in the degradation of metallopolymers. Quantitative investigations are necessary on the loss of weight of specimens and the evolution of volatile products, and their nature and the structural changes in the solid residue must be established; these may give more definite information on the mechanism of the degradation of metallopolymers. The investigation of purely thermal degradation is especially important, since the degradation of metallopolymers in air leads to oxidation of the highly disperse metals, so that degradation of the polymer is then affected actually by the metal oxide.

The introduction of certain disperse metals retards the oxidative degradation of organosilicon polymers [126,146,147]. This was explained by the orienting influence of the particles, which are able to become centres for the formation of secondary structures: i.e. physical factors are regarded as having the predominant effect on thermal degradation. Other authors [148,149] are inclined to attribute the enhanced stability of polysiloxanes when filled with metals to the formation during degradation of a new polymer with the metal heteroatom in the chain: i.e. they explain the stabilisation effect by the chemical action of the metal. The role of the physical or the chemical factor is obviously decisive in each specific case, but the influence of the other factor can be by no means excluded.

The above methods of preparation, mechanism of formation, and physicochemical properties of products obtained by the interaction of polymer macromolecules with the surface of colloidal metal particles at their instant of formation indicate that a chemisorption bond is established in these products between polymer and metal. This allows such two-phase systems of limiting homogeneity to be classed as a separate group under the name "metallopolymers". The chemisorption interaction of the macromolecules with the metal surface, the high degree of dispersion of the metal particles, and also the uniformity of their distribution in the bulk of the polymer guarantee a considerable improvement in the physicomechanical and physicochemical properties of metallopolymers in comparison with ordinary polymers filled with metals.

The simplicity of the methods of preparation combined with the series of valuable specific properties of metallopolymers opens up wide possibilities for their application in the national economy. Metallopolymers based on film-forming and lacquer-depositing polymers may find application as corrosion-resistant and other protective coatings. The exploitation of, for instant, the magnetic, semiconducting, ferromagnetic, catalytic, and antifriction properties of metallopolymers is most promising in practical terms.

Detailed investigations are required on the mechanism of the thermal and thermo-oxidative degradation of metallopolymers obtained from a variety of metals and macromolecular compounds. Such investigations would serve as a basis for producing metallopolymers possessing high thermal stability, which would considerably expand their field of application.

Further examination of the mechanism of the formation of metallopolymers based on the most diverse classes of macromolecular compounds and various metals would make possible a general theory of the formation of metallopolymers.

Researches on the formation of metallopolymers by the polymerisation or polycondensation of monomers and oligomers on the freshly formed surface of highly disperse metals would be especially interesting for both theory and practice, involving both problems of polymerisation and structure formation on solid surfaces and those of the strengthening of filled polymers.

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Structural Course of the Polymerisation of Diynes

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Examination of the available information shows that polymers of diverse structure—linear (with polyene and cumulene fragments), cyclolinear (including ladderlike), and three-dimensional—can be obtained by the polymerisation of diynes having conjugated and non-conjugated triple bonds. The structural course of the process is determined by the nature of monomer and catalyst and the conditions. Linear organometallic polymers, whose main chain comprises alternating double bonds and atoms of Group IV elements, can be obtained by the polyaddition of hydrides of these elements to $\alpha\omega$-diynes. A list of 58 references is included.

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I. INTRODUCTION

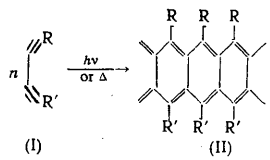
The polymerisation of acetylenic compounds, especially diynes, has been much less studied than that of alkenes and dienes. During recent years, however, polymers based on acetylenic monomers have been attracting increasing attention from research workers in connection with the intensive search for new materials possessing high thermal and thermo-oxidative stability with specific magnetic, catalytic, electrophysical, and other properties.

Whereas the polymerisation of mono- and di-substituted derivatives of acetylene usually leads to the formation of substituted polyenes (Ref.1 and Ref.2, p.378) and/or substituted cyclomers (Ref.2, p.327, and Refs.3 and 4), diynes having conjugated and non-conjugated acetylenic bonds may yield polymers in which the main chain of the macromolecule has a polyene, cumulene, or aromatic cyclic (including ladderlike) structure.

II. SYNTHESIS OF POLYMERS FROM DIYNES WITH CONJUGATED TRIPLE BONDS

It has been discovered comparatively recently[5-11] that certain crystalline monomers of the type R.[C:C]$_2$.R′ (diacetylenic dicarboxylic acids, alkadiynediols, diurethanes, anacycline), which are stable in solution or in a melt, become coloured when illuminated or when heated rapidly to a temperature below the melting point. The colour is red — violet, dark blue, or black depending on the nature of the substituents R and R′, and more or less soluble polymers are formed with degrees of polymerisation of 3 — 20.

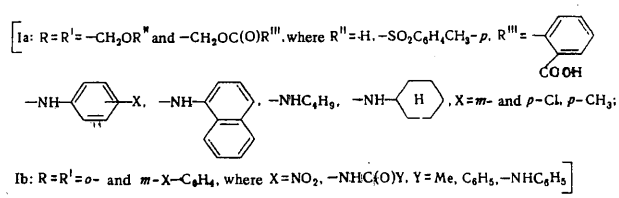
From a study of the ultraviolet spectra of the resulting polymers and the discovery of phthalic acid among their oxidative decomposition products it was suggested[5-8] that the energy communicated to the monomer in the crystalline state, i.e. with a parallel arrangement of the diyne chains, was used to serve only one pair of π-electrons in each triple bond. This destroyed the rigidity of the diyne molecule, and polymers having a substituted acene structure were formed:



(I) (II)

This interpretation, which disregarded the specific nature of the substituents R and R′, has found a place in subsequent reviews[12,13].

More detailed investigation of reactions of this type has shown[14-17] that in general such behaviour is exhibited only by those diynes which, because of the nature of their substituents



can form hydrogen bonds or develop dipole — dipole interactions.

Solid-phase polymerisation requires that the triple bonds in the monomer molecules should be arranged in such a way that the process can occur without any great change in the crystal lattice of the monomer. For this reason *ortho*-substituted compounds of type (Ib) are sometimes less reactive than the corresponding *meta*-derivatives, while *para*-isomers of (Ib) do not undergo polymerisation at all[17]. The modification of R.C:C.C:C.R (where R = CH_2.O.CO.NH.C_6H_5) free from dioxan also does not polymerise, since dioxan is responsible for the necessary packing of the monomer molecules in which the phenylurethane groups are bound by hydrogen bonds to neighbouring diyne and dioxan molecules[18].

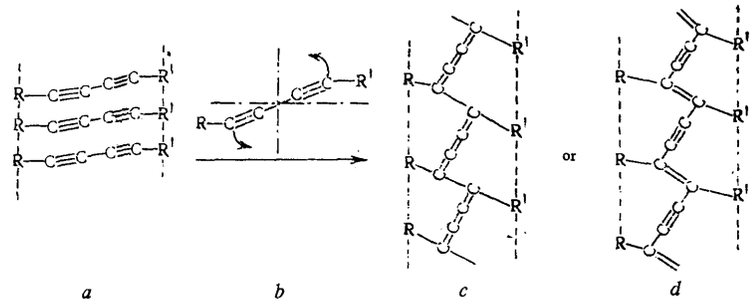


Figure 1.

Individual molecules are evidently regularly arranged in the crystal lattice of the monomers in the form of a "ladder" (Fig.1*a*), the "rungs" of which are formed by diyne fragments, and the "uprights" by hydrogen bonds or groups with strong dipole — dipole interaction (shown by the broken lines in Fig.1). Reaction occurs as a result of the rotation of each individual "rung" about its centre (Fig.1*b*) or shearing of the whole "ladder", while the separate "crossbars" are joined by 1,4-addition to form three cumulative double bonds in the unit[14-17] (Fig.1*c*) or perhaps an enyne structure[18] (Fig.1*d*).

Polymer systems obtained by the polycondensation of diynediols with di-isocyanates or dichlorides of dicarboxylic acids exhibit analogous structural changes to those observed in the polymerisation of monomeric diacetylenic derivatives in the solid state[19]:

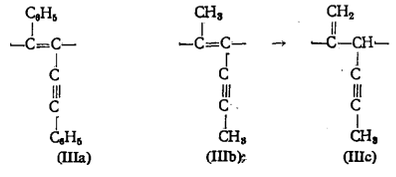
$$\mathrm{HO{-}X{-}(C{\equiv}C)_2{-}X{-}OH + OCN{-}Y{-}NCO \rightarrow}$$
$$\rightarrow \ldots{-}O{-}X{-}(C{\equiv}C)_2{-}X{-}OC(O)NH{-}Y{-}NHC(O){-}\ldots,$$

where $X = CH_2$, $CH_2(OCH_2CH_2)_2$; $Y =$ $(CH_2)_6$, $p\text{-}C_6H_4CH_2C_6H_4\text{-}p$.

$$\mathrm{HO{-}CH_2(C{\equiv}C)_2CH_2{-}OH + ClC(O)(CH_2)_4C(O)Cl \xrightarrow[-HCl]{\text{pyridine}}}$$
$$\rightarrow \ldots{-}O{-}CH_2(C{\equiv}C)_2CH_2{-}O{-}C(O)(CH_2)_4C(O){-}\ldots$$

In the case of polymers the replacement of a diyne by a cumulene or an enyne group leads to intermolecular cross-linking. Since the reaction is catalysed by radical initiators (benzoyl peroxide and azoisobutyronitrile) and is retarded by radical inhibitors (quinol), while ionic systems have no effect on the process, a radical mechanism of polymerisation is extremely probable.

The thermal and catalytic polymerisation of conjugated diynes follows a different course in solution or in a melt. The polymerisation of diphenylbutadiyne (I: R = R′ = C_6H_5) on the tri-isobutylaluminium — titanium tetrachloride catalytic system yields a linear polymer with a substituted polyene structure (IIIa), but on thermal polymerisation in the melt, i.e. above the melting point of the monomer, a block copolymer is formed consisting of substituted polyene (IIIa) and acene (II: R = R′ = C_6H_5) fragments (deduced from the results of ultraviolet, infrared, nuclear magnetic resonance, and electron spin resonance spectroscopy, luminescent, thermochemical, and X-ray examination, and also study of the chemical reactions of the products)[1,20-29].



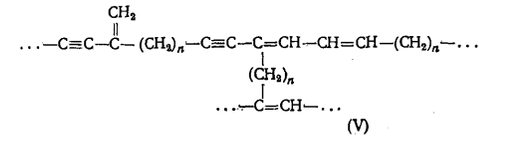
Heat-treatment and bromination, which cause intramolecular cyclisation of polydiphenylbutadiynes, increase the number of acene segments in the macromolecule[30], but in no case is a polymer obtained having a completely acene (ladderlike) structure.

The thermal polymerisation of dimethylbutadiyne (I: R = R′ = CH_3), like that of diphenylbutadiyne, involves predominantly formation of a block copolymer, consisting of (II: R = R′ = CH_3) and (IIIb) units. However, this is accompanied by the production of not more than 3% of methylene side-groups (IIIc) because of intramolecular isomerisation[31], which is responsible for the ready oxidisability and subsequent cross-linking.

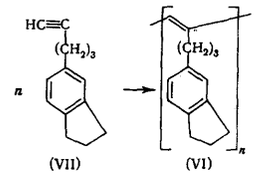
III. POLYMERISATION OF DIYNES WITH NON-CONJUGATED TRIPLE BONDS

The course of the polymerisation of diynes of the type HC:C.X.C:CH (IV) is determined by the nature of the group X separating the triple bonds and by the reaction conditions.

The polymerisation of diynes (IV) in which X = $[CH_2]_n$ (where $n = 2-5$) on the complex catalytic system $Ni(CO)_2.2(C_6H_5)_3P$ leads to the formation of compounds of high molecular weight[32]. The high-melting insoluble polymer from hexa-1,5-diyne (IV: X = $[CH_2]_2$) has the structure (V)



as a result of simultaneous linear polymerisation and dehydropolycondensation. Hepta-1,6-diyne (IV: X = $[CH_2]_3$) gives (together with the aromatic trimer 1,3-di(indan-5-yl) propane) a 75 — 80% yield of a soluble resinous product of degree of polymerisation <20, which infrared spectroscopy shows to be a substituted polyene (VI). This structure results from polymerisation at the triple bond of the dimer (VII) obtained initially[32]:



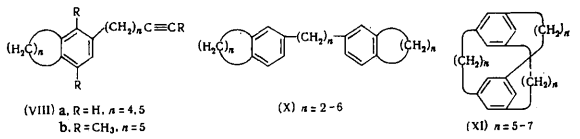
The number of 1,2,4-trisubstituted aromatic groups in polyocta-1,7-diyne is less than in polyhepta-1,6-diyne. Under these conditions nona-1,8-diyne forms only an insoluble polymer containing no aromatic groups. Copolymers of diynes with equimolecular quantities of hept-1-yne contain both aromatic groups and conjugated double bonds.

Thus the number of aromatic groups in products of the polymerisation of non-conjugated diynes of the type (IV) on the catalytic system $Ni(CO)_2.2(C_6H_5)_3P$ decreases in the sequence

hepta-1,6-diyne > octa-1,7-diyne ≫ hexa-1,5-diyne, nona-1,8-diyne

This may be determined by the conformations of the intermediate complexes of the diynes with the catalyst.

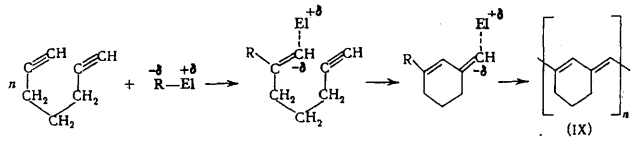
The polymerisation on the catalyst $Hg[Co(CO)_4]_2$ of diynes (IV) in which X = $[CH_2]_n$ and n = 4, 5 leads to the formation of a small quantity of dimers (VIIIa; R = H, n = 4, 5)



(VIII) a. R = H, n = 4, 5; b. R = CH_3, n = 5 (X) n = 2-6 (XI) n = 5-7

and soluble polymers, whereas undeca-2,9-diyne yields only insoluble products under the same conditions[33]. The corresponding dimer from this latter compound (VIIIb: R = CH_3, n = 5) is obtained in 44% yield under conditions of high dilution[33]. The dimer (VIII) formed initially is evidently converted by polymerisation at the triple bond into a polymer of structure analogous to that suggested in Ref.32.

According to American workers[34] hepta-1,6-diyne (IV: X = $[CH_2]_3$) is converted on Ziegler — Natta catalysts by a mechanism of intra- and inter-molecular polymerisation into a polymer whose absorption spectra and chemical reactions (dehydrogenation, halogenation, and ozonolysis) suggest a cyclic polyene structure (IX):



(IX)

Under the same conditions octa-1,7-diyne and nona-1,8-diyne (IV: X = $[CH_2]_4$ and $[CH_2]_5$) give mainly cross-linked polymers. The soluble products of the polymerisation of octa-1,7-diyne contain seven-membered rings in the main chain, formed similarly to the rings in (IX), and perhaps long side-chains as a consequence of independent linear polymerisation at triple bonds. Of the monomer units in the soluble portion of polynona-1,8-diyne 25 — 30% contain one unchanged acetylenic group[34].

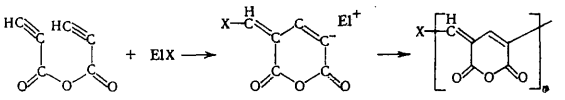
These results contradict those obtained by other investigators[33,35,36]. The polymerisation of hepta-1,6-diyne on the catalytic system $(C_2H_5)_3Al - TiCl_4$, as on the catalyst $Ni(CO)_2.2(C_6H_5)_3P$, gives a polymer having the structure (VI)[35]; but octa-1,7-diyne[33] and nona-1,8-diyne[33,36] form small amounts of cyclic trimers (X) and (XI) together with soluble and insoluble polymers. Since the infrared and nuclear magnetic resonance spectra of the trimers were identical with those of the polymers, the polymerisation of non-conjugated alkadiynes on Ziegler — Natta catalysts was supposed[33,36] to involve polycyclotrimerisation.

The copolymerisation of hepta-1,6-diyne with phenylacetylene probably yields a structure in which (VI) and $CH{:}C(C_6H_5)$ units alternate[35].

As with the polydimethylbutadiyne discussed above structure (V(should be characterised by migration of a hydrogen atom from the methylene side-group into the main-chain, which is responsible for the ready oxidisability of the resulting structure of type (IIIc). In fact, if freshly isolated polyhepta-1,6-diyne contains ~2% of oxygen, subsequent treatment and storage lead to an increase in the oxygen content to 10% and a loss of solubility by the polymer[35].

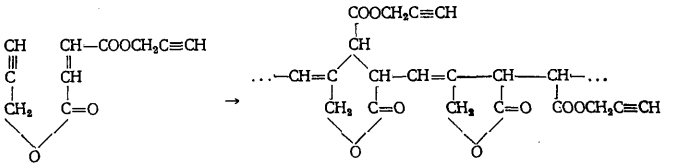
Acetylenic α-carboxylic acid anhydrides of general formula R.C:C.CO.O.CO.C:C.R (R = H, Alk, Ar) in the presence of anionic catalysts in an inert organic solvent at 50 — 100°C give black polymeric powders; these are insoluble in water and in most organic solvents but soluble in dimethylformamide[37]. The yield of polymer (3 — 92%) increases with rise in temperature and increase in duration of the process. In dimethylformamide halide ions are active catalysts — even such a weak nucleophile as the chloride ion[38].

The polymerisation of propiolic anhydride (IV: X = CO.O.CO) involves an intramolecular cyclisation step by a mechanism analogous to that discussed above for hepta-1,6-diyne:



where El = Na, K and X = CNS, CN, Hal. Contamination with propiolic acid inhibits polymerisation and depresses the molecular weight of the resulting polymers[37-39]. Acetylenic α-carboxylic acid anhydrides do not undergo polymerisation with cationic, radical, or thermal initiation (with respectively the ether complex of boron trifluoride, benzoyl peroxide, and a toluene solution at 100°C)[39].

Diprop-2-ynyl maleate (IV: X = $CH_2.O.CO.CH{:}CH.CO.O.CH_2$), in the presence of radical initiators in bulk and in solution at 70 — 130°C, is converted by inter- and intramolecular interaction between double and triple bonds into a polymer containing lactone units in the main chain[40]:



Diethynylarenes can be regarded as monomers intermediate in structure and properties between conjugated and non-conjugated diynes. A study of the crystal optics and spectra in the solid-phase polymerisation of single crystals of *p*-diethynylbenzene (IV: X = *p*-C_6H_4), initiated by ultraviolet radiation and by cobalt-60 γ-rays at ~20° and 77°K, has shown[41-43] that the polymer chains grow along a definite axis (N_p) of the refractive-index ellipsoid of the monomer crystal, which forms an angle of about 53° with the plane of the benzene rings.

Polymerisation involves predominantly one acetylenic group in each *p*-diethynylbenzene molecule (Fig.2). The chain evidently grows "head to tail", since a "head to head" construction requires that the inner carbon atoms of the triple bonds should come closer together, which is hardly possible in a crystal.

The reason why the crystal lattice of the monomer remains undisturbed is that the acetylenic groups of different molecules are close together, and the regrouping of atoms required for polymerisation is accomplished both by the formation from a triple bond of a longer double bond and also perhaps by some displacement of the molecules or deflection of acetylenic groups. These displacements accompanying polymerisation lead to the accumulation of mechanical stresses near the end of the polymer chain in the crystal, which causes the chain to terminate. The mechanical stresses produced may also be responsible for the absence of branching in the growing chain and the participation in polymerisation of only one acetylenic group from each molecule.

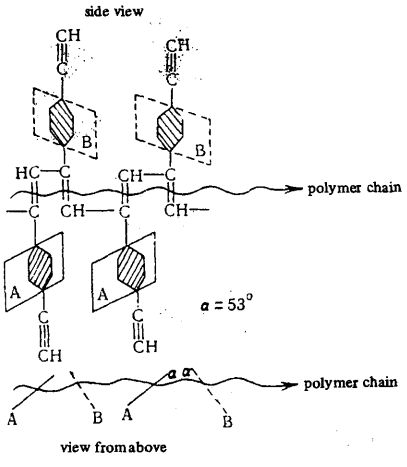


Figure 2.

Polymers of different structure are obtained when the process is conducted in solution or in a melt, as with the polymerisation of conjugated diynes.

The thermal (100 — 300°C) or catalytic polymerisation of *p*-diethynylbenzene, or its copolymerisation with phenylacetylene, diphenylacetylene, and several other acetylenic derivatives, yields insoluble and infusible polymers, probably of planar or three-dimensional structure[44-47].

In the presence of cobalt and other transition-metal complexes, diethynyl compounds (IV: X = $[p\text{-}C_6H_4]_n$, $p\text{-}C_6H_4.El.C_6H_4\text{-}p'$; n = 1 — 3, El = O, Se, etc.) in bulk or solution form by polycyclotrimerisation polymers with aromatic groups in the main chain[48-50].

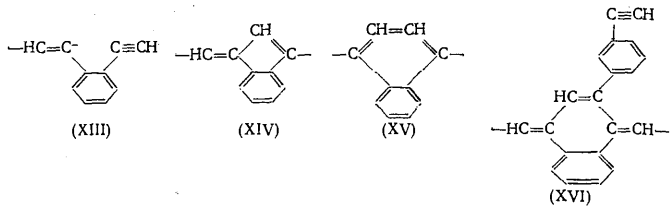
The copolymerisation of mono- and di-ethynyl derivatives enables the degree of branching in the products to be controlled. Copolycyclotrimerisation can in general be represented by the scheme

$$HC{\equiv}C{-}X{-}C{\equiv}CH + HC{\equiv}CR \rightarrow \left[\begin{array}{c} -Ar- \\ | \\ R \end{array}\!\!\begin{array}{c} \\ \\ \end{array}\!\!\begin{array}{c} -Ar- \\ \\ \end{array}\right]_n$$

(XII)

The actual structure is probably more complicated than (XII). Thus a study by infrared spectroscopy and ozonolysis of the copolymerisation of *p*-diethynylbenzene with phenylacetylene on the tri-isobutylaluminium — titanium tetrachloride catalytic system has established[51] that the soluble copolymerisation products contain polyene segments together with phenylene fragments, independently of the initial molar ratio of monomers and components of the catalytic system.

A polymer consisting of the units (XIII) — (XVI)[52]



has been obtained by coordination, radical, and cationic polymerisation of *o*-diethynylbenzene (IV: X = $o\text{-}C_6H_4$)—on the systems $R_2AlCl - TiCl_4$, $R_3Al - TiAcac$, $R_2AlCl - TiAcac$, and $RAlCl_2 - TiAcac$ (R = C_2H_5; Acac = acetylacetonate); isobutyronitrile; and titanium tetrachloride respectively. The polymer obtained in the presence of titanium tetrachloride contained no cyclic groups; with radical and coordination polymerisation the degree of cyclisation of the polymer was respectively 30% and 50 — 70%. The polymer evidently consists mainly of (XIII) and (XIV) units, and the chain grows by "head to head" addition — e.g. (XV), (XVI).

IV. SYNTHESIS OF ORGANOMETALLIC POLYMERS BY POLYADDITION

The method for obtaining linear organometallic polymers is based[53-55] on the quite easy addition to a carbon — carbon triple bond of hydrides of Group IV elements in which all but two hydrogen atoms have been substituted by organic groups. The polyaddition of the "dihydrides" RR′ ElH_2 to αω-diynes can be represented by the scheme

$$n\,RR'\,ElH_2 + n\,HC{\equiv}C{-}X{-}C{\equiv}CH \rightarrow n\left[\begin{array}{c} R \\ | \\ H\text{-}El\text{-}CH{=}CH{-}X{-}C{\equiv}CH \\ | \\ R' \end{array}\right] \rightarrow$$

(XVII)

$$\left(\begin{array}{c} R \\ | \\ -El-CH{=}CH{-}X{-}CH{=}CH- \\ | \\ R' \end{array}\right)_n$$

(XVIII)

where R, R′ = Alk, Ar; El = Si, Ge, Sn; X = $[CH_2]_n$, $p\text{-}C_6H_4$, ElRR′. Since a triple bond is considerably more reactive than a double bond under the conditions of synthesis, the intermediate compound (XVII) probably passes into the polymer (XVIII)[55]. The properties of the resulting polymers (high decomposition temperatures, their infrared spectra, electrical conductivities, and activation energies of conduction) indicate that *d*-orbitals of the elements are involved in chemical bond formation[54].

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The information surveyed above shows that polymers varying widely in structure — linear (with polyene and cumulene units), cyclolinear, ladderlike, and three-dimensional — can be obtained from diynes depending on the nature of the monomer, the catalyst, and the conditions of polymerisation.

Since diacetylenic derivatives are able to form polymeric products not only by addition polymerisation at the carbon — carbon triple bonds but also in other ways — the most important of which are addition of unsaturated

compounds (1, 3- and 1, 4-cycloaddition[56,57]) and oxidative dehydropolycondensation[58]—further study of the reactions of diynes leading to the formation of polymers of diverse structure is desirable and promising.

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Internal Reflection Spectroscopy. Applications in Chemistry and Industry

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Published information on the application of internal reflection spectroscopy (IRS) in chemistry and industry is systematically discussed, and the theory of IRS is briefly reviewed. The apparatus and experimental techniques are described. 297 References.

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I. INTRODUCTION

Many papers dealing with the application of internal reflection spectroscopy (IRS) in chemistry and in related areas of science and industry have appeared in recent years.

The importance of IRS stems primarily from the fact that systems which are difficult or impossible to study by absorption methods can be examined by this method. In contrast to absorption methods, which rely on the transmission of light through the experimental medium, IRS is based on the phenomenon of total internal reflection.

The principle of the method is the following: during total internal reflection, a beam of light can penetrate from the optically denser into the optically less dense medium to a depth of the order of one wave length. If the less dense medium is absorbing, the beam is attenuated and reflection is not total. If the experimental medium is strongly absorbing, its attenuated total reflection (ATR) spectrum can be obtained by measuring with a suitable spectrometer its reflectivity R ($R = I/I_0$, where I_0 is the intensity of the incident light and I is the intensity of the reflected light).

Since total internal reflection does not involve any loss of radiant energy, the method known as multiple attenuated total reflection (MATR)† can be used to measure the spectra of very weakly absorbing media such as thin films and monomolecular layers.

The internal reflection (IRS) spectra of bulk materials, measured under standard conditions, are very similar to their transmission spectra, and in the case of very thin layers the two types of spectrum are practically identical. Hence, IRS spectra can be interpreted in much the same way as transmission spectra. Furthermore, IRS spectra often yield more detailed information on the structure of the sample than transmission spectra.

† OPO and MOPO are the Russian terms for the IRS methods known in English as ATR and MATR (attenuated total reflection and multiple attenuated total reflection). Non-Russian publications sometimes refer to FTR (frustrated total reflection), which is best rendered in Russian as NPVO. The term FMIR (frustrated multiple internal reflection), often encountered in the Western literature, is synonymous with MATR. The physical significance of the methods used in IRS is perhaps most clearly indicated by the terms ATR and MATR (in Russian, OPO and MOPO).

Almost the whole of the spectrum, from ultraviolet to far infrared, can now be explored by IRS.

In practice, the most important results have been obtained by i.r. IRS. The availability of commercial i.r. spectrometers with suitable attachments has greatly increased the scope of i.r. IRS: in particular, chemical, physicochemical, and biochemical processes have been investigated directly in media hitherto inaccessible by conventional methods.

Because its sensitivity and (in some cases) its precision are higher than those of i.r. transmission spectroscopy, i.r. IRS has been used to investigate surfaces, and it has also been applied in analytical procedures. It is now widely used in chemical and related industrial practice as an efficient and reliable method of process control.

The use of total internal reflection to study optical properties of materials is not an entirely new approach. As early as 1914, Mandel'shtam[1] and, somewhat later, Baryshanskaya[2] had used the phenomenon of total internal reflection to investigate fluorescence in thin layers, relying on Eikhenval'd's theoretical model[3]. A much more recent review of the possibilities offered by this method has been published by Hirschfeld[4].

Taylor and Glover[5] used total internal reflection to investigate the spectrum of an aqueous solution of potassium permanganate, and Korobko-Stefanov[6] discussed the advantages of this method in studies of strongly absorbing media.

However, the widespread penetration of IRS into research techniques began in the 1960's, when the remaining theoretical and experimental difficulties were finally overcome.

Unfortunately, existing Russian reviews of the practical application of IRS [7,8] are lacking in both breadth and depth. The only bibliography of the subject[8] dates back to 1967, and is therefore wholly inadequate.

Many review articles have been published outside the Soviet Union[9-17], but none of these consider work published since 1967. However, the number of publications has increased very rapidly in the last few years, and the scope of IRS has grown very significantly. None of this recent work is dealt with in existing reviews, whether Russian or foreign.

The aim of the present review is to discuss as fully as possible the applications of IRS in chemistry and in related areas of science and technology, and to familiarise the reader with the underlying theory, the apparatus, and the experimental methods.

II. THEORETICAL BASIS OF INTERNAL REFLECTION SPECTROSCOPY

Total internal reflection occurs when a light beam strikes the boundary between a medium of high optical density (n_1) and a medium of lower optical density ($n_2 < n_1$) at an angle greater than the critical angle of incidence (θ_c).[18] The critical angle is defined by the expression

$$\sin\theta_c = n_{21} \qquad (1)$$

where n_{21} is the relative refractive index ($n_{21} = n_2/n_1 < 1$), and n_1, n_2 are the absolute refractive indices of the two optically transparent media.

The condition for total internal reflection is written

$$\theta > \theta_c = \arcsin n_{21}. \qquad (2)$$

However, as pointed out by Newton[19], the light penetrates into the optically less dense medium during total internal reflection.

This optical penetration effect, which could not be explained by the corpuscular theory of light, is now clearly understood in terms of the electromagnetic theory.

As pointed out by Eikhenval'd[3], the electromagnetic field associated with the light wave does not suffer a discontinuity at the boundary between the two media during total internal reflection: it penetrates from the medium n_1 into the medium n_2, where it decays exponentially. The decreasing amplitude E of the electrical oscillations of the light wave in the second medium is given by the expression

$$E = E_0 e^{-\gamma z} \qquad (3)$$

where $\gamma = 2\pi(\sin^2\theta - n_{21}^2)^{1/2}/\lambda_1$, E_0 is the amplitude at the interface, z is the distance from the interface into the medium of lower refractive index, λ_1 is the wave length of the light in the denser medium.

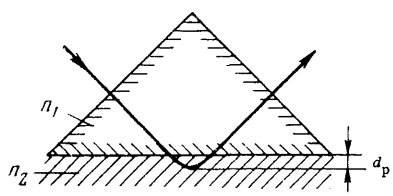

Figure 1. Penetration of light into the medium of refractive index n_2 during total internal reflection (d_p is the depth of penetration).

We must stress that in total internal reflection the intensity of the reflected light (I) is equal to the intensity (I_0) of the incident light: the penetration of the light into the second medium does not cause any loss of radiant energy. According to Eikhenval'd, the incident beam "strays into the second medium" where it follows a curvilinear path "before re-emerging, unaltered, in the first medium as the reflected beam" (see Fig. 1).

Defining d_p as the depth of penetration for which the amplitude E decreases by a factor of e, we obtain

$$d_p = \frac{\lambda_1}{2\pi(\sin^2\theta - n_{21}^2)^{\frac{1}{2}}} \qquad (4)$$

Examination of Eqn. (4) shows that: 1) for angles $\theta \gg \theta_c$ the depth of penetration is less than one wave length, 2) for $\theta = \theta_c$ the depth of penetration is very large, 3) the depth increases with critical angle, and 4) it increases with the wave length.

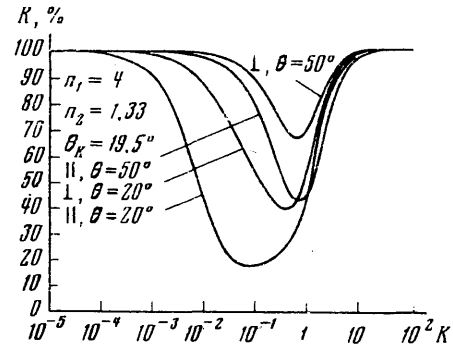

Figure 2. Plots of R against K for different values of θ and for different polarisations.

If the light penetrates into an absorbing medium, then $I \neq I_0$. In this case the reflectance R depends not only on the absorption coefficient K, but also on θ, n_{21}, and λ in Eqn. (4). The functional dependence, as shown in Fig. 2, is very complicated. The variation of R with K, θ, n_{21}, and polarisation of the light can be calculated in two ways. One method is to express the reflectivity as a function of the above variables.

The calculations are usually made by applying the Fresnel formulae, suitably modified for attenuated total reflection conditions. The modifications consist in replacing the refractive index n_2, which adequately characterises the optical properties of a transparent medium, by a complex refractive index[23] n_2^*, which characterises the optical properties of the absorbing medium:

$$n_2^* = n_2(1 - iK), \qquad (5)$$

where n_2 and K are the effective refractive index and the effective absorption coefficient.

The relationship between K and α (the absorption coefficient in the Beer — Lambert law) is given[24] by

$$\alpha = \frac{4\pi n_2 K}{\lambda_0}, \qquad (6)$$

where λ_0 is the wave length of the light in a vacuum, related to the wave length in a denser medium by the expression $\lambda_0 = \lambda_1 n_1$.

For ATR conditions, the Fresnel formulae become[25]

$$R_\perp = \left| \frac{(n_{21}^{*2} - \sin^2\theta)^{\frac{1}{2}} - \cos\theta}{(n_{21}^{*2} - \sin^2\theta)^{\frac{1}{2}} + \cos\theta} \right|^2 \qquad (7)$$

$$R_\parallel = R_\perp \left| \frac{(n_{21}^{*2} - \sin^2\theta)^{\frac{1}{2}} - \sin\theta\tan\theta}{(n_{21}^{*2} - \sin^2\theta)^{\frac{1}{2}} + \sin\theta\tan\theta} \right|^2, \qquad (8)$$

where the subscripts $\perp$ and $\parallel$ indicate that the vector of the electrical oscillations is perpendicular ($\perp$) or parallel ($\parallel$) to the plane of incidence.

Calculations of R as a function of K, θ_c, and θ, and also of polarisation, have been reported and discussed in a number of papers[9,24-29]. We shall confine ourselves to a consideration of some general rules which relate specifically to the practical exploitation of the ATR method.

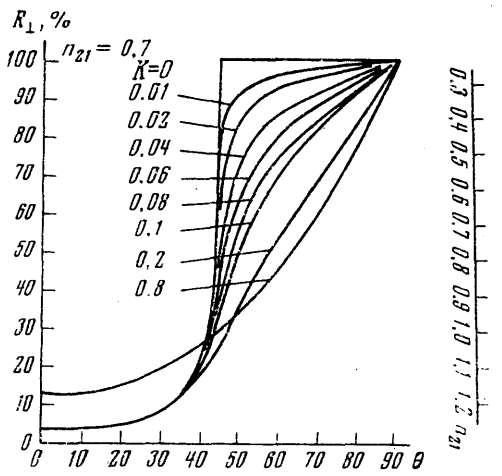

Figure 3. $R_\perp$ as a function of K and θ.

It is evident from Figs. 2, 3, and 4 that the method offers maximum sensitivity in the range $0 < K < 0.2$, which includes the i.r. absorption bands of most organic compounds.

We note also that the reflectivity depends not only on K, but also on θ, θ_c, and polarisation: R decreases as θ decreases and as θ_c increases.

Other conditions being equal, $R_\perp < R_\parallel$.

R falls off sharply as $\theta \to \theta_c$; in other words, the conditions for maximum sensitivity and therefore precision of the ATR method are found[26,28] close to the critical angle of incidence, the best choice of which depends on the value of K.[26]

However, the IRS bands observed at the optimum critical angles are distorted relative to the transmission spectra: they are broadened towards the long-wave end of the spectrum, and their peaks are shifted towards lower frequencies[7,9-11,13,29-31]. Yet, it would be desirable to obtain IRS spectra as similar as possible to the corresponding transmission spectra.

Calculations based on the Fresnel formulae have shown that undistorted IRS spectra can be obtained from very weakly absorbing samples only at angles $\theta \gg \theta_c$.[29,30,32]

The values of R for weakly absorbing samples can be calculated by means of simple expressions, derived from Eqns. (7) and (8) by expanding them into a power series and retaining terms up to K^3:[29,32]

$$R_\perp = 1 - \alpha \cdot d_{\text{eff}\perp} \quad (9)$$

$$R_\parallel = 1 - \alpha \cdot d_{\text{eff}\parallel} \quad (10)$$

where d_{eff} is an effective thickness having the same order of magnitude as the wave length.

It follows from Eqns. (9) and (10) that the role of the effective thickness is analogous to that of the optical path length in transmission spectroscopy, and that this parameter can be calculated from the expressions[9,20,29,33,34]:

$$d_{\text{eff}\perp} = \frac{n_{21}\cos\theta\lambda_1}{\pi(1-n_{21}^2)(\sin^2\theta - n_{21}^2)^{\frac{1}{2}}} \quad (11)$$

$$d_{\text{eff}\parallel} = \frac{n_{21}\cos\theta(2\sin^2\theta - n_{21}^2)\lambda_1}{\pi(1-n_{21}^2)[\sin^2\theta(1-n_{21}^2) - n_{21}^2](\sin^2\theta - n_{21}^2)^{\frac{1}{2}}} \quad (12)$$

It is not hard to show that Eqns. (9) and (10) are analogues of the Lambert – Beer equation for the case of very weak absorption[9,35], and therefore they can be re-cast in the form

$$R = e^{-\alpha d_{\text{eff}}} \quad (13)$$

Thus, the Lambert – Beer law is formally applicable to the undistorted IRS spectra[26,32], and we may use these IRS spectra for quantitative measurements in the same way as transmission spectra.

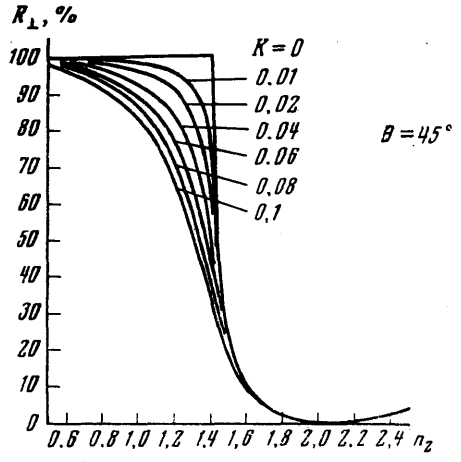

Figure 4. $R_\perp$ as a function of K and n_2.

Although these generalisations of the Fresnel equations provide a theoretical foundation for the practical application of the ATR method, they do not give a physical picture of the interaction of light with the absorbing medium. It should also be noted that the use of Eqns. (7) and (8) in daily laboratory work is complicated by the need for electronic computation[20].

Hence, an alternative solution of the problem could be attractive if it relied on simple mathematical expressions describing the mechanism of light absorption and the main features of IRS spectra in cases of practical interest ($0 < K < 0.2$) without resorting to the use of computers.

Let us consider the case of weak absorption. As stated above, in this case R can be found from Eqns. (9) – (12), whence it follows that d_{eff}, and therefore also n_{21} and θ, are independent of α. From the same equations we can show that the product $\alpha . d_{\text{eff}}$ is simply the fraction of radiant energy absorbed by the medium of lower refractive index. Thus, the behaviour of the electric field in a weakly absorbing medium can be discussed independently of α.[9,20,29,32-34]

According to Harrick[20], the absorption a, i.e. the interaction between the light beam and the weakly absorbing medium over the whole of the penetration path, can be described by the equation

$$a = \alpha \frac{n_{21}}{\cos\theta} \int_0^\infty E^2 dz \qquad (14)$$

where $E = E_0 \cdot e^{-\gamma z}$ is the amplitude of the electric field in the less dense medium relative to the amplitude of the incident light.

From Eqn. (14) we find

$$\frac{n_{21}}{\cos\theta} \int_0^\infty E^2 dz = \frac{a}{\alpha} \qquad (15)$$

where the expression on the left-hand side denotes the effective thickness[9,20,33,34]

$$d_{\text{eff}} = \frac{n_{21}}{\cos\theta} \int_0^\infty E^2 dz \qquad (16)$$

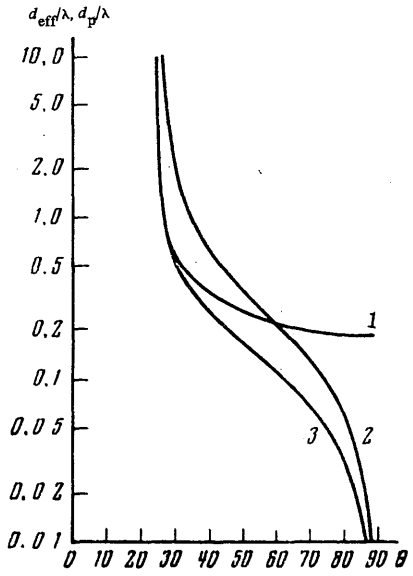

Figure 5. Relative depth of penetration and relative effective thickness as a function of θ (n_{21} = 0.423): *1)* d_p/λ, *2)* $d_{\text{eff}_\parallel}/\lambda$, *3)* $d_{\text{eff}_\perp}/\lambda$.

It follows from Eqn. (14) that the absorption depends not only on the value of α, but also on the value of the integral, which defines the total intensity of the light over the whole of the penetration path. Evidently, this intensity is a function of the amplitude E_0 at the phase boundary on the side of the less dense medium. The value of E_0 as a function of the angle of incidence and of the polarisation of the light can be calculated from the equation for the standing electromagnetic wave produced at the phase boundary on the side of the denser medium by the superposition of the incident and the reflected light. These calculations, carried out by Harrick[20,33,34], have shown that: 1) E_0 is a maximum for $\theta = \theta_c$; 2) E_0 decreases as θ increases; 3) E_0 vanishes for $\theta = \pi/2$; 4) E_0 vanishes for $E_{0\perp} < E_{0\parallel}$.

We shall now discuss the dependence of d_{eff}, and therefore also of the absorption, on the factors which enter into Eqn. (16).

We have two cases, depending on whether the thickness d of the absorbing layer is greater or smaller than the depth of penetration. For "thick" layers ($d > d_p$) we obtain the following formula [from Eqn. (16)] for the effective thickness:

$$d_{\text{eff}} = \frac{n_{21} E_0^2 d_p}{2\cos\theta} \qquad (17)$$

It follows from Eqn. (17) that the effective thickness of "thick" layers depends on four factors. The physical significance of the first three (n_{21}, E_0, and d_p) has already been discussed; the fourth ($1/\cos\theta$) determines the area over which light interacts with the sample.

Fig. 5 shows the variation of d_{eff} (which determines the interaction between the tailing electric field and the weakly absorbing medium) with angle of incidence and with polarisation. It is evident that d_{eff} is greatest near the critical angle, and reaches a maximum [see Eqn. (17)] when the refractive index n_1 of the internal reflection element (IRE)‡ is very close to the true refractive index n_2, i.e. when $n_{21} \to 1$. Hence, to obtain the strongest possible bands in IRS spectra we must choose an IRE with a refractive index close to that of the experimental medium (n_2) at the maximum of the dispersion curve (Fig. 6), and use near-critical angles of incidence[26]. Under these conditions the quantities n_{21}, E_0, and d_p, which determine d_{eff}, have their maximum values.

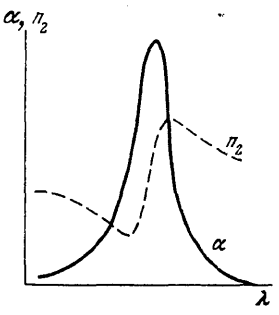

Figure 6. Absorption coefficient α (full line) and refractive index n_2 (broken line) as a function of wave length in the region of the absorption band.

As θ increases, E_0 and d_p fall off, causing a decrease in d_{eff} and hence in absorption[36]. When $\theta = \pi/2$, $E_0 = 0$, and therefore $d_{\text{eff}} = 0$ (i.e. there is no absorption). We note that when $\theta = 45°$, $d_p = (d_{\text{eff}_\perp} + d_{\text{eff}_\parallel})/2$.

It has been shown[20,33-35] that formulae (9) — (13), which are strictly applicable only to weak absorption (they can be obtained from (14) and (17) [20]), can in fact be used over a fairly wide range of K values ($0 < K < 0.2$), since they differ by only 10% from the exact Fresnel formulae when R falls to 10% (see Fig. 2).

‡ In IRS the optically transparent, denser medium is sometimes called the IRE.

Eqn. (17) can be used to explain the difference between the IRS spectra obtained with "thick" layers and the transmission spectra of the same materials. Since d_p increases with λ, the absorption also increases with λ. Hence, the intensity of the bands in the IRS spectra increases with wavelength[10,11,20,29,33,34].

As stated above, IRS spectra obtained with θ close to θ_c appear distorted. To identify the cause of the distortion we turn to Fig. 6, whence it is evident that n_2 (as well as α) varies with wave length. The largest value of n_2 is found on the long-wave side of the absorption band. Since the critical angle reaches a maximum and the difference $\theta - \theta_c$ (for a given θ) reaches a minimum on the long-wave side of the absorption peak, it is not surprising to find an increase in n_{21}, E_0, and d_p (and therefore an increase in absorption) on the long-wave side of the peak. As a result, the absorption maximum is shifted towards lower frequencies, and the band shows some broadening in the same direction[7,9-13,29-31].

Obviously, the distortion of the IRS spectra arises from the fact that the ATR method is sensitive to changes in both the optical constants K and n_2. This suggest that IRS can be used to evaluate these constants[24,25,28,37-49].

In order to obtain an IRS spectrum free from the distortion associated with anomalous dispersion we must choose conditions such that d_{eff} is not sensitive to changes in the coefficient n_2. It can be seen from Fig. 5 that when the angle θ is much greater than θ_c, i.e. when the difference $\vartheta - \theta_c$ is large, the fluctuations in this difference due to changes in the critical angle have very little influence on the depth of penetration. The same can be said of E_0, which is insensitive to changes in θ_c if $\theta \gg \theta_c$, as demonstrated by Harrick[9]. Therefore, it is essential to work with an angle of incidence much greater than the critical angle if the aim is to obtain an IRS spectrum almost identical to the transmission spectrum. However, small differences in frequency (of the order of a few cm^{-1}) are nevertheless to be expected[50].

Starting from the refractive index n_2 of the experimental medium, measured by normal refractometric methods, the expected absorption coefficient K, and the condition[29] $K/(\sin^2\theta - n_{21}^2) \ll 1$, it is possible to choose an angle of incidence and an IRE refractive index such that the IRS spectrum is free from the distortion associated with anomalous dispersion. We can readily show that this condition is satisfied for small K values, and as K increases for $\theta \gg \vartheta_c$.

However, the IRS spectrum plotted at large angles of incidence has a low intensity[7,9-11,30,35,51]. Stronger bands can be obtained by the MATR method, which produces spectra both undistorted and intense[7,9-11,30,35,52-56].

In this method, d_{eff} is increased in proportion to the number of reflections (N), and therefore the absorption is increased by a factor of N. Evidently, Eqn. (13) for the MATR method must be re-written[20,35]

$$R^N = e^{-\alpha \cdot d_{eff} N} \qquad (18)$$

Clearly, by adopting the MATR method we can not only increase the intensity of the IRS method but also use it at higher sensitivity.

We shall now turn to the case of "thin" layers ($d < d_p$). In this case the electric field penetrates beyond the thin absorbing layer into the underlying optically transparent medium§. Since the layer is very thin, the electric field may be assumed to be constant within the film[20]. Then, using Eqn. (16), we obtain

$$d_{eff} = \frac{n_{21} E_0^2 d}{\cos\theta} \qquad (19)$$

Thus, with "thin" layers as with "thick" layers the parameter d_{eff} depends on four factors. We can evaluate d_{eff} for a "thin" layer using the formulae proposed by Harrick[9,20,33,34]¶:

$$d_{eff\perp} = \frac{4n_{21} \cdot \cos\theta \cdot d}{1 - n_{31}^2} \qquad (20)$$

$$d_{eff\parallel} = \frac{4n_{21}\cos\theta\,[(1 + n_{32}^4)\sin^2\theta - n_{31}^2]\,d}{(1 - n_{31}^2)[(1 + n_{31}^2)\sin^2\theta - n_{31}^2]} \qquad (21)$$

where $n_{21} = n_2/n_1$; $n_{32} = n_3/n_2$; $n_{31} = n_3/n_1 < 1$ are the relative refractive indices. Formulae (20) and (21) are accurate when

$$\frac{2\pi d}{\lambda_1} < 0{,}1 \text{ and } K_2 < 0{,}1$$

Eqns. (19) – (21) lead to a number of generalisations applicable to IRS spectra obtained with "thin" layers.

It follows from Eqn. (19) that d_{eff} is independent of the depth of penetration. Hence, the intensity of the bands in the IRS spectra of "thin" layers does not increase with wave length. Furthermore, we can see from Eqns. (20) and (21) that d_{eff} is limited for $\theta = \theta_c$, where θ_c = arc sin n_3/n_1. Clearly, the IRS spectrum of a "thin" layer—unlike the spectra of "thick" layers—is free from anomalous dispersion distortions and is practically identical to the transmission spectrum.

It is important to note that the IRS spectrum of "thin" layers can be obtained even when the true refractive index of the thin layer is greater than the refractive index of the IRE. Furthermore, and in contrast to "thick" layers for which $d_{eff\parallel} > d_{eff\perp}$, the parameter $d_{eff\parallel}$ can be greater or smaller than $d_{eff\perp}$ in "thin" layers, depending on whether the ratio n_{32}^4/n_{31}^2 in Eqn. (21) is greater or smaller than unity.

It follows from (20) and (21) that d_{eff} for "thin" layers can be much greater than the physical thickness of the layer if $n_3/n_1 \to 1$. By using MATR, the sensitivity of the method can be dramatically increased[58] to $\sim 10^{-14}$ mole.

We had previously stated that light polarised in a parallel direction interacts more strongly with the absorbing medium than light polarised at right angles[59], which is true only for isotropic media. In anisotropic media the interaction will depend on the orientation of the dipoles. Hence, ATR and MATR methods can be used to study anisotropic media[20,25,27,60-62].

III. APPARATUS AND EXPERIMENTAL TECHNIQUES

The apparatus used to record IRS spectra consists of a standard spectrophotometer with a special attachment in the cell compartment. The optical system of the attachment is designed according to the optical and geometrical features of the IRE and of the spectrometer. Depending on the IRE, the attachment can provide single or multiple reflections. In single-reflection attachments the IRE may

§ The theory of multilayer systems, with reference to the ATR method, has been discussed by Hansen[57].

¶ Formulae (20) and (21) are given[20] without proof, but a derivation of these formulae was published later[25]. However, formula (21) is somewhat different from the corresponding formula obtained in Ref. 25.

be in the form of a prism[15,54,63-65] (mainly for work in the u.v. and visible regions), a hemisphere, or a hemicylinder[24,35,37,66-71] (for i.r. measurements).

The use of a hemicylinder is convenient because it allows an arbitrary choice of angle of incidence and hence it can replace several prisms with different angles of incidence. Furthermore, it is easy to obtain a parallel beam within the hemicylinder[9,24,25,35,68,70] over a wide range of angles of incidence, and therefore the angle of incidence can be calculated unambiguously and with great precision (~0.5′)[66]. This level of precision is essential, for example, in determinations of optical constants by the two-angle method[25,46].

Attachments using a hemicylindrical IRE have been designed for the IKS-14,[67] Hilger H-800,[68] and UR-20 [70] spectrophotometers. The operation of these attachments is easily understood from Fig. 7.

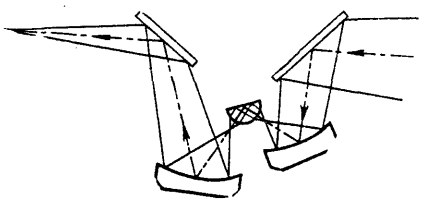

Figure 7. Single reflection attachment.

Single-reflection attachments have one serious drawback: they cannot produce intense, undistorted spectra. This drawback is overcome in multiple-reflection attachments, which can accept IRE's of different geometrical configurations such as plates with fixed or variable angles of incidence, and with single[10,11,15,72-77] or double[9,15,20,78] light transmission. IRE's can be trapezoidal[79] or rosette-shaped[80], with multiple light transmission, or in the form of a light-guide[15,81]. An IRE with a curved surface has been described[82,83]. The most commonly used of these elements is the multiple internal reflection (MIR) plate with fixed angle of incidence and single light transmission. This is because both the construction and the calculations are simpler with these plates. In the simple geometry of the plate, the number of reflections is easily calculated:

$$N = \frac{L}{t}\cot\theta \qquad (22)$$

where L is the length and t is the thickness of the plate.

It follows from Eqn. (22) that the number of reflections increases as the angle of incidence decreases. The number of reflections increases in proportion to the length, and in inverse proportion to the thickness of the plate. However, it should be remembered that the length of the plate cannot be increased indefinitely without total extinction of the light beam as a result of optical imperfections in the polished surfaces. The scattering by these imperfections is a function of wave length, and is most pronounced in the u.v. region[58]. Hence, the reflectivity of the plate depends on the quality of its optical finish[35,54]. The thickness of the plate, also, is limited, and cannot be decreased below the width of the spectrometer slit[10,11,35].

It should be noted that any divergence of the light beam within the plate causes ambiguity in the angle of incidence[9,35] even though it may be beneficial in ensuring total illumination of the surface of the plate[10,11].

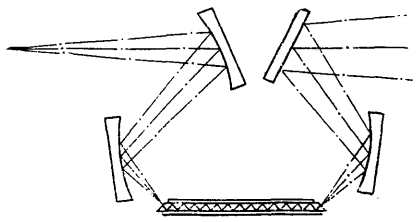

Figure 8. Multiple reflection attachment.

MIR plates are now commonly used in commercial attachments (see Fig. 8), made both in the Soviet Union and abroad. Attachments for the IKT-14,[71] UR-20 [84,85], and various Perkin — Elmer spectrometers[54-56] have been described in detail.

Attachments using an MIR plate as the IRE are used in the u.v. and the visible region[54], and also in the i.r. region[76] and in the far infra-red[86]. MIR plates giving up to 50 — 300 reflections have been constructed[87-89].

Cells for special investigations have been developed using MIR plates. Some of these, produced[54,55] by the firm of Wilks Scientific Corporation (USA), are particularly interesting because they are equally suitable for analytical work and for physicochemical research.

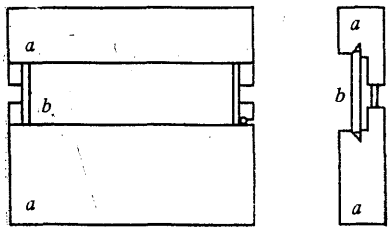

Figure 9. Cell for viscous liquids: (*a*) Teflon holder, (*b*) IRE plate.

Fig. 9 shows a cell for the analysis of high-boiling compounds (lubricants, oils, adhesives, and other viscous materials). The cell consists of a Teflon holder and an IRE in the form of a plate. The IRS spectrum is obtained by spreading the material on the surface of the plate. 25 reflections are possible.

The microcapillary cell (Fig. 10) is used to examine fractions isolated by gas — liquid chromatography. It consists of a Teflon holder and two thin MIR plates, between which the substance to be analysed is placed. Because of the large number of reflections (~50), the sample size can be very small (~10^{-4} g).

The cell shown in Fig. 11 is used for liquid samples. The gap between the MIR plate and the metal holder is not critical, because the absorption does not depend on the thickness of the layer of sample.

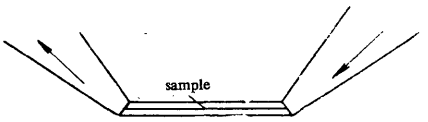

Figure 10. Micro-capillary cell.

The combined cell and reaction vessel (Fig. 12) and the flow-through cell (Fig. 13) have been designed for studies of the kinetics and mechanisms of chemical reactions[88].

In spectrophotometric studies of powders, paper, tissues, rubber, polymers, films, and various coatings, the solid-sample cell shown in Fig. 14 is used. Mechanical pressure is applied to increase the area of contact between the plate and the experimental material.

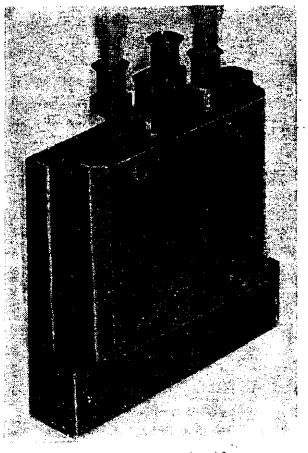

Figure 11. Liquid sample cell.

Cells for direct spectroscopic studies of aerosol particles[90], and for measurements in high vacuum[9] and at high temperatures[54,55], have also been described. Special attachments in which the IRE extends beyond the cell compartment of the apparatus have been developed for studies on large samples[10,11].

Differential spectra can be obtained, if necessary, by using single and multiple reflection cells. However, it is not always possible to compensate exactly for the differences between two IRE's. With isotropic media, the residual background absorption can be compensated with polarisers[91] or variable-area cells[54]. In addition to the various attachments, special spectrometers for IRS spectroscopy have been described[10,11,54,55,92], but in every case the essential component, which determines the quality of the spectra, is the IRE. Obviously, the material used to fabricate the IRE must have some special optical, physical, and chemical properties.

The material must have: 1) a high refractive index, so as to give undistorted spectra with samples of widely different refractive indices; 2) high purity and optical transmission, since the length of the optical path in the MIR

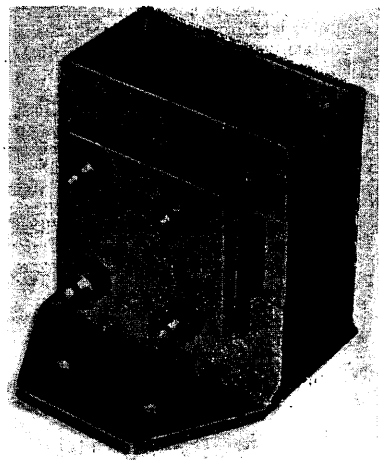

Figure 12. Reaction cell.

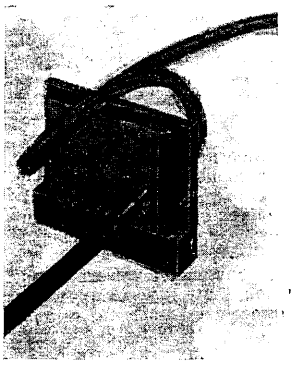

Figure 13. Flow-through cell.

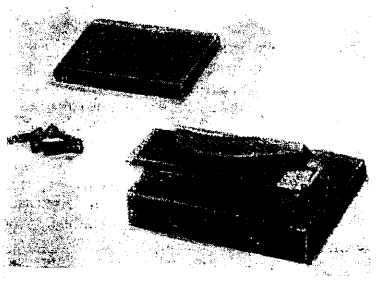

Figure 14. Solid-sample cell.

plate can be 100 mm or more; 3) high elasticity, hardness, and mechanical strength, since the IRE must not be easily deformed, scratched, or bent; 4) chemical stability, since the IRE material must not dissolve in or react with the material being analysed.

Characteristics of materials.

No.	Material	Chemical composition	n_D	θ^*_K	Spectral region, μm	Max. temp., °C	Remarks
1	Germanium		4.0	14.5	2—11.5	125	Hard, brittle, chemically stable. Used in the i.r. region.
2	Silicon		3.5	16.6	2—6.5 40—300	300	Hard, brittle, chemically stable. Used in the i.r. and far i.r. region.
3	KRS-5	42%—TlBr 58%—TlI	2.5	23.6	1—40	125	Elastic, soft, insoluble in many solvents. Sparingly soluble in water. Used in the i.r. region.
4	Irtran-4	ZnSe	2.4	24.6	2—16	300	Hard, stable, insoluble in water. Used in the i.r. region.
5	KRS-6	40% TlBr 60% TlCl	2.2	27.0	0.4—25	100	Softer,than KRS-5. Used in the i.r. region. Can be used in the visible.
6	Silver chloride	AgCl	2.0	30.0	1—20	200	Very soft, insoluble in water. Used in the i.r. region.
7	Sapphire	Al_2O_3	1.7 (above 2 at $\lambda < 0.2$ μm)	36.0	0.18—6		Very hard. Used in the u.v. and visible region.
8	Quartz (fused)	SiO_2	1.43 (1.65 at $\lambda < 0.2$ μm)	44.4	0.18—0.75		Used in the u.v. and visible region

*θ_K values calculated relative to air.

In addition, the IRE material must: 5) be easy to grind and polish, and 6) retain its transparency at high temperatures.

Because of these stringent requirements, the materials used to obtain transmission spectra are not always suitable for IRS. The literature dealing with materials for internal reflection spectroscopy is extensive[9-17,34,54-56,72,85,93]. Some properties of materials commonly used in IRS are listed in the Table.

IV. APPLICATIONS OF INTERNAL REFLECTION SPECTROSCOPY

As stated above, internal reflection spectra are qualitatively similar to transmission spectra if the distortion resulting from anomalous dispersion can be overcome. (Suitable conditions are discussed in Section II). Hence, existing data on the transmission spectra of related compounds can often be used to interpret IRS spectra. This allows IRS methods to be applied to a wide variety of problems, including the identification of various compounds, studies of their structure and reactivity, and a wide range of associated problems.

However, IRS has a number of advantages over transmission spectroscopy: it is unique in its ability to examine materials in any state of aggregation, of any consistency, and of practically any size or thickness.

1. Types of Material

The IRS method has no special advantage over transmission spectroscopy in work with liquids and some solutions, but in practically every other case it is greatly superior, and in some cases it is the only possible method.

Powders. The study of powders by i.r. spectroscopy is a very common problem. Conventional techniques (pressing into tablets with alkali halides, preparation of mulls, etc.)[94] are laborious and often unsatisfactory: they tend to contaminate the sample and to disturb its crystal structure, and chemical interaction between the sample and the matrix cannot always be avoided. Furthermore, the spectra are sometimes incomplete or otherwise unsatisfactory, due to scattering or masking by the bands of the diluent.

IRS methods are free from all these drawbacks. The only pre-treatment needed is to spread the sample on an adhesive tape[54], which is then pressed against the IRE. With amorphous powders the procedure is even simpler: the sample is deposited directly on the internal reflection plate[54]. Sands, various precipitates[95], and other fairly coarse (up to 300 μm particle size) powders have been analysed in this way, and have always yielded high-quality spectra (Fig. 15).

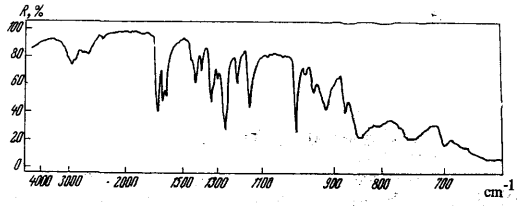

Figure 15. Internal reflection spectrum of sorbic acid powder. IRE—Ge plate (25 reflections).

Solid bodies. Solid bodies cannot be examined directly by transmission spectroscopy. A sample must first be removed, finely powdered, and examined by a standard method. In some cases (e.g. coal analysis[96]) the preparation of the sample may take up to 8 hours.

On the other hand, the study of solid bodies (including coals[97]) by IRS methods is quite straightforward: special attachments have been developed[10,11,54] for recording spectra from samples of any size.

The difficulties encountered in studying single crystals by transmission spectroscopy[98] are well known: again, this type of sample can yield IRS spectra without difficulty[60,99-103]. The IRS method is particularly effective in studies of anisotropic media: in particular, it is greatly superior to transmission spectroscopy for studying dichroism[60-62,99].

Films. The examination of fairly thick films by the classical spectroscopic methods presents a number of difficulties. Even at thicknesses of a few tens of microns[98] analysis of the film by classical methods may become impossible. In direct contrast, films are perhaps the best type of sample for IRS studies (Fig. 16). In addition to solving various problems in the physics of films[104], these methods have been used successfully for film identification[54] (including films of metal hydroxides[7,105]). Coatings on films[7] are easily analysed, including measurements of thickness[107] and composition[106,107]. IRS methods are seen at their best in the analysis of multilayer films[7,108,109], since they can yield identifiable spectra for the individual layers.

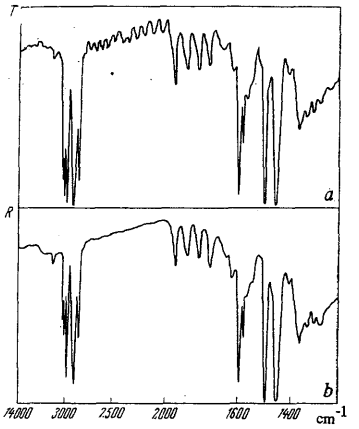

Figure 16. Transmission (*a*) and IRS (*b*) spectra of a polystyrene film. IRE—KRS-5 plate (25 reflections).

Viscous materials. Viscous materials are not easily studied by transmission spectroscopy in their natural form, yet they are almost the ideal type of sample for IRS[54]. For example, IRS spectra for a large number of adhesives have been obtained very easily[79], including industrial adhesives[110,111] and adhesive coatings[112].

Melts. Fairly complicated techniques are available for measuring the i.r. spectra of melts. They become very much simpler when IRS methods are used[113,114].

Liquids and solutions. In studies of the i.r. spectra of liquids, and some solutions, the use of IRS methods is hardly justifiable. However, the u.v. transmission spectra of liquids and concentrated solutions are almost impossible to measure. Furthermore, the scope of i.r. spectroscopy of solutions is often limited by the difficulty of finding a suitable solvent, since most solvents have strong absorption bands and therefore they can only be used over a limited region of the spectrum. Water is one of these solvents, and in many cases aqueous solutions are the only form in which the material of interest can be investigated. With biologically active substances and their model compounds aqueous solutions are vitally important because they most closely resemble natural (*in vivo*) conditions. However, the study of aqueous solutions still presents considerable difficulties[115], and several important regions of the spectrum remain inaccessible even with the thinnest available cells.

With the introduction of IRS methods the scope of aqueous i.r. spectroscopy has become much wider, and at the same time the experimental procedures have been simplified. The i.r. spectra of aqueous solutions can now be measured over practically the whole of the spectral region by using the available range of crystals (KRS-5,[115] AgCl,[116,117] Irtran-2,[118] Ge [95])†, by choosing the ATR[116-122] or the MATR[115,123,124] method as required by the problem, and by taking advantage of the most up-to-date equipment[117,119].

The possibilities and the advantages of the IRS method in comparison with the transmission method have been demonstrated by measurements on aqueous solutions of acetylcholine[125], various aminoacids[115,116,118-120], and carbohydrates[115,120,126]. IRS methods are widely used to study aqueous solutions of inorganic and organic acids and their salts[16,115,117,118,120-122,127-132], and other compounds[115,120], and also the structure of water itself[121,129,133]. IRS methods are particularly effective in studies of multiphased systems, e.g. aqueous emulsions of disperse and turbid media, etc.[95,118,120], which cannot as a rule be examined by conventional transmission methods. The IRS spectra of concentrated aqueous solutions have also been examined in the u.v. region[72,81].

The IRS technique has greatly extended the range of solvents which can be used in i.r. spectroscopy. Thus, universally acceptable solvents such as alcohols, dimethylformamide, dimethylsulphoxide, etc. can now be exploited by the i.r. spectroscopist. A comparative study[134] of the solvents most commonly used in chemistry has shown that their transmission bands are much broader in i.r. IRS spectra than in conventional i.r. absorption spectra.

2. Applications

Because of the unique features of the IRS method, its potential applications in chemistry and in related areas of science and technology are many. Some examples of the application of IRS in areas where the method appears particularly promising are discussed below.

a) Study of chemical reactions

Molecular spectroscopy is undoubtedly one of the most powerful methods of studying various types of chemical change, and important problems in chemical kinetics and reaction mechanisms. However, the scope of transmission spectroscopy in this particular area is severely limited. Thus, it is seldom possible to study a reaction without a solvent, or in concentrated solutions; unfortunately the commonest solvents are strongly absorbing, and therefore the reaction systems cannot be studied by transmission methods even in dilute solutions.

All these difficulties can be fully or partially overcome by resorting to IRS methods, whose extensive technical arsenal (various crystals with different angles of incidence and number of reflections, special reaction vessels[54,55]) allows almost any reaction to be investigated either in solution (in one of the increasing number of usable solvents[134]) or without a solvent.

A good example of the advantages of IRS over ordinary transmission methods is provided by Roberts' work[135] on

† It must be noted that KRS-5 is sparingly soluble in water, particularly in hot water[95], and that AgCl can react with aqueous solutions giving rise to corrosion of the steel parts of the cell[16,95].

reactions involving carbonium ions, based on measurements of u.v. IRS spectra. Carbonium ions absorb very strongly in the u.v., and they can be studied only at high dilution. On the other hand, they are so highly reactive that unwanted side-reactions with the solvent are almost unavoidable. For these reasons, the study of carbonium ion reactions by normal u.v. spectroscopy is not a practical proposition.

On the other hand, IRS methods have been found very effective in this case, and studies of carbonium ion reactions (including intermediates) have been successfully carried out by these methods over a range of concentration, temperature, and pressure.

Infrared IRS is widely used to study polymerisation reactions[76,136-138], including high-temperature polymerisation[138], which do not lend themselves to conventional transmission spectroscopic investigation (Fig. 17).

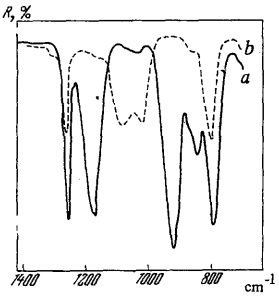

Figure 17. IRS spectra of hexamethylcyclotrisilazane during hydrolysis: (*a*) initial compound, (*b*) hydrolysis product. IRE—KRS-5 plate (25 reflections).

IRS is one of the most effective methods of monitoring surface reactions on opaque materials. For example, the effect of u.v. radiation on the stability of polymers and the effect of inhibitors on the course and the rate of reactions on polymer surfaces have been studied[139] by IRS spectroscopy. The behaviour of modifiers and other polymer additives under the influence of light has also been examined[140]. IRS has been used to study surface oxidation[141], the oxidative polymerisation reactions involved in the drying of certain oils[142], and various other processes on polymer surfaces[143].

b) Surface phenomena and adsorption

The future of IRS in the study of these important chemical problems is assured[144,145]. In particular, IRS methods are among the few which can give information on surface states in semiconductors and on their influence on the electrical properties of the surface[144]. In this case the application of the method stems from the fact that the reflectivity is a function of the electric charge at the surface, which is itself influenced by external electric fields or by adsorption. Harrick[27,53,82,146] was the first to use IRS in the study of surface states, but the method was soon adopted by other workers[147-149]. More recently, IRS has been used to study a wide range of problems in semiconductor surface chemistry, including the chemical nature and the behaviour of solid and liquid surface films formed by the action of electrolytes, during etching, etc.[73,150-157], and also adsorption processes on semiconductors[27,158].

Adsorption is the branch of chemistry where the advantages of IRS are most clearly evident, as shown by the large number of papers published on this subject. Among the most interesting are studies of the adsorption of hydrocarbons[82], fatty acid derivatives[154-159], and other organic and inorganic substances[159-161] including gases[27,158].

The various modifications of carbon are technically important as adsorbents, but the study of these materials by the traditional methods of transmission and reflection spectroscopy (particularly in the i.r. region) often presents insuperable practical difficulties arising from their very strong absorption[162] (which can exceed the absorption of organic compounds by 10^2-10^3). However, by using multiple reflection techniques in very sensitive spectrometers we can identify the functional surface groups which determine the adsorption properties of the different carbons, measure their concentration, and examine various problems bearing on the nature of the adsorption process. In particular, we can answer questions such as: how do adsorbates affect the structure of the surface, which functional groups are involved in sorption processes, what is the nature of the sorption bond, etc.[96,141,162-164].

c) Electrochemistry

The most important problems in electrochemical research are to establish the mechanism of the electrode reactions, to identify the intermediate activated states of the products formed by electron transfer, etc. Information of this type cannot be obtained directly from electrochemical measurements. Other methods, including transmission spectroscopy, are also unsuitable.

IRS, on the other hand, is ideally suited to the study of electrochemical processes *in situ*.

The theory of IRS developed by Hansen[165] for multilayer systems has been widely applied in studies of electrochemical reactions by u.v. and i.r. internal reflection spectroscopy.

The electrode for studies in the u.v. region usually consists of a glass prism or plate coated with a thin conducting layer of tin oxide[166-169], gold[149,170-172], platinum and palladium[173], or antimony[171]. For work in the i.r. region the electrode is either pure germanium[174] or germanium coated with a metallic film (e.g. gallium)[88,175].

A good example of the successful application of u.v. IRS in electrochemistry is a series of studies[166-168,173] of the electrochemical oxidation of *o*-toluidine, in which the kinetics and the mechanism of the reaction were examined under different conditions, the electrolysis products were identified on the electrode surface, and their concentration was measured. A similar study of eosin-Y has also been published[165,170,171].

Other examples of the use of IRS in the u.v. region for electrochemical studies include an investigation of discrete states at the electrode — solution interface[147,176,177] and studies of the reduction of 8-quinolinol, tetramethylbenzidine, and various carbonyl compounds[88,175]. Electrolysis mechanisms were investigated, the reduction products were identified, and their concentration was determined. The effect of electrode potential on the intensity of the spectral bands due to intermediate products was also found (Fig. 18).

d) Biochemistry, clinical chemistry, and pharmacology

Molecular spectra (and, in particular, vibrational spectra) are widely used in biochemical research. Significant advances have been made in recent years[178-180],

but the preparation of samples for spectroscopic measurements remains a complicated and laborious procedure[180], involving many preliminary operations such as homogenisation, dehydration, and pressing into alkali halide disks, which can lead to losses and contamination of the sample. However, the most serious shortcoming of these techniques is the danger of altering the properties of delicate biological samples.

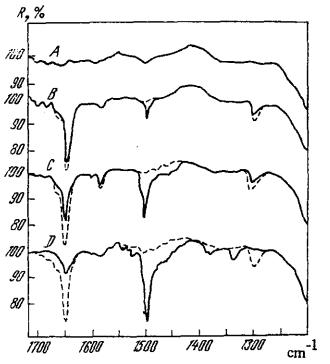

Figure 18. IRS spectra of *p*-benzoquinone (broken line) and its electrolysis products (full line): *B* at 0.7 V, *C* at 1.1 V, *D* at 2.0 V. *A* is the spectrum of the solvent. IRE—germanium plate (25 reflections) coated with a layer of gallium.

IRS methods have opened an entirely new chapter in biochemistry and clinical chemistry, because they enable biological tissues to be examined without pre-processing. Thus, spectra have been obtained from whole blood[126], bone tissues and collagens[181], tendons[181,182], etc.

One of the main advantages of the IRS methods is their unique ability to examine not only the tissues themselves but also numerous processes occurring within the tissues as a result of various influences. For example, spectra have been obtained from the upper integument of the brain cortex of the white rat, undergoing narcosis[76]. IRS methods have been used also to study stimulated chemical changes in animal tissues under the influence of biologically active preparations[183]. One of the most important discoveries has been the selectivity of these preparations towards different organs: for example, spectral changes were detected in kidney and liver tissues after the injection, but not in other tissues. Thus, IRS methods can, in principle, monitor the distribution of biologically active substances within the organism, and therefore they can be used to study the mechanism of biological interactions[183].

The use of IRS in biochemical studies of normal and pathogenic animal and human tissues may lead to significant advances in the diagnosis and study of various diseases. Results so far obtained are extremely promising. Thus, spectra have been obtained from normal and from pathological erythrocytes in human blood[76]. Infrared IRS spectra have been recorded, and studied, from the tissues of various human organs[184]: spleen, liver, blood vessels, etc. Significant differences have been found between the spectra of the aorta of a new-born infant and that of an adult suffering from arteriosclerosis. We may therefore classify IRS among the methods available for comparative studies of the chemical composition and properties of healthy and of pathological tissues. The use of IRS to study healthy and diseased tissues in the human eye (cornea, and crystalline lens) has also been proposed[184].

New prospects in biochemical and clinical research (e.g., in the diagnosis of skin diseases) may be expected from the latest refinements in the design of IRS apparatus. Thus, special attachments have been developed[185] to take IRS spectra from the surface of practically any part of the human body. These provide detailed information on the skin retention of ointments, creams, and other preparations, and on the nature of their interaction with the skin (Fig. 19).

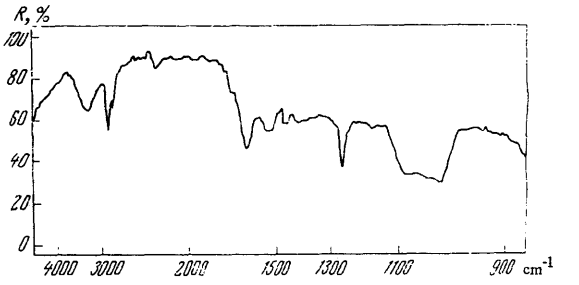

Figure 19. IRS spectrum of human skin treated with an ointment. IRE—AgBr plate.

One of the most interesting biochemical applications of IRS is the study (and, in some cases, the identification) of micro-organisms such as bacteria and algae. By using special membrane filters to "accumulate" the micro-organisms, their spectra can be recorded[95,186,187], and furthermore the organisms can be identified, since the spectra of, say, two varieties of algae show some distinct differences[95]. In principle, mixed cultures can be analysed from their IRS spectra with the help of a computer.

Among the many other biological applications of IRS, the following are particularly interesting: a study of the structure of liquid water in crystalline animal haemoglobin[76], a study of the surface reactions of bio-polymers[188,189], and also measurements of the u.v. spectra of chlorophyll[79] and of the i.r. spectra of carbohydrates[120,126,190], aminoacids[118-120], steroid hormones[191], and various biologically active substances and preparations[160,192,193].

IRS methods are very attractive in pharmacology[194], since they can be used in the structural analysis and quality control of medicinal preparations[195].

e) Chromatography

Infrared spectroscopy is one of the most effective methods of analysis and identification of chromatographic fractions. However, this method cannot always be applied: in order to achieve the optimum separation conditions, it is often necessary to work with very small samples, which may lie below the limits of sensitivity of standard methods of analysis.

In gas chromatography, the problem can be overcome by using the capillary multiple reflection cell described in the previous Section[54,185,196], which may be connected

directly to the chromatographic fraction collector. This method overcomes the loss of sample which is unavoidable in normal methods, and it offers very high sensitivity (down to 0.01 μl) by virtue of the large number of reflections possible (up to 50)[196]. The apparatus can be used with substances covering a wide range of boiling point (60 — 200°)[185, 196].

Typical examples of the use of IRS in chromatography include the analysis of fractions of steroids[191], pesticides[192], adhesives[110], and other substances[112], with samples weighing only a few microgrammes[192] (see Fig. 20).

Thin-layer chromatography and paper chromatography also involve very small samples, which cannot be analysed by normal i.r. spectroscopy after being fractionated and extracted from the substrate. Larger samples are sometimes collected by combining several peaks[192], but the procedure is time-consuming.

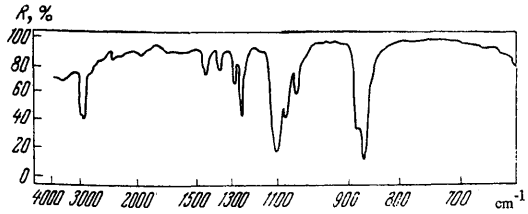

Figure 20. IRS spectrum of a chromatographic dioxan fraction isolated from a 0.7 μl sample of dioxan — acetone mixture. IRE—KRS-5 (50 reflections).

Considerable time saving, and simpler experimental procedures, can be achieved by resorting to IRS methods. Thus, it is sometimes possible to record spectra and to identify the fractions directly from the surface of the chromatogram, and even to analyse a mixture quantitatively[197]. In other cases[191,192] the chromatographic spot is extracted with a suitable solvent and the solution is applied to the IR plate. With this technique, a few microgrammes of sample are sufficient to give a strong spectrum, particularly if a plate capable of 50 or more reflections is used[54].

f) Industry

The important new features of IRS (as compared with transmission spectroscopy) offer great scope not only in scientific and research work but also in industrial laboratories responsible for the analysis of production runs. Molecular spectroscopy may now find general application as a method of process control and quality assurance in industry, whereas until relatively recently the method had been applied only in a few specialised areas.

The outlook can be illustrated by some examples.

1. Paper. IRS methods are already widely applied in the analysis of various types of paper, cardboard, etc. They are used also in the analysis of pulp and unbleached paper[198,199], and to identify and to determine the composition of paper coatings[200,201] including bonding[7,202-204] and colouring agents[16,106]. Different types of article have been analysed: paper-coated aluminium foil[205], cardboard boxes and labels[199], stamps[206]. IRS methods have been applied to specific problems such as identifying the contaminants of the matting in paper-making machinery[199], and also in determining the stability of paper coatings under the influence of temperature, light, etc.[54,204].

2. Wood. IRS methods have been used to solve problems related to the composition of wood, and to analyse various wood coatings[126].

The chemical composition of its surface determines many important properties of wood, such as its ability to bond to other surfaces. IRS spectral studies of different types of wood[207] have shown that the chemical composition of wood near a cut surface is very dependent on the angle of the cut. In particular, the xylene content of the surface region can vary by a large factor, depending on the angle of the cut.

3. Textiles. The development of IRS methods has led to the solution of a number of problems in the textile industry. Thus, both natural[54,105,208-210] and synthetic[54,99,126,210,211] fibres and fabrics have been successfully identified, glass fibres have been studied[105], and the composition of their surface coatings has been determined[105,111,208]. Because of the high sensitivity of the IRS methods, minor components of surface coatings can be detected[111] at concentrations below 1%. Other successful applications of IRS include the quantitative analysis of fibre compositions (for example, the ratio of cotton to nylon in semi-synthetic fabrics[31]), and the analysis of residues of finishing materials[208], which may include impurities harmful to the fabric[111].

4. Leather. The different types of natural[212] and synthetic[7,111] leather can easily be identified by IRS methods; it is possible also to analyse coatings and residues of finishes on the leather surface.

5. Polymers. Articles made from polymers are extensively used in industry and in everyday life. They can all be identified and analysed by IRS methods. These methods can also be applied for process control in the production of polymers[76,136,213], and for the analysis of finished articles[7,24,69]. In conjunction with special pyrolysis attachments, IRS methods can give useful information on polymer additives and fillers[185,211,214,215].

The use of IRS methods to analyse and identify polymers in the footwear industry[110], and also in the packaging and other industries[108], has also been reported.

6. Foodstuffs. I.r. IRS spectra have been measured on many food products, including margarine, gelatin[70,126], and milk powder[182]. By using membrane filters[187], components present in suspension in liquid foodstuffs can be analysed (for examples, yeasts in different types of beer[186]). In principle, IRS enables the quality of any foodstuff to be assessed and the presence of adulterants to be detected.

7. Cosmetics. The analysis of cosmetic articles by IRS methods is much more effective than analysis by the classical transmission spectroscopy methods, used until recently[216]. The most varied types of cream can be analysed[189,217] (including cream present on the skin[185]), and also toothpaste[182,217], liquid soap[218], foam[54], shampoo[218], domestic liquid detergents[218], and others[219].

The importance of i.r. spectroscopy as an operational method of quality assurance and process control in industry is well known[220]. The development of IRS has

greatly extended the scope and the range of the industrial applications of i.r. spectroscopy: as stated above, i.r. spectroscopy can now be applied in the paper, textile, food, and other industries as an analytical method. IRS may have an important part to play in the solution of some urgent industrial problems (e.g. effluent analysis[95,115]).

In the chemical industry, IRS offers exciting new prospects in the area of direct process control (e.g., on-line product analysis[24,221,222]).

Problems of these types can seldom be solved by the classical methods of spectroscopic analysis, which are severely limited by the need to use extremely thin optical cells. On the other hand, analysers based on the IRS principle can be used in a wide variety of automatic process control loops handling any type of liquid system, including very viscous liquids.

Industrial i.r. IRS analysers have been developed[223,224], and have been used successfully under factory conditions[224].

g) Trace analysis

One of the main attractions of the IRS method is its very high sensitivity, which enables quantities of the order of $10^{-6}-10^{-7}$ [54,87,95,191,193] or even 10^{-9} [35] g of sample to be detected and identified. It is thought[58] that even lower limits of detection may be practical. Hence, the IRS method is very attractive for the detection of very small concentrations of harmful and dangerous substances (a very important problem in chemical plant, storage areas, etc.).

An IRS trace analyser[139] has been developed for the detection of toxic vapours from rocket fuels, which may build up to dangerous concentrations in rocket storage sheds. A more recent modification of this equipment is used[160] to detect traces of organo-phosphorus compounds in air. The key component of the apparatus is a germanium multiple reflection plate coated on both sides with a thin platinum film which acts as the adsorption surface. Under the best conditions (film thickness 500 — 800 Å, surface temperature 15 — 20°) the apparatus can detect the presence of 10^{-7} g litre^{-1} of dimethylmethylphosphonate in air in 30 s.

The function of the platinum coating is to ensure that the adsorption is reversible: the adsorbate can be removed from the surface in a few seconds, simply by flushing the apparatus with air, and the sensitivity of the surface remains constant over long periods.

Similar devices can be used[90] to detect solid particles.

3. Quantitative Measurements

It was pointed out in Section II that the reflectivity of the surface can be approximately described by an equation analogous to the Lambert — Beer law if the refractive index and the angle of incidence of the IRE are correctly chosen. The formal optical density $\ln(R_0/R)$ then becomes a linear function of the concentration c.

From Eqn. (13) we have

$$\ln\left(\frac{R_0}{R}\right)_\nu = \alpha_\nu \cdot c \cdot d_{\text{eff}} \qquad (23)$$

Eqn. (23) can be used to calculate the concentration of the material of interest by the procedures and methods of quantitative transmission spectroscopy.

The practical aspects of quantitative analysis by IR spectroscopy were discussed by Wilks[31], who examined the dependence of the precision, reproducibility, and sensitivity of the method on factors such as the material of the plate, the number of reflections, the angle of incidence, the area of the plate covered by the sample, the position and uniformity of the sample, and the effectiveness of the contact.

It should be noted that, because of the linear dependence of the effective thickness upon wave length, the IRS band intensities are not directly comparable with those of transmission spectra. It can be shown, however, that the integral intensity of a band in the IRS spectrum is equal to the G integral in the transmission spectrum, obtained by integrating over the logarithm of the frequency[46,76]. Thus, the IRS method offers a simple way of determining the integral band intensities in the spectra of pure liquids and solutions[32].

The ATR and, particularly, the MATR method show great promise in routine analysis, when absolute methods are very seldom necessary and the main objective is to establish the effect of varying many factors. Relative methods are fully adequate in these circumstances. Typical applications of IRS methods in routine analysis include the quantitative analysis of aqueous and alcoholic solutions[72,95,112,117,118,124,127], and of coatings on paper[201,203], fabrics[203], and films[107,219]. Other reported applications of quantitative IRS methods include the compositional analysis of alkyd resins[215] and adhesives[112], semi-synthetic fabrics[31], and paper pulp[198]. Quantitative analyses of medicinal products[195], cosmetics[218,219], chromatographic fractions[197], and mixtures of powders[31] have also been mentioned. It has been shown that the method can measure the concentration of electrochemical reaction products on electrode surfaces[197], and the concentration of functional groups on adsorbent surfaces[164], and that it can be used to monitor polymerisation processes quantitatively[138]. Lastly, analysers for the quantitative control of continuous industrial processes have been developed[223,224].

The precision of quantitative IRS methods is always of the order of a few per cent[117,124,198,215,218], which is as good as in ordinary transmission spectroscopy. However, the former technique has a number of advantages over the latter, such as freedom from interference errors (Fig. 16). IRS methods also have some operational advantages by being less time consuming than transmission methods (mainly because of the simpler sample preparation procedures).

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Many examples of the successful application of IRS in important areas of science and technology have been listed in this review. However, the list is by no means exclusive. It may be said, without exaggeration, that the scope of IRS, and therefore the area of application of ATR and MATR methods, is almost limitless. It would be difficult to enumerate all the areas of science and technology in which IRS methods have been successfully applied.

IRS has been used to study the liquid-crystal state[225], electrophoresis[54] and diffusion[9], and in mineralogy[103]; it has also been used to analyse asphalt[226] and tiles[156]. ATR and MATR methods are used to analyse pollutants in air[227], to determine the composition of cigarette smoke[95] and exhaust gases[186], and to identify inks[186] and wire coverings[54]. IRS methods have been proposed for the analysis of sludge deposits[95] and lunar dust[87]. There are reports of the successful use of IRS in philately[75,206] and in forensic science[10]. IRS methods may be useful in establishing the authenticity of paintings from the composition of the paints[185], which may be determined by direct IRS measurements on the painting itself. Wilks, one of the

founders of practical IR spectroscopy, rightly points out that the limitations of the IRS methods, and the specific areas of science and technology where these methods can be applied, are mainly determined by the ingenuity of the investigator.

In conclusion, we note that IRS methods can be generally recommended, in all cases where the conventional methods of transmission spectroscopy are difficult or impossible to apply. The number of such cases is ever-increasing: many new problems in science and technology are soluble in principle, but they present insuperable difficulties arising from the limitations of transmission spectroscopy methods. Therefore, a more extensive penetration of molecular spectroscopy into chemistry and industry is almost unthinkable unless accompanied by a wider application of IRS methods in research and industrial laboratories.

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Many new publications have appeared while the present review was being prepared. The most important is undoubtedly Harrick's monograph[228], translated into Russian with an appendix by V. M. Zolotarev in which IRS equipment commercially available in the Soviet Union is described.

Two reviews[229,230] deal with general problems, and discuss some practical aspects of the application of IRS methods. In the latter, formulae for calculating effective thickness are obtained from a new mathematical treatment[231] of the problem.

Many interesting review papers can be found in the proceedings of a conference on applied spectroscopy held in 1970 in the USA.[232]

Section III of the present review, dealing with apparatus and techniques, would be incomplete without mention of some multi-purpose attachments for plotting u.v. and i.r. spectra[233], for adsorption studies[234], for low-temperature work[235,236], for studies of solids undergoing pyrolysis[237], and also of an attachment in which the light passes twice through the IRE.[238]

Mention must be made also of a number of interesting papers dealing with experimental methods, including the possibility of applying compensation measurements in IRS,[239] the optimum conditions for recording the spectra[240], and still further examples of the use of internal reflection spectroscopy with widely different types of sample including disperse media[241], suspensions[242], single crystals[243,244] and powders[245,246], and in particular metal oxides[247].

The practical applications of IRS methods continue to grow, as shown by the large number of papers published in the recent past. Among the most noteworthy we include IRS studies of paints[248] and textiles[249], of cellulose[250], of various foodstuffs[251], and of organic impurities in water[252].

IRS methods are being used on an increasing scale to study chemical reactions. Some of the more recent examples include studies of the interaction of proteins with polysaccharides[253], or resorcin with formaldehyde[254], and studies of the formation of elastomers in the solid phase[255] and studies of electrochemical reaction mechanisms[256-260].

In biochemistry the MATR method has recently been used in process control (separation of steroids by thin-layer chromatography[261]); in pharmacology it has been used to identify medicinal compounds and preparations[262-264].

IRS continues to be widely used in studies of surface phenomena and adsorption. The most recent papers on these topics deal with the physiochemical processes occurring in the surface layers of polymers during photochemical oxidation[265-267], under the influence of a corona discharge[268], in the presence of ozone[269,270], and they also describe further studies of various processes in polymers[271-274]. Adsorption[234], surface phenomena on semiconductors[275-279], and corrosion inhibitors[280] have also been investigated. In addition, IRS has been used to study the surface orientation of polymers[281] and biopolymers[282,283], the behaviour of surface-active molecules at an interface[284], solutions of alkali metals in liquid ammonia[285], adhesion between epoxy resins and cellulose[286,287], the hydrolysis of glass surfaces[288], and also a number of films and surface coatings[289-291].

Furthermore, the ATR method continues to be widely used to measure optical constants[292-297].

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RUSSIAN CHEMICAL REVIEWS
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The Pre-exponential Factors for Unimolecular Gas-phase Reactions

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The principal concepts and methods whereby the pre-exponential factors for unimolecular gas-phase reactions may be found have been examined. The methods are based on the transition state theory which accounts successfully for all experimental data. The reactions have been classified taking into account the typical structure of the activated complex. The question of the effect of molecular structure on the value of the pre-exponential factor has been examined for each group of reactions. The general postulates have been illustrated by examples. The data employed embrace about 800 reactions.
The bibliography includes 177 references.

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I. INTRODUCTION

Extensive information is now available concerning the pre-exponential factor A for unimolecular reactions of polyatomic molecules. The fundamental principles of the theory, which permitted a successful explanation of the experimental data, were formulated many years ago with the aid of the transition state method[1]. However, a detailed quantitative treatment with extension of the theory to different classes of compounds became possible only in the 1960's, in the first place due to the large-scale introduction in practice of the computational method of the Rice–Ramsperger–Kassel–Marcus (RRKM) theory and in the second place due to the marked increase in the number of experimental data. The data of recent years are the most accurate and frequently refer to long series of similar compounds, which is also important. The aim of the present review is to give a general and systematic account of the available data on gas-phase reactions.

II. THE VALUE OF THE PRE-EXPONENTIAL FACTOR

In 1928 Polanyi and Wigner[2] were the first to examine the question of the magnitude of the pre-exponential factor in unimolecular reactions using for this purpose mainly data for reactions in solutions[3] and introduced the concept of the "normal" pre-exponential factor, which has similar magnitude to molecular vibration frequencies (10^{12}–10^{14} s^{-1}). It is remarkable that at that time only three gas-phase reactions were known (decomposition of azomethane and N_2O_5 and the racemisation of pinene), which can now be classified, making certain assumptions, as unimolecular;

Table 1. The range of values of pre-exponential factors and certain other characteristics of unimolecular reactions.

No.	Class of compound	Reaction	Group according to Table 2	Number of compounds for which the following parameters are available				
				$\lg A$ (s^{-1})	$k(p)$	IE*	k (e)	Calcn. based on RRKM theory
1	2	3	4	5	6	7	8	9
1	alkanes	dissociation of C–C bond	1	—, —, 10 (Refs. 6 & 7)	1 (Ref.8)	—	2 (Ref.9)	5 (Refs.8 & 9)
		dissociation of C–H bond $CH_4 \rightarrow CH_3 + H$	2	—, —, 1 (Ref.6)	—	—	1 (Ref.9)	1(Refs.8 & 9)
		loss of H_2 $CH_4 \rightarrow CH_2 + H_2$	—	—, 1, — (Ref.10)	—	—	—	—
2	unsaturated hydrocarbons	dissociation of C–C bond	1	—, —, 5(Refs.6,7 & 11)	—	—	7(Ref.12)	7 (Ref.12)
3	aliphatic-aromatic hydrocarbons	dissociation of C–C bond	1	—, —, 5(Refs.6,7 & 13)	—	—	—	—
		dissociation of C–H bond	2	—, 6, –(Refs.6 & 14)	—	—	—	—
4	ketones and diacetyl	dissociation of C–C bond $RCOR' \rightarrow R' + R\dot{C}O$	1	—, 3,9(Refs.15–24)	—	—	—	—
5	alkyl cyanides	dissociation of C–C bond $R\dot{C}CH \rightarrow R\cdot + \dot{C}CN$	1	—, 1,2(Refs.15 & 25)	—	—	—	—
		loss of H_2 $CH_3CH_2\dot{C}N \rightarrow CH_2{=}CHCN + H_2$	3	—, 1, — (Ref.25)	—	—	—	—
		loss of HCN $CH_3CH_2CN \rightarrow C_2H_4 + HCN$	3	—, —, 1 (Ref.25)	—	—	—	—
6	free alkyl radicals	dissociation of C–C bond	1	—, 7,3 (Ref.26)	—	4 (Refs.27, 28 & 29)	7(Refs.9& 30)	7(Refs.9, 28–30)
		dissociation of C–H bond	2	—, 3, 2 (Ref.26)	—	1 (Ref.9)	2 (Ref.9)	2 (Refs.8 & 9)
		isomerisation	4	2, —, —(Refs.31 & 32)	—	—	—	—
7	acetyl radicals	dissociation of C–C bond $R\dot{C}O \rightarrow R' + CO$	1	1, —, 3(Ref.26)	—	—	—	—
8	alkoxy-radicals	dissociation of C–C bond $R\dot{C}O' \rightarrow R' + \rangle C{=}O$	1	3,1,1 (Ref.26)	—	—	—	—
9	$ROCH_2\cdot$ radicals (R = CH_3 or H)	dissociation of R–O bond	1,2	—, 2, —(Ref.26)	1 (Ref.8)	—	—	1 (Ref.8)
10	amines and amides	dissociation of C–N bond	1	—, 2, 2 (Refs.15 & 33)	—	—	—	—
		loss of CH_4	3	—, —, 1 (Ref.22)	—	—	—	—
		loss of NH_3	3	—, —, 1 (Ref.22)	—	—	—	—
11	azo-compounds	dissociation of C–N bond $R{-}N{=}N{-}R \rightarrow R\dot{N}_2 + R$	1	1, 2, 10 (Refs.15, 22 & 34)	1 (Refs.35 & 36)	1(Ref.36)	—	1(Refs.35 & 36)
12	aliphatic nitro- and halogenonitro-compounds	dissociation of C–N bond $RNO_2 \rightarrow R + NO_2$	1	—, —, 28 (Ref.37)	3 (Reg.38)	—	—	—
13	difluoroamines	dissociation of C–NF_2 bond	1	—, —, 3 (Ref.39)	—	—	—	—
14	difluoro-aminoalkyl radicals	dissociation of C–N bond $-\dot{C}-C(NF_2)- \rightarrow \rangle C{=}C\langle + NF_2$	1	1, 7, — (Ref.36)	—	—	—	—
15	hydrazine and its derivatives	dissociation of N–N bond	1	—, 3, 1 (Refs.15 & 26)	1 (Ref.40)	—	—	1 (Ref.41)
16	tetrazenes $R_2N{-}N{=}N{-}NR_2$	dissociation of N–N bond	1	—, 1, 1 (Ref.42)	—	—	—	—
17	nitramines $R_2N{-}NO_2$	dissociation of N–N bond	1	—, —, 3 (Refs.43 & 44)	—	—	—	—
18	nitrosamines $R_2N{-}NO$	dissociation of N–N bond	1	—, —, 1 (Ref.48)	—	—	—	—
19	dialkyl peroxides	dissociation of O–O bond	1	—, 1, 6 (Refs.45,46 & 47)	—	—	—	—
20	diacyl peroxides $RC(=O){-}O{-}O{-}CR(=O)$	dissociation of O–O bond	1	—, —, 3 (Ref.49)	—	—	—	—

Table 1 contd.

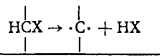
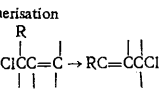
No.	Class of compound	Reaction	Group according to Table 2	Number of compounds for which the following parameters are available				
				lg$A$ (s^{-1})	k (p)	IE*	k (e)	Calcn. based on RRKM theory
1	2	3	4	5	6	7	8	9
21	hydroperoxides	dissociation of O–O bond	1	—, 3, 4 (Refs.45 & 50)	—	—	—	—
22	nitrites RO—NO	dissociation of O–N bond	1	—, 1, 4 (Refs.22 & 45)	—	—	—	—
23	nitrates RO—NO_2	dissociation of O–N bond	1	—, —, 3 (Ref.45)	—	—	—	—
24	inorganic oxides N_2O_4, N_2O_5, NO_3F, Cl_2O_7	loss of NO_2, OF, or ClO_3	1	—, —, 4 (Ref.15)	1 (Ref.51)	—	—	1 (Ref.52)
25	organomercury compounds	dissociation of Hg–C bond	1	—, 1, 4 (Refs.14,15,20,21 & 53)	1 (Ref.53)	—	—	—
		dissociation of Hg–Hal bond	2	—, 1, 2, (Refs.14,15,20 & 21)	—	—	—	—
26	compounds MR_n M=Zn, Cd, Sb, Bi, Pb, Sn, Ge, Si	dissociation of M–C bond	1	1, 4, 5 (Refs.15,54–57)	—	—	—	—
27	sulphones RSO_2—R	dissociation of C–S bond	1	—, —, 3 (Ref.58)	—	—	—	—
28	sulphides Rh CH_2—SCH_3	dissociation of C–S bond	1	—, 1, —(Ref.59)	—	—	—	—
29	$\dot{R}SO_2$ radicals	dissociation of C–S bond	1	—, 1, 1 (Ref.33)	—	—	—	—
30	cyclohexadienes	dissociation of C–H bond	2	—, 2, — (Ref.60)	—	—	—	—
31	organic chloro-derivatives of different classes	dissociation of C–Cl bond	2	—, 2, 2 (Refs.14,25,61–63)	—	—	—	—
32	organic bromo-derivatives of different classes	dissociation of C–Br bond	2	—,12,— (Refs.14,15,25,61–63)	—	—	—	—
33	organic iodo-derivatives of different classes	dissociation of C–I bond	2	—, 4, — (Refs.15,64 & 65)	—	—	—	—
34	inorganic oxides and fluorides FNO_3, F_2SO_3, $FClO_3$, $FClO_2$, $ClNO_2$, SF_4	elimination of F, O, or Cl	2	—, 5, 2(Refs.15, 66–69)	—	—	—	—
35	acetaldehyde	elimination of H	2	—	—	—	1 (Ref.70)	1 (Ref.70)
36	chloroalkyl radicals	loss of Cl	2	—, 7, — (Ref.26)	—	—	4 (Ref.71)	4 (Refs.71–73)
37	halogenomethanes	elimination of HX 	—	—, 5, — (Refs.15,66 & 67)	1 (Ref.74)	—	—	1 (Ref.75)
38	cyclic hydrocarbons, cyclo-olefins	dehydrogenation	3,4	—, 8, — (Refs.6,60,66 & 77)	—	—	—	—
39	fluoroalkanes	elimination of HF	3	—, 3, — (Refs.78–82)	—	1 (Ref.83)	17 (Refs.84–87)	4 (Refs.86 & 87)
40	AlR_3	elimination of isobutene	3	1, —, — (Ref.88)	—	1 (Ref.88)	—	—
41	chloroalkanes	elimination of HCl	3	17, 46, 1 (Refs.89–94)	1 (Ref.95 & 96)	2 (Refs.95 & 97)	3 (Refs.97–99)	4 (Refs.52,95–97, 100–102)
			4	—, 1, — (Ref.94)	—	—	—	—
42	bromoalkanes	elimination of HBr	3	—, 17, — (Refs.90 & 103)	1 (Ref.104)	—	3 (Ref.101)	3 (Ref.101)
43	iodoalkanes	elimination of HI	3	1, 5, 2 (Refs.90,103,105 & 106)	—	—	—	1 (Ref.64)
		dissociation of C–I bond	2		—	—	—	1 (Ref.64)
44	neo-$C_5H_{11}Cl$	γ-elimination of HCl	—	—, 1, —(Ref.107)	—	—	—	—
45	chloroalkenes	isomerisation 	3	2, —, —(Ref.90)	—	—	—	—

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Table 1 contd.

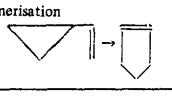
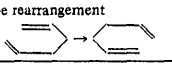
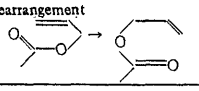
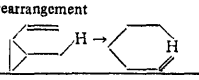
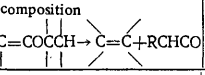
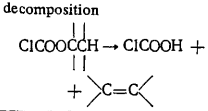
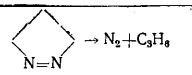
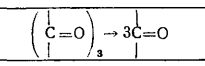
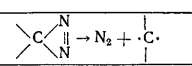
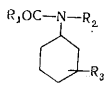
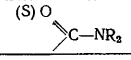
No.	Class of compound	Reaction	Group according to Table 2	Number of compounds for which the following parameters are available				
				lg$A$ (s^{-1})	k (p)	IE*	k (e)	Calcn. based on RRKM theory
1	2	3	4	5	6	7	8	9
46	alcohols	loss of H_2O	3	—, 2, — (Ref.103)	—	—	—	—
47	mercaptans	loss of H_2S	3	—, 1, — (Ref.108)	—	—	—	—
48	acetic acid	loss of H_2O	3	—, 1, — (Refs.25 & 109)	—	—	—	—
		loss of CH_4	3	1, —, — (Ref.25)	—	—	—	—
49	alkyl azides	loss of HN_3	3	—, 1, 2 (Refs.110 & 111)	—	—	—	—
50	halogenosilanes	$XCCSiR_3 \rightarrow \rangle C{=}C\langle + XSiR_3$	3	2,2, — (Ref.103)	—	—	—	—
51	acetic anhydride	$(CH_3CO)_2O \rightarrow CH_2{=}CO + CH_3COOH$	3	—, 1, — (Ref.103)	—	—	—	—
52	vinylcyclopropanes	isomerisation 	3	—, 6, 4 (Refs.15 & 112)	—	—	—	—
53	methyl thiocyanate	isomerisation $CH_3SCN \rightarrow CH_3NCS$	3	—, —, 1 (Ref.15)	—	—	—	—
54	alkyl isothiocyanates	elimination of HNCS $RNCS \rightarrow \rangle C{=}C\langle + HNCS$	3	—, 3, — (Ref.113)	—	—	—	—
55	alkyl isocyanides	isomerisation $CH_3NC \rightarrow CH_3CN$		—, 1, 1— (Ref.114)	2 (Refs.115 & 116)	2 (Refs.115 & 116)	—	2 (Refs.115 & 116)
56	mononitroalkanes	elimination of HNO_2 $HCCNO_2 \rightarrow \rangle C{=}C\langle + HNO_2$	4	7, 9, 0 (Ref.117)	—	—	—	—
57	trimethylacetyl choride	$Me_3CC(=O)Cl \rightarrow C_4H_8 + CO + HCl$	4	1, —, — (Ref.118)	—	—	—	—
58	dienyls and diynyls	Cope rearrangement 	4	13, —, — (Refs.6 & 119)	—	—	—	—
59	allyl vinyl ethers	non-aromatic Claisen rearrangement	4	4, —, — (Ref.6)	—	—	—	—
60	allylic esters	rearrangement 	4	8, 6, — (Ref.6)	—	—	—	—
61	1-alkyl-2-vinylcyclo-propanes	rearrangement 	4	5, —, — (Ref.6)	—	—	—	—
62	linear conjugated polyenes	cyclisation	4	4, —, — (Ref.6)	—	—	—	—
63	unsaturated cyclic systems	isomerisation	4	3, —, — (Ref.6)	—	—	—	—
64	esters	decomposition $RCOOCCH \rightarrow RCOOH + \rangle C{=}C\langle$	4	9, 77, 4 (Refs.88, 103 & 120)	—	—	—	—
65	unsaturated esters	rearrangement	4	8, 6, — (Refs.112 & 120)	—	—	—	—
66	acetals	decomposition $RCH(OCOR')_2 \rightarrow RCHO + (R'CO)_2O$	4	12, —, — (Refs.25 & 103)	—	—	—	—
67	*cis*-1,3-dienes	1,5-migration of hydrogen	4	10, 6, — (Refs.6 & 121)	—	—	—	—
68	γ-unsaturated alcohols, β-unsaturated acids, β-ketoacids	elimination of ketone (aldehyde, CO)	4	6, 2, — (Refs.15 & 103)	—	—	—	—

Table 1 contd.

No.	Class of compound	Reaction	Group according to Table 2	Number of compounds for which the following parameters are available				
				lg$A$ (s^{-1})	k (p)	IE*	k (ε)	Calcn. based on RRKM theory
1	2	3	4	5	6	7	8	9
69	alkyl vinyl ethers	decomposition 	4	5, —, — (Refs.103 & 112)	—	—	—	—
70	dicarbonates	decomposition	4	—, 15, — (Refs.103 & 120)	—	—	—	—
71	chloroformates	decomposition 	4	1, 3 — (Ref.103)	—	—	—	—
72	cyclopropane and its derivatives	structural isomerisation	5	1,4,23 (Refs.6,15,112,122-125)	7 (Refs.122,126, 127 & 128)	1 (Ref.126)	2 (Refs.129&130)	3 (Refs.52,72,104,126, 127,131 & 132)
		geometrical isomerisation	5	—,—,4(Refs.6 & 59)	11 (Ref.26)	11 (Ref.26)	—	1 (Ref.126)
73	bicyclic compounds containing the cyclopropane ring	rearrangement with opening of cuclopropane ring	5	—,2,2 (Refs.6,112 & 124)	—	—	—	—
74	oxiran and its derivatives	structural isomerisation	5	—,1,2 (Refs.6,133,134 & 135)	2 (Refs.70 & 134)	1 (Ref.70)	1 (Ref.133)	1 (Ref.70)
75	cyclobutane and its derivatives	decomposition	5	—,—,23(Refs.5 & 112)	3 (Refs.126 136-140)	1 (Ref.126)	—	3 (Refs.52,126 & 136)
		geometrical isomerisation	5	—,—,6 (Refs.6 & 112)	—	—	—	—
76	bicyclic compounds containing the cyclobutane ring	structural isomerisation with opening of cyclobutane ring	5	1,1,3 (Refs.6 & 112)	—	—	—	—
77	oxetan and its derivative	structural isomerisation	5	—,—,2 (Refs.6, 141 & 142)	—	—	—	—
78	cyclobutene and its derivatives	structural isomerisation	5	—,20,2(Refs.6 & 112)	3 (Refs.126, 143-146)	1 (Ref.146)	—	3 (Refs.126,132,146,147)
79	bicyclic compounds containing the cyclobutene ring	isomerisation	5	—, 1,3 (Ref.6)	—	—	—	—
80	1-pyrazolines		5	—,—,10 (Ref.148)	—	1 (Ref.149)	—	—
81	cyclic radicals	decomposition	5	—,—,2 (Ref.6)	—	—	—	—
82	trimers		—	—,—,4 (Refs.15 & 25)	—	—	—	—
83	olefins	*cis-trans*-isomerisation	5	6,7,1, (Refs.15,112 & 150)	1 (Ref.132)	—	—	1 (Refs.52 & 132)
84	diazirines		5	—, 3,1, (Refs.151 & 154)	2 (Refs.151 & 153)	—	—	—
85	cyclic compounds	retrodiene reactions	5	—,5,2, (Refs.6,76,155 & 156)	—	—	—	—
86	*ortho*-substituted acetanilides 	rotation about C-N bond	—	4,4 — (Ref.157)	—	—	—	—
87	amides and thioamides 	rotation about C-N bond	—	1,3,— (Refs.15 & 158)	—	—	—	—
88	FN=NF	*cis-trans*-isomerisation	5	—,1, — (Ref.159)	—	—	—	—
89	alkyl halides	rotation about C-C bond	—	4,9, —(Refs.160 & 161)	—	—	—	—
90	O=N—NMe_2 O=N—$OCMe_3$	rotation about N-N and N-O bonds	—	—,2, —(Ref.15)	—	—	—	—

Note. Column 7 lists data on all types of kinetic isotope effects in both thermally and chemically activated systems. The first, second, and third numerals in column 5 indicate the numbers of reactions with lg A less than 12, in the range 12–14, and greater than 14 respectively.

they all have lg $A > 14$. All earlier theories of unimolecular reactions (the Rice–Ramsperger, Kassel, and Slater theories) yielded a normal value of A,[4,5] which to a considerable degree helped to confirm the validity of this concept.

In 1952 the proportion of reactions with normal values of A were 60% according to Kondrat'ev's data[4] and that of reactions with lg $A > 14$ was 16%. At present about 800 unimolecular reactions are known, for which the parameters of the Arrhenius equation have been determined (Table 1). Of these 47% have lg $A = 12$–14, 33% have lg $A > 14$, and 20% have lg $A < 12$. On the whole, pre-exponential factors lie in the range between 10^9 and 10^{17} s^{-1}. The absolute number of reactions with A exceeding 10^{14} or below 10^{12} s^{-1} is very large. Therefore the concept of the "normal" pre-exponential factor is now of purely conventional significance; it reflects the frequently encountered situation where the structure of the activated compound differs little from that of the initial molecule.

III. CALCULATION OF THE PRE-EXPONENTIAL FACTOR

The high or low experimental values of A can only be accounted for with the aid of statistical theories of unimolecular reactions based on the activated complex (AC) method. The modern RRKM theory[9,162,163] yields the following expression for the rate constant at a high pressure:

$$k_\infty = \alpha \frac{kT}{h} \frac{Q^{\neq}}{Q} e^{-E_a/RT}, \qquad (1)$$

which is the same as the classic Eyring formula and is equivalent to the formulation[1]

$$k_\infty = \alpha \frac{kT}{h} e^{\Delta S_0^{\neq}/R} \cdot e^{-\Delta H_0^{\neq}/RT}, \qquad (2)$$

where α is the statistical factor for the reaction, $Q^{\neq}$ and Q are the partition functions of the activated complex and the initial molecule, E_a is the true activation energy, i.e. the height of the potential barrier at 0°K, and $\Delta S^{\neq} = S_0^{\neq} - S_0$ and $\Delta H_0^{\neq} = \Delta H_0^0 + (H_T - H_0^0)^{\neq} - (H_T - H_0^0)$ are the entropy and enthalpy of formation of one mole of activated complex.

The relation between E_a and the activation energy E at a temperature T is illustrated in Fig. 1 (E_{vibr} and $E_{vibr}^{\neq}$ are the vibration energies of the active internal degrees of freedom of the reactant and the activated complex, $E_{t\text{-}r}$ is the energy of the internal translational and rotational motions in the activated complex, r and t are the numbers of internal rotations, and E_0 and $E_0^{\neq}$ are the zero-point energies of the initial molecule and the activated complex respectively).

If it is assumed that the experimental activation energy U, determined from the Arrhenius equation

$$k_\infty = Ae^{-U/RT}, \qquad (3)$$

is equal to E, then the following relations are valid:

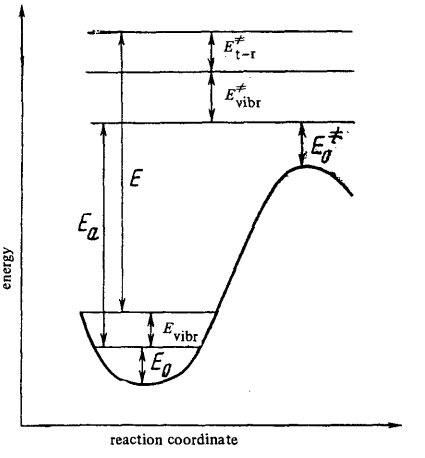
$$U = E_a + E_{t\text{-}r}^{\neq} + E_{vibr}^{\neq} - E_{vibr} = E_a + (r - t + 2)RT/2 + RT^2(d\ln Q^{\neq}/dt - d\ln Q/dT), \qquad (4)$$

$$k_\infty = \alpha \frac{ekT}{h} e^{\Delta S^{\neq}/R} e^{-U/RT}, \qquad (5)$$

$$\ln A = 1 + \ln\alpha + \ln\frac{kT}{h} + \frac{\Delta S^{\neq}}{R}, \qquad (6)$$

$$\ln A = \ln\frac{\alpha ekT}{h} + \ln\frac{Q^{\neq}}{Q} + T\left(\frac{d\ln Q^{\neq}}{dt} - \frac{d\ln Q}{dt}\right). \qquad (7)$$

When account is taken of the changes in the moments of inertia of the overall rotation owing to the greater size of the activated complex, then the term $\frac{1}{2}\ln(I_A^{\neq}I_B^{\neq}I_C^{\neq}/I_AI_BI_C)$ must be added to the right-hand side of Eqn. (7). All the difficulties of the theoretical calculation of A from Eqn. (7) reduce to the necessity of determining the vibration frequencies and the moments of inertia of the overall and internal rotations in the activated complex. Since the same partition function can be obtained with the aid of a wide variety of frequency sets, there is always a considerable uncertainty in the choice of the structure of the activated complex.



Schematic representation of the energy levels in a unimolecular reaction.

The RRKM theory provides the greatest scope for overcoming this uncertainty. On the basis of a single model of the activated complex, it is possible to calculate within the framework of this theory a wide variety of characteristics of unimolecular reactions, which are susceptible to experimental determination. They include the following[5,9].

1. The pressure dependence of the rate constant $k(p)$.
2. The primary and secondary isotope effects in thermally activated systems: $(k_H/k_D)_{prim}$ and $(k_H/k_D)_{second}$.
3. The reverse isotope effect in the region where k varies with p: $(k_H/k_D)_{rev}$.
4. The dependence of the rate of reaction on the excess energy above the threshold value: $k(\epsilon)$.
5. The isotope effect in chemically activated systems: $k(\epsilon)_H/k(\epsilon)_D$.

Unfortunately not all these characteristics are sufficiently sensitive to changes in the vibration frequency in the activated complex. Measurements of the dependence of k on p and of the isotope effects in thermally activated systems are the most useful[9,146,164]. It was shown recently[126,146] that in reactions with a reverse isotope effect the position of the point of intersection of the $k(p)$ curves for isotopic molecules depends greatly on the structure of the

activated complex and thus may be used successfully to test activated complex models.

Reactions involving the decomposition of the molecule into two radicals have yet another extremely important characteristic which makes it possible to infer the structure of the activated complex: the rate constant for the recombination of radicals (see p. 718). Similarly the rate constant for the addition of an atom or a radical to an olefin helps us to understand the structure of the activated complex in the reverse reaction involving the decomposition of the free radical into an olefin and an atom (or a radical).

Calculations for activated complex models based on the RRKM theory using, in addition to the pre-exponential factor, at least one other experimental characteristic have been made for approximately 60 reactions (Table 1). However, in the majority of cases this involves the calculation of the rate of decomposition of chemically activated species, i.e. a characteristic which is relatively insensitive to the activated complex parameters [9]. There are comparatively few calculations concerning the $k(p)$ relation and the isotope effect.

The most complete attempts to determine the structure of the activated complex by adjusting the calculated $k(p)$ curves to coincide with experimental plots have been made for ethane [8,9], hexafluoroethane [165], ethyl chloride [52,95–97,100,101], methyl isocyanide [115,166], ethyl isocyanide [116], cyclopropane [52,126,131,132], 1,1-dichlorocyclopropane [167], cyclobutane [52,126], cyclobutene [126,132,146,147], methylcyclobutene [136], azomethane [35,36], and alkyl [9,28] and certain other radicals [71]. In many cases [100,136,167] it was established that the detailed structure of the activated complex is very difficult to determine, since different models yield similar results. Probably this difficulty will increase with increase of the complexity of the molecular structure and of the activation energy [136,167].

Models using two characteristics, $k(p)$ and the reverse isotope effect at low pressures, have been optimised for the following reactions: decomposition and isomerisation of cyclopropane [126,165] and cyclobutane [126,146], isomerisation of methyl isocyanide [112] and ethyl isocyanide [116], and decomposition of ethyl chloride [100]. One may assume that the interpretation of the structure of the activated complex for these reactions and also for the decomposition of ethane, hexafluoroethane, azomethane, and alkyl radicals has been made fairly reliably. Examples of activated complex models will be quoted below.

One should note that the accuracy of the geometrical structure and of the vibration frequencies of the activated complex achieved in these calculations greatly exceeds the accuracy required for the calculation of the pre-exponential factor. Therefore, from the standpoint of the estimation of A, the importance of calculations based on the RRKM theory consists primarily in a convincing demonstration of the validity of the transition state method for reactions of polyatomic molecules at high pressures and the fact that, for all fundamental types of unimolecular reactions (which will be dealt with below), a detailed analysis has been made of activated complex models in individual examples.

Recently successful attempts have been made to develop semiempirical methods for the calculation of A. [103,168–170] In the main they refer to reactions proceeding via a cyclic transition state. The methods are based on approximate hypotheses concerning the structure of the activated complex and employ experimental values of $\Delta S^{\neq}$ [from Eqn. (5)] in order to find the contributions of the individual structural elements of the activated complex to the total entropy of activation. Either the values of the contributions or the methods of their determination are then standardised.

Mulyava and Shevchuk [168] proposed a method based on the additivity of bond entropies in molecules and activated complexes for the calculation of $\Delta S^{\neq}$. Using the bond classification of the kind usual in additive schemes [171,172] and the concept of the activated bond in the activated complex [173], they calculated the corresponding bond entropies and also corrections for symmetry, cyclisation, conjugation of double bonds, and the presence of cumulative double bonds. A fairly high accuracy in the calculation of $\Delta S^{\neq}$ was demonstrated on a number of examples, but for its large-scale application the method probably requires a more detailed formulation. A similar procedure for the estimation of $\Delta S^{\neq}$ but with a less detailed subdivision into components was proposed by Szabó and Berces [174].

The method of calculation of A for cyclic activated complexes proposed by O'Neal and Benson [103] is less formal. On the basis of a physically clear albeit approximate activated complex model, these workers proposed simple rules for the calculation of individual structural contributions to activation entropy from molecular characteristics. The method is applicable to calculations for more than one hundred reactions and yields an excellent agreement with experiment. Within the framework of this method, it is easy to predict the effect of substituents on $\Delta S^{\neq}$ for the reaction (the method is described in greater detail on p. 720).

The success of the approximate methods of calculation of $\Delta S^{\neq}$ for cyclic activated complexes can be accounted for to some extent by the comparatively low sensitivity of this quantity to changes in the activated complex parameters. In order to predict A to within a factor of three, it is sufficient to take into account the most fundamental changes in the types of motion on formation of the activated complex, i.e. those associated with low-frequency vibrations and internal rotation. Probably the same accuracy can be achieved also in the estimation of A for bond dissociation reactions [170,175].

IV. CLASSIFICATION OF REACTIONS

In terms of the pre-exponential factor and the typical structure of the activated complex, reactions can be divided into the five main groups indicated in Table 2.

Table 2. Classification of reactions.

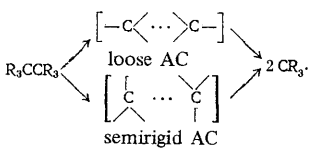
No.	Group of reactions	Reactions investigated	Reactions with lg$A$ in the range			Number of series with different numbers of reactions				
			<12	12–14	>14	1–5	6–10	11–15	16–20	20
1	decomposition into two radicals	171	7	40	124	17	4	2	—	2
2	decomposition into an atom and a radical	52	—	43	9	7	3	1	—	—
3	elimination or isomerisation via a four-membered ring	130	24	93	13	17	2	—	1	1
4	ditto via a five- or six-membered ring	227	98	125	4	8	1	5	2	1
5	reactions via a biradical transition state (ring opening, *cis-trans*-isomerisation)	146	8	50	88	7	5	1	—	3

The assignment of reactions to particular groups is specified in column 4 of Table 1. The classification does not embrace about 50 reactions. The characteristic features of each group of reactions will be examined in subsequent sections.

Table 2 also shows the distribution of reactions with respect to homologous reaction series. Evidently in gas-phase reactions there are comparatively few long reaction series. Nevertheless, large series in which the effect of structure on A is shown (and for which the most reliable experimental data are as a rule available) are in fact the most valuable for understanding the structure of the activated complex and for developing semiempirical methods for calculating A. Studies undertaken specially to investigate the greatest possible number of reactions with the same mechanism and the same reaction centre probably merit attention.

V. DISSOCIATION OF THE MOLECULE INTO TWO RADICALS OR INTO AN ATOM AND A RADICAL

In the decomposition of a molecule into two radicals via homologous bond dissociation, for example the reaction $R_3C-CR_3 \rightarrow 2CR_3$, two types of activated complex structures are distinguished—the loose and semirigid structures. The following notation can be introduced:



(8)

A characteristic feature of the loose activated complex is a considerable extension of the bond undergoing dissociation and free (or almost free) three-dimensional rotation of the separating fragments. The structure of such a complex is close to that of the reaction products. The reverse radical recombination process occurs in almost every collision in the case of a loose activated complex and the recombination rate constant k_r is of the order of $10^{10.5}$ litre mole^{-1} s^{-1}. The recombining radicals are held at a considerable distance by polarisation forces and are oriented arbitrarily reliative to one another [1,15]. The barriers to recombination via a loose activated complex are very small. A loose activated complex is typical in the dissociation of strong bonds between small radicals. It has been demonstrated rigorously for the decomposition of ethane, hexafluoroethane, and certain other compounds.

If $k_r < 10^{10}$ litre mole^{-1} s^{-1}, then the activated complex can be assigned to the semirigid type. In its formation from the molecule, the R_3C-C rocking vibrations do not pass to free rotation but merely undergo a decrease in their frequency. A complete liberation of the rotations of CR_3 radicals does not occur until the critical point has been passed. The formation of a semirigid activated complex from radicals requires a specific orientation of the latter and the transformation of rotational into vibrational motion. Therefore recombination via a semirigid complex involves a loss of entropy.

Judging from the recombination rate constants (Table 3), in most cases the decomposition of molecules into two radicals proceeds via a semirigid activated complex.

In the formation of an activated complex of any type from the initial molecules in reaction (8), the following changes in internal degrees of freedom are possible.

1. A decrease of the frequency of deformation vibrations associated with the dissociating bond (C–C). Two of these pass into the out-of-plane vibrations of the CR_3 radicals formed in the activated complex. The decrease of frequency in this process can be measured with the aid of the secondary α-deuterium isotope effect [164,176]. Judging from the available data, one can assume without much error that in all cases the frequency changes by a factor of two.

The frequencies of the four rocking vibrations of R_3C-C characterising the rocking of the CR_3 groups relative to one another decrease by a factor of 2–3 in a semirigid complex and by a factor of 6–10 in a loose complex. The latter decrease is almost equivalent to free rotation of the fragments about axes perpendicular to the internal axis of inertia. The decrease of the rocking vibration frequencies makes the principal contribution to the entropy of a loose activated complex.

Table 3. Rate constants for the recombination of radicals [45].

Radicals	$\lg k_r$ (litre mole^{-1} s^{-1})	Bond strength, kcal mole^{-1}
R + R R + OR	10—11	80—90
R + NO R + NO_2	9—10	50—60
RO + NO RO + NO_2 RO + OH RO + OR	7—9	35—40

2. The freeing of internal rotation relative to the dissociating bond when the rotation was hindered in the ground state. The increase of activation entropy owing to the freeing of the hindered internal rotation depends little on the partition function for free rotation and factors such as the size of the rotating groups or the symmetry number do not play a significant role. The barrier to internal rotation has the main effect. The maximum contribution to $\Delta S^{\neq}$, which may occur when the height of the barrier is in excess of 10 kcal mole^{-1}, is about 3 Gibbs mole^{-1}.

3. The change in the frequency of torsional vibrations relative to the R–C bonds, i.e. the change in the rotational motion of the groups R adjoining the reaction centre. The decrease of the torsional vibration frequency, which may accompany a change in the geometry of the R_3C fragment and a decrease of the repulsion between the groups R and which can be very large in principle, occurs comparatively rarely, since usually adjacent groups inhibit fairly strongly their mutual rotation both in tetrahedral and in planar CR_3 structures.

On the other hand an increase of the frequency of the torsional vibrations of an adjacent group (and hence a decrease of A) are frequently observed in the decomposition of free radicals or olefins, when the barrier to internal rotation relative to the terminal bond being formed increases owing to the conjugation of the free valence produced. Usually one bond is involved in such conjugation and therefore the effect is small.

When account is taken of all three factors enumerated above, it is usually possible to explain satisfactorily the experimental data.

The decomposition of the molecule into an atom and a radical, $R_3CX \rightarrow R_3C\cdot + \cdot X$, is analogous to the decomposition into two radicals. The difference is that in the

elimination of an atom the number of deformation vibrations which are altered in the activated complex is a factor of two less than in the elimination of a radical and moreover the effect associated with rotation relative to the bond undergoing dissociation is missing. For the majority of reactions investigated, the activated complex has a semirigid structure and the entropy change $\Delta S^{\neq}$ is small. A loose activated complex has been postulated only for the decomposition of methane [9]. However, in this case too A exceeds 10^{14} s^{-1} only slightly owing to the small total number of parameters which are altered.

Table 4. Dissociation of the C–C bond.

Compound	Activated complex	$\lg A$ (s^{-1})
$H_3C—CH_3$	loose	16.3—17
$F_3C—CF_3$	ditto	17.6
$Me_3C—CMe_3$	semirigid	16.3
$CH_3—CH_2CH=CH_2$	ditto	15.8
$CH_3—CH_2Ph$	»	14.5
$CH_3—CH_2CHCH_3$	»	13.5—15

Example 4. Dissociation of the C–C bond. In C–C bond dissociation reactions, A varies from $10^{13.5}$ to 10^{17} s^{-1}. Typical cases are presented in Table 4. [6]

The ethane and hexafluoroethane decomposition reactions provide a classic example of a loose activated complex and have the highest values of A. In the case of hexamethylethane the complex is semirigid, but A is also very high. Possibly in this case the rotation of adjacent groups, i.e. the decrease of the frequencies of the torsional vibrations of the CH_3 groups in the transition state, has an effect. Much lower values of A are observed in the decomposition of unsaturated and aliphatic-aromatic compounds and also of free radicals, owing to conjugation and the increase of the barriers to internal rotation in the radical formed (Table 5 presents a model which explains quantitatively the observed pre-exponential factors).

Example 2. Azo-compounds. The high values of A (10^{17} s^{-1}) observed in the decomposition of azo-compounds can be explained by the simultaneous dissociation of two C–N bonds and by a loose structure of the activated complex. Table 6 presents a model of such a transition state for the decomposition of azomethane [35] ($\lg A = 17.3$). A free activated complex probably occurs also in the decomposition of $C_2H_5N_2C_2H_5$.

However, for large groups R in R–N=N–R, free activated complexes are unlikely and therefore the corresponding values of A should not exceed 10^{15} s^{-1}. The values of A of the order of 10^{17} s^{-1} quoted in the literature for large molecules of azo-compounds are probably erroneous. Recent data confirm this [34].

Example 3. Peroxides, hydroperoxides, nitrites, and nitrates (Table 7). A general characteristic of all these compounds is a comparatively rigid structure of the activated complex (recombination rate constant 10^7–10^9 litre $mole^{-1}$ s^{-1}) and the fact that the dissociation of O–O or O–N bonds results not only in a freeing of rotation about these bonds but also in a decrease of the barrier to the internal rotation of the group R, i.e. the effect of adjacent groups is bound to be shown to some extent in this case. It can be particularly appreciable for peroxides. Unfortunately accurate calculations have not been made for these compounds. The attempts to explain the high values of A in the decomposition of peroxides without taking into account the rotation of R were unsuccessful [47].

Table 5. Models of the transition states for the dissociation of the C–C bond [8, 28, 52] (vibration frequency, cm^{-1}).

Vibration	$C_2H_6 \rightarrow \left[-\overset{\cdot}{C}\cdots\overset{\cdot}{C}-\right]$		$H_3C—CH_2CH=CH_2 \rightarrow \left[{}^{1}H_3C\cdots{}^{2}CH_2\cdots{}^{3}CH\cdots{}^{4}CH_2\right]$		$H_3C—CH_2CHCH_3 \rightarrow \left[{}^{1}H_3C\cdots{}^{2}CH_2\cdots{}^{3}CH—{}^{4}CH_3\right]$	
	molecule	AC	molecule	AC	molecule	AC
$^{1}C—{}^{2}C$ stretch, CH_3 def.	993 1375 1375	0 840 840	1055	0	1055	0
$^{1}CH_3—{}^{2}C$ rock.	820	144	765	190	1442	724
$^{1}C—{}^{2}CH_2$ rock.	820	144	1165	290	1152	576
(either $^{1}C—{}^{2}CH_2$ rock. or	1155	144	960	240	972	486
$^{1}C—{}^{2}C—{}^{3}C$ skelet.)	1155	144	435	375	435	215
$^{1}C—{}^{2}C$ tors.	275	142	225	56	194	97
$^{2}C—{}^{3}C$ tors.	—	—	102	250	102	250
$^{2}C—{}^{3}C$ stretch.	—	—	845	1200	1008	1350

Example 4. Aliphatic nitro-compounds. In the study of the pyrolysis of aliphatic nitro- and α-halogenonitro-compounds, data were obtained for bond dissociation in the longest reaction series in the group of reactions involving decomposition into two radicals [37]. Here all the theoretically predicted contributions to the increase of $\Delta S^{\neq}$ and in particular the effect of the free rotation of the alkyl groups in the radical formed have been detected and measured experimentally (Table 8).

Table 6. Decomposition of azomethane

$$CH_3—N=N—CH_3 \rightarrow \left[-C\cdots N=N\cdots C-\right] \rightarrow N_2 + 2CH_3.$$

Vibration	Molecule	Activated complex
C–N stretch.	922	0
	1 100	0
N=N stretch.	1576	2 000
CH_3 def.	1370 (2)	580 (2)
CH_3 rock.	1013 (4)	free rock.
skelet. def.	593	550 (2)
	350	
	300	
$I_A \cdot I_B \cdot I_C$	$2.85 \cdot 10^{-115}$	$4.33 \cdot 10^{-115}$

In all cases the activated complexes have a semirigid structure (the $CH_3 + NO_2$ recombination rate constant is $10^{9.5}$ litre $mole^{-1}$ s^{-1}). In nitromethane the barrier to internal rotation about the C–N bond is very low and the only factor which alters $\Delta S^{\neq}$ is the decrease of the deformation vibration frequencies of CH_3–N and C–NO_2. In all

Table 7.

Compound	Activated complex	lg$A$ (s^{-1})
Peroxides	R—O···O—R	15.4—16.1
Hydroperoxides	R—O···O—H	13.4—13.7
Nitrites	R—O···NO	14.1—14.4
Nitrates	R—O···NO_2	14.4—14.7

Table 8. Decomposition of aliphatic nitro-compounds.

No.	Compound	No. of substances investigated	Contribution by different factors				$\Delta S^{\neq}$, gibbs moles^{-1}
			rocking vibration	$^{*}NO_2$ rot.	NO_2 rot	R rot.	
1	$CH_3—^{*}NO_3$	1	+	—	—	—	3.06
2	$X_3C^{*}NO_2$, $X_2C(NO)_2^{*}NO_2$, $XC(NO_2)_2^{*}NO_2$ (X = Cl, Br, I)	9	+	+	—	—	6.2—8.4
3	$X_2C(NO_2)^{*}NO_2$, $XC(NO_2)_2^{*}NO_2$, $X_2(NO_2)C—^{*}NO_2$ (X = H, F, NO_2)	5	+	+	+	—	9—10.4
4	$RCXNO_2—^{*}NO_2$, (X = H, F, NO_2)	7	+	+	+	+	13.7—15
5	RCX_2NO_2 (X = Cl, Br)	3	+	+	—	—	6.2—8.0

other compounds the effect associated with the freeing of hindered internal rotation is shown. In the absence of large halogen atoms (Cl, Br, and I) from the α-position (third row in Table 8), $\Delta S^{\neq}$ increases slightly, which may be attributed to a decrease of the torsional vibration frequencies of the NO_2 groups in the radicals formed [$\cdot C(NO_2)_3$, $\cdot CH(NO_2)_2$, $\cdot CHFNO_2$]. A similar but much larger effect is observed for the alkyl group the rotation of which in the transition state becomes completely free (fourth row in Table 8). This conclusion has been confirmed by a number of independent findings[38].

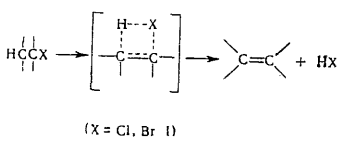
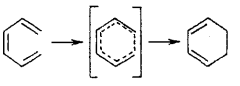
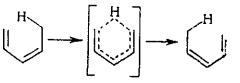
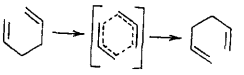
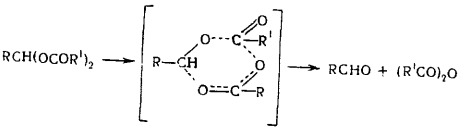
VI. REACTIONS INVOLVING A CYCLIC TRANSITION STATE

In reactions which proceed via a cyclic activated complex, the loss of free or partly hindered internal rotation has the greatest influence on A. There is no fundamental difference between the third and fourth groups of the proposed classification (Table 2). The difference is merely quantitative. In a four-membered transition state, only one or two internal rotations can be lost and in a six-membered state the loss of 2–4 rotations is possible. Accordingly, in the fourth group of reactions (Table 2), low values of A are encountered much more frequently than in the third group. Certain cases where it is possible to follow clearly the change in A owing to the increase of the number of restricted internal rotations are presented in Table 9.

In a cyclic transition state the decrease of entropy due to the disappearance of internal rotations is partly compensated by the appearance of low-frequency out-of-plane ring vibrations. It is not possible to determine by any simple method the frequency of these vibrations taking into account all the ring atoms. Therefore O'Neal and Benson[103], who developed a method for the calculation of A in four- and six-centre unimolecular reactions, proposed for the activated complex a model with a so called loose cyclic structure in the formation of which internal rotations are transformed into semifree partial torsional bond vibrations, It is assumed further that the order of the bonds being loosened and formed changes by 1/2 with a corresponding change in the deformation, stretching, and torsional vibration frequencies. This hypothesis standardises the method of calculation of $\Delta S^{\neq}$. To simplify the calculation, the activation entropy is divided into four parts:

1. $\Delta S^{\neq}_{vibr}$—the entropy change owing to the change in the deformation and stretching vibration frequencies. For each principal cyclic framework, $\Delta S^{\neq}_{rot}$ is constant.

Table 9. Four- and six-membered rings.

Reaction	No. of rotations lost	lg$A$ (s^{-1})
 (X = Cl, Br I)	1	12—13
	2	11—11.8
	2	11—12
	3	10—11.5
	4	9—10.5

2. $\Delta S^{\neq}_{rot-vibr}$—the entropy arising owing to the restriction of the free internal rotations (which are converted into torsional vibrations about bonds with an order of 3/2).

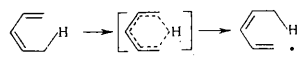
3. $\Delta S^{\neq}_{sym}$—the overall symmetry correction: $\Delta S^{\neq}_{sym} = R \ln \sigma$, where σ is the statistical factor of the reaction.

4. $\Delta S^{\neq}_{cor}$—a correction term which must be introduced into $\Delta S^{\neq}_{r-t}$ in order to take into account the barriers to internal rotation in the initial molecule. The effect of substituents on A is in fact taken into account in terms of $\Delta S^{\neq}_{cor}$.

Despite the considerable simplifying assumptions made in the calculation of activation entropy, in most cases the calculated A differ by not more than a factor of two from the average experimental values[103]. Within the framework of a single reaction series, where the main variable parameter is $\Delta S^{\neq}_{cor}$, the accuracy of the prediction of A may be very high.

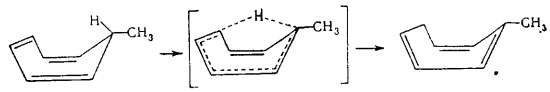
In many cases a purely qualitative examination of the direction of change in the barrier to rotation makes it possible to explain fine effects of the structure and substituents on A. The examples quoted, the experimental data for which were taken from Refs. 6 and 103, illustrate this.

Example 5. 1,5-Migration of hydrogen. Ten cases of hydrogen migration [reaction (9)] have been investigated[9]. Two rotations are lost in the activated complex and $\lg A = 11-11.8$:

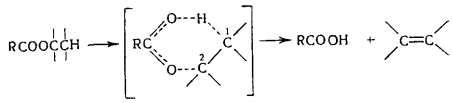


(9)

However, for 7-methylcyclohepta-1,3,5-triene, where there is no internal rotation, $\lg A$ has the normal value of 12.6:



Example 6. Esters. The value of A. In the transition state for the reaction

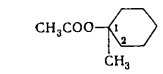
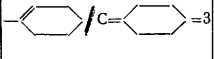
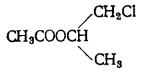


the rotations about the $O-\overset{2}{C}$ and $\overset{1}{C}-\overset{2}{C}$ bonds disappear, which explains the decrease of the pre-exponential factor to $10^{11}-10^{11.8}$ s^{-1}. The substituents in the 1- and 2-positions increase the barrier to internal rotation and smooth out the differences between the initial state and the activated complex. Substituents in the 2-position may be expected to have a greater effect, since they influence also the $\overset{1}{C}-\overset{2}{C}$ bond and what is particularly important, the $O-\overset{2}{C}$ bond, which has a very low barrier to internal rotation (Table 10).

Table 10. Effect of substituents on A for the decomposition reactions of esters.

Substituent	lg A
1-Phenyl	12.0
2-Phenyl	12.4
1,2-Diphenyl	12.7
1-Alkyl (linear)	12.0
1-Alkyl (branched)	12.6
1,1-Dialkyl	12—13

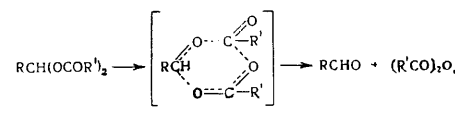
Table 11.

Reactant	Observed ratio	Statistical ratio
	 =3	0.67
	$\frac{CH_3CH=CHCl}{CH_2=CHCH_2Cl} = 1.1$	0.67

Example 7. Esters. Mode of Cleavage. When the elimination reaction can occur in two ways, the pathway for which the transition state includes bonds with highest barriers to internal rotation is preferred. On the basis of this simple postulate, one can explain all cases where the composition of the products differs from their relative proportions based on a purely statistical distribution (Table 11).

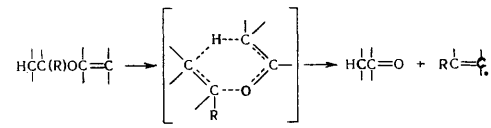
In the first example quoted in Table 11, the transition state involves preferentially the $\overset{1}{C}-\overset{2}{C}$ bond of the cyclohexane ring instead of the $C-CH_3$ bond and the second includes the $C-CH_2Cl$ bond instead of $C-CH_3$.

Example 8. Acetals.



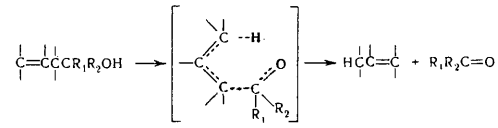
R	lg A
H	9.23
alkyl	10.3
CCl_3	11.1

Example 9. Alkyl vinyl ethers.



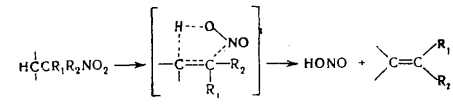
R	lg A
H	11.60
CH_3	12.58

Example 10. β-Hydroxyolefins.



R_1	R_2	lg A
H	H	11.65
H	CH_3	11.93
CH_3	CH_3	12.40

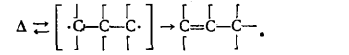
Example 11. Mononitroalkanes [117].



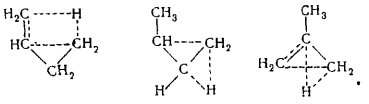
R_1	R_2	A/σ
H	H	11.5—11.8
H	alkyl	11.9—12.2
alkyl	alkyl	12.5—12.8

VII. REACTIONS INVOLVING A BIRADICAL TRANSITION STATE

The first elementary step in the geometrical isomerisation of olefins and cyclic hydrocarbons and also in the decomposition and structural isomerisation of the latter consists in the dissociation of a C-C bond and proceeds via an activated complex which has the properties of a biradical [112,169,170]. In many cases an excited biradical is probably an intermediate, which can lead to the formation of products and to the reverse reaction



The reversibility of the first stage hinders the interpretation of the kinetic data [126]. For certain structural isomerisations, it is postulated that the dissociation of a C–C bond and hydrogen migration can occur in a single elementary step via a transition state which differs from the biradical state [132]. From this standpoint, the following activated complex structures are possible for the structural isomerisation of methylcyclobutane:



Product but-1-ene but-2-ene isobutene

However, it is assumed that the cyclisation, associated with hydrogen transfer, involves a very loose structure and does not prevent rotation about the C–C bond.

In most cases the pre-exponential factors for these reactions are enhanced (up to $10^{15.5}$ s^{-1}), the main reason for which is the appearance of internal rotations about single bonds in the linear system produced.

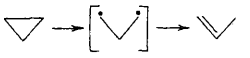
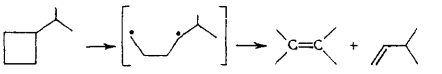
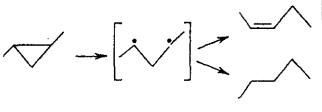
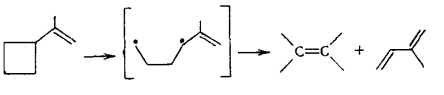
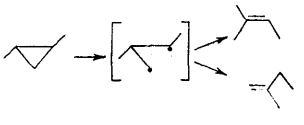
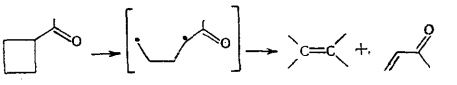
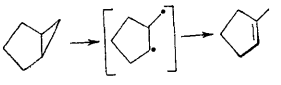
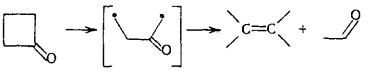
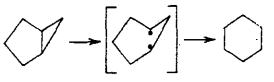
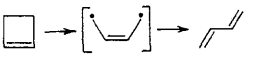
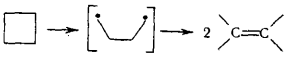
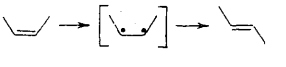
The presence of substituents prevents internal rotation and limits the increase of A. A double bond in the α-position relative to the free valence has a similar effect, since conjugation leads to an increase of the barrier to internal rotation. On the basis of these general considerations, even when the treatment is confined for simplicity to the hypothesis of a purely biradical structure of the activated complex, it is possible to understand the typical values of A observed in these reactions, which are listed in Table 12.

Quantitative calculations based on the RRKM theory have been made for only a few reactions of this type [52,126,132], but these confirm satisfactorily the decisive role of internal rotations. Pre-exponential factors have been evaluated by semiempirical calculations of activation entropies for reactions involving a biradical state [169,170,175]. A recent handbook [177] describes methods for the semiempirical calculation of A for all types of unimolecular reactions.

In conclusion one may note yet again that, despite the large number of theoretical treatments of unimolecular reactions, the real possibility of estimating pre-exponential factors of decomposition and isomerisation rate constants for polyatomic molecules at high pressures is nowadays based almost entirely on the classical formula (1) of the transition state theory. The more detailed RRKM statistical theory, the general validity of which has been confirmed by the success of its application, yields for k_∞ a formula identical with Eqn. (1). The possibility of taking into account anharmonic interactions in the activated molecule by postulating an activated complex with a somewhat predetermined structure in the RRKM theory) and the explanation on this basis of the high values of the pre-exponential factor constitute a brilliant achievement of the statistical theory. As a result, among problems concerning unimolecular reactions, that of the pre-exponential factor is the most completely resolved. Its solution is based on hypotheses concerning the structure of activated complexes in various elementary processes, which have arisen as a result of long experience gained in the application of the transition state theory to real systems. Despite their qualitative nature, in the vast majority of cases these hypotheses are sufficient to estimate correctly the critical values of A for reactions of the given type and to predict the dependence of A on molecular structure. Recently, in connection with the development of the RRKM theory, the possibility of a quantitative approach to the modelling of the activated complex structure has also appeared.

In the calculation of the pre-exponential factor, one may restrict the treatment to specifying the geometrical structure, the vibration frequencies, and the barriers to internal rotation in the activated complex, which can be frequently done using the corresponding characteristics

Table 12.

No.	Reaction	lg A	No.	Reaction	lg A
1		15.45	7		15.63
2		14.05 14.13	8		14.61
3		13.28 13.21	9		14.50
4		13.89	10		14.50
5		13.29	11		13.26
6		15.62	12		14.10

of the reactants and the reaction products or any of their analogue among stable compounds. When the reaction mechanism is well known, A can be in its turn an important source of information about the structure of the activated complex. This factor has been used successfully to develop empirical and semiempirical methods for the calculation of A, which nowadays play a dominant part in the interpretation and prediction of pre-exponential factors[168,170,177]. The scope of these methods depends entirely on the accumulation of experimental data and their reliability depends on fundamental studies involving the calculation of activated complex structures (for example within the framework of the RRKM theory). Together with considerable achievements in this field, the experimental and particularly theoretical studies which have been made are still inadequate and require further development.

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Formation of Free Radicals from Molecular Complexes

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The Review summarises results from various branches of chemistry having as a common theme the part played by donor-acceptor molecular complexes in the generation of free radicals. Attention is paid mainly to liquid-phase reactions. One section deals with polymerisations involving molecular complexes. A list of 200 references is included.

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I. INTRODUCTION

The theoretical importance of the formation of free radicals by the interaction of valency-saturated molecules was at one time pointed out by Semenov[1], but the experimental information which has been accumulated on this problem is still very limited[2]. Processes in which the appearance of radicals is preceded by preliminary donor–acceptor interaction of the molecules, leading to the formation of various types of complexes, have been better studied.

The importance of molecular complexes in chemistry is immense. During the twenty years that have elapsed since Mulliken worked out the principles of the modern theory of donor–acceptor interaction in complexes great progress has been made in elucidating the structure, geometry, and thermodynamic and spectral characteristics of the complexes. Detailed accounts of these topics are to be found in monographs[3,4]. Nevertheless, relatively few studies have been made of the part played by complexes in chemical reactions.

Reviews on the production of free radicals from complexes cover the literature up to 1963–1964.[5-7] In the present Review attention is paid mainly to various mechanisms by which free radicals are formed and to possible explanations of such processes in energetic terms. Use is made chiefly of results published during 1965–1970. Complexes formed by metal salts are not considered, nor are stable free radicals, aspects which have already been discussed in detail[8-11]. However, we have considered several papers in which free radicals were recorded and the existence of a complex can be inferred from the properties of the reactants.

II. MECHANISMS OF THE FORMATION OF FREE RADICALS FROM MOLECULAR COMPLEXES

1. Involvement of Complexes in Radical Reactions

Three tasks are involved in studying the part played by molecular complexes in the formation of free radicals: the existence of molecular complexes in the system must be proved, then free radicals must be detected or a radical reaction mechanism demonstrated, and finally a connection must be established between complex formation and the appearance of radicals. The last task is usually the most complicated.

Donor–acceptor interaction between reactant molecules changes their electronic structure and reactivity. Complex formation may be expected to increase the reaction velocity when interaction between donor and acceptor lowers the free energy of the transition state more than the energy of the ground state[12]. Such changes obviously occur in many biochemical processes, in particular in enzymic reactions, where the entropy factor plays a large part in the transition state[13]. The existence of molecular complexes can often be shown in the reactions of relatively small organic molecules, but it is not easy to prove that they are involved in forming the product[14]: the complex may be produced in parallel with the main reaction.

Let us examine the simple schemes of consecutive and parallel reactions

$$A + D \overset{K}{\rightleftarrows} \pi \xrightarrow{k_1} P, \qquad (I)$$

$$\pi \overset{K}{\rightleftarrows} A + D \xrightarrow{k_2} P, \qquad (II)$$

where A is an acceptor, D a donor, π the complex, and P the product. A choice between (I) and (II) cannot be based on the usual kinetic measurements[14,15]. Indeed, the low activation energy leads to rapid and reversible formation of a complex in solution at room temperature[14]. Rate constants for the formation and the dissociation of π–π complexes of 1,3,5-trinitrobenzene with deuterated fluorenes have been measured recently by quadrupole relaxation as respectively $(0.61–1.7) \times 10^{10}$ M^{-1} s^{-1} and $(0.53–1.5) \times 10^{10}$ s^{-1}.[16]

If a reaction occurs and a complex is formed in a system, and the latter can be monitored e.g. by means of its optical absorption, the disappearance of the complex in the system according to Eqn. (I) is described, for the normally chosen experimental conditions $[D]_0 \gg [A]_0$, by the equation

$$\ln\frac{[\pi]_0}{[\pi]} = \ln\frac{[A]_0}{[A]} = \frac{k_1 K [D]_0}{K[D]_0 + 1} t. \qquad (1)$$

If the complex coexists with formation of the final product [Eqn. (II)], we have

$$\ln\frac{[\pi]_0}{[\pi]} = \ln\frac{[A]_0}{[A]} = \frac{k_2 [D]_0}{K[D]_0 + 1} t. \qquad (2)$$

In both cases the reaction follows a first-order law, and the mechanisms cannot be distinguished[15].

Direct evidence of the formation of intermediate complexes has been obtained only for certain reactions in the gas phase[17].

With liquid-phase processes the problem of the participation of complexes in the reaction can be solved by a detailed study of the intermediate species. Correlations between various properties of the complexes and the reaction rate constants are also usually regarded as evidence of their involvement in the chemical process. Correlations have been observed between the reactivity of donor and acceptor and the stability of their complexes with substances which do not react with them [18]. The equilibrium constants of complex formation have been found to correspond with the rate constants in the interaction of a given acceptor with a series of donors [11,15]. A correlation exists between reactivity and changes in optical charge-transfer spectra [19].

A kinetic method, in which the reaction is conducted in different solvents, has also been proposed [20] for making a choice between schemes (I) and (II). The reaction of tetrachlorophthalic anhydride with triethylamine, which resembles the Menshutkin reaction and depends on the polarity and the polarisability of the solvent molecules, was investigated. The apparent first-order rate constant, determined experimentally from the decrease in the acceptor concentration, is connected with the equilibrium constant of complex formation and with the concentration of the donor, present in excess, by the relation $k_{exp} = k'[D]_0/(1 + K[D]_0)$. If the complex takes part in the reaction, we have $k' = k_1 K$. The values of k_1 and K can be obtained by reducing the above equation to the form [15,20]

$$1/k_{exp} = 1/k_1 + 1/k_1 K \cdot 1/[D]_0 . \qquad (3)$$

With parallel formation of the complex (scheme II) we have $k' = k_2$. If the rate constant of the Menshutkin reaction k^M is used to characterise the solvent, a definite regularity in the dependence of $\lg k_1$ on $\lg k^M$ should be observed if the complex takes part in the reaction. If, however, the complex is not involved in the reaction, a large scatter of the points should be obtained in the corresponding dependence of $\lg k_2$ on $\lg k^M$. On this basis it was concluded [20] that the charge-transfer complex is an intermediate product, and that the reaction occurs according to scheme (I).

Another approach to elucidating the part played by the complex in the reaction consists in lowering the temperature. This permits the study of intermediate products that are unstable at room temperature [21-23] and also diminishes the rate of all stages in schemes (I) and (II). With sufficient retardation of the most rapid stage of the reaction, an S-shaped rate curve representing accumulation of the reaction product may be observed experimentally if the product is formed from the complex (consecutive reaction). Here it is desirable that none of the elementary rate constants should differ too greatly in absolute magnitude. A negative temperature coefficient is also of interest: if the acceleration of the reaction when the temperature is lowered is associated with formation of an intermediate complex, this agrees with schemes (I)—not with (II). [15]

We have been discussing above the simplest consecutive and parallel reactions (schemes I and II). It is often suggested that two intermediate species, e.g. π- and σ-complexes [6,14], are involved in formation of the products. Thus for the scheme

$$A + D \overset{K}{\rightleftarrows} \pi \xrightarrow{k_3} R \xrightarrow[+D]{k_4} P \qquad (III)$$

(in which R is the second complex or free radical) the time variation in the concentration of the product P is expressed by the equation

$$[P] = \frac{k_3 k_4 [D]_0 [\pi]_0}{k_3 - k_4 [D]_0} \left[\frac{1 - e^{-k_4 [D]_0 t}}{k_4 [D]_0} - \frac{1 - e^{-k_3 t}}{k_3} \right] \qquad (4)$$

provided that $[D]_0 \gg [A]_0$ and with rapid equilibrium formation of π. In this case a sigmoid curve for the product can be observed comparatively easily. Fig. 1 shows theoretical rate curves for the accumulation of P with different ratios of k_3 to $k_4[D]$. [24] Schemes of type (III) should be found especially frequently with radical reactions, since the free radicals formed from the complex react readily with the starting materials to give the reaction products.

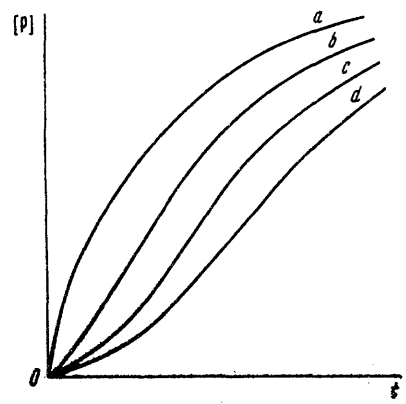


Figure 1. Theoretical rate curves for the accumulation of the reaction product according to: *a*) scheme (I); and according to scheme (III) with different values of $k_4[D]$: *b*) $8k_3$; *c*) $2k_3$; *d*) $1.2k_3$.

Evidence of the formation of the σ-complex from the π-complex—not directly from the original molecules—has been obtained from a spectrophotometric investigation of the reaction between N-substituted aromatic amines and chloranil in solution [22]. A kinetic study has been made of this process [23]. With low concentrations of donor and acceptor very little of the "external" (π) complex is present at room temperature, but it is observed on cooling to −80°C (the process is reversible). Formation of the "internal" (σ) complex in this case requires a further drop in temperature (to −196°C) in order to accumulate the π-complex, followed by a return to −80°C. When the π-complex is present in appreciable concentrations at room temperature, cooling to −80°C is sufficient for the σ-complex to be formed. Thus there exists a critical concentration of the π-complex necessary for further reaction [22]. A similar phenomenon is observed in several radical reactions involving an intermediate complex [25,26].

Formation of the same products by photoexcitation of the complex in the charge-transfer band as in the dark thermal reaction may be used as an argument that the complex is involved in the reaction even in the absence of illumination. This criterion has been applied, for example, to the reaction of acid chlorides with aromatic

amines[27] and to free-radical reactions involving tetranitromethane[25]. The formation of donor–acceptor complexes also favours photochemical reactions. Complex formation usually shifts the absorption maximum to longer wavelengths, and absorption may increase at a given wavelength. Thus complex formation has the effects firstly of increasing the efficiency of the absorption of light and secondly of permitting the use of irradiation with photons of lower energy and the avoidance of several side-reactions.

2. Possible Modes of Breakdown of the Complex into Radicals

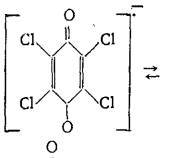
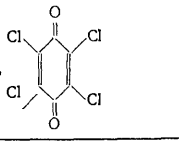
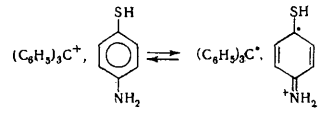
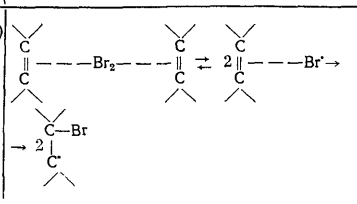
The wave function of a donor–acceptor complex in the ground state is given by a linear combination of wave functions of non-bonding and bonding configurations. There exist complexes with weak interaction, when the term describing a structure without charge transfer has the highest value in the wave function; and complexes with strong interaction, which are represented mainly by a structure with a transferred charge. In our opinion the nature of the ground state of the complex and of the radicals formed after charge transfer indicate that four main cases can be distinguished. These are given in Table 1 together with actual examples illustrating the general schemes.

Scheme 1. This shows that, if a complex consists in the ground state of two neutral molecules, an electron transition in the complex will lead to an excited state that is more polar than the ground state. In this case replacement of a less by a more polar solvent will shift the charge-transfer band to longer wavelengths. The effect is usually small, since solvent molecules require a finite time for reorientation around the polar excited state, while the ground state is only slightly solvated. Complete transfer of charge in such cases will yield two oppositely charged radicals.

Scheme 2a. In the ground state the complex consists of charged particles. Most complexes of this type that have been studied are pyridinium halides[6]. The position of the charge-transfer band in such complexes is strongly dependent on the polarity of the solvent. In polar solvents the ionic ground state is more strongly solvated than is the excited state, and this leads to a short-wavelength shift of the charge-transfer band. In this case complete transfer of an electron from donor to acceptor yields two uncharged radicals.

Scheme 2b. Free radicals are produced most easily in the case of complexes having strong interaction, when an electron is transferred spontaneously from the highest occupied orbital of the donor to the lowest vacant orbital of the acceptor. The radical pair thus formed can be regarded in some cases as a new ground state of the complex. When it is excited, charge transfer takes place in the opposite direction, and the excited state corresponds to the original structure[30]. Such cases are usually observed in solid crystalline paramagnetic complexes. Salts of radical-ions have been most thoroughly studied among solid-phase complexes. Such complexes have high electrical conductivity and are usually strongly paramagnetic[34]. Salts of radical-ions can be obtained both by the complete transfer of an electron from donor to acceptor and from "ready made" ions of the substances involved[35]. Such complexes show interesting behaviour in solution. In media of low polarity charge-transfer bands can be observed corresponding to the transfer of an electron from anion to cation. With increase in polarity of the solvent this band moves to shorter wavelengths[36], i.e. in the opposite direction to that for neutral complexes. The position of the charge-transfer band in such complexes corresponds to low energies, and can be observed in the infrared[30,36–40]. Assignment of the charge-transfer band may be made difficult by the absorption due to radical-ions. It should be noted that the ionic ground state of a complex in the solid phase is not necessarily preserved in solution. The electron spin resonance signal also frequently vanishes on passing into solution[41].

Table 1. Mechanisms and examples of the formation of free radicals from molecular complexes.

No.	Starting materials	Complex: gound state	Complex: excited state	Example	Ref.
1	A+D	(A, D)	$(A^{\cdot-}, D^{\cdot+})$	$C_6H_5NH_2$, $(NC)_2C{=}C(CN)_2 \rightleftarrows [C_6H_5\dot{N}H_2]^{\cdot+}$, $[(NC)_2C{=}C(CN)_2]^{\cdot-}$	28
2a	$A^+ + D^{\cdot-}$	$(A^+, D^{\cdot-})$	$(A^{\cdot}, D^{\cdot})$	$C_6H_5\overset{+}{N}CH_3I^{\cdot} \rightleftarrows C_6H_5\dot{N}CH_3$, $I^{\cdot}$	29
2b	A + D	$(A^{\cdot-} D^{\cdot+})$	(A, D)	$[(CH_3)_2NC_6H_4\overset{+}{N}(CH_3)_2]^{\cdot+}$,  $\rightleftarrows (CH_3)_2NC_6H_4N(CH_3)_2$, 	30
3a	A + $D^{\cdot-}$	$(A, D^{\cdot-})$	$(A^{\cdot-}, D^{\cdot})$	$C(NO_2)_4$, $C_6H_5O^{\cdot} \rightleftarrows [C(NO_2)_4]^{\cdot-}$, $C_6H_5O^{\cdot}$	31
3b	$A^+ + D$	(A^+, D)	$(A^{\cdot}, D^{\cdot+})$		32
4	D+X—Y	(D, X—Y)	(D, X˙ Y˙)		33

Spontaneous electron transfer usually occurs with donors of low ionisation potential I_D and acceptors of high electron affinity E_a. The best known donors, e.g. tertiary aromatic amines, have I_D = 6–7 eV. The electron affinity of such acceptors as tetracyanoethylene, tetracyanoquinodimethane, and chloranil is 2.4–2.6 eV according to the most recent results[42,43].

Schemes 3a and 3b. If the complex is formed by neutral and ionic components, one of the radicals will be neutral after electron transfer, and the other charged. Relatively few such examples are known[44].

Scheme 4. Cases are also possible in which one of the components of the complex breaks down into radicals in the course of complex formation, while the other remains unchanged, at least initially. Such a scheme corresponds formally to homolysis of the molecule as a consequence of its bonding into a complex, and will be examined in greater detail in Section III, 2.

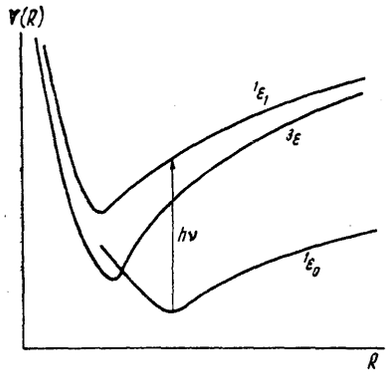


Figure 2. Potential-energy curves of ground and excited states of complex.

Study of the detailed mechanism of the formation of radicals from complexes has begun during recent years. Use is made mainly of the excitation of neutral molecules in the charge-transfer band combined with methods enabling short-lived intermediate species to be investigated. When the complex absorbs light of energy corresponding to the charge-transfer band and insufficient to excite the starting materials, it passes into the lowest excited singlet state (Fig. 2, curve $^1\epsilon_0$). This involves passage of an electron from a donor orbital to the lowest unoccupied orbital of the acceptor, while the total spin multiplicity is maintained. The electronic constitution and the structure of ground and excited states of the complex differ greatly. This leads to a considerable difference between the excited state formed in conformity with the Franck–Condon principle and the equilibrium excited state. As a result, mirror-image symmetry may not be satisfied between the absorption spectrum (i.e. the charge-transfer band) and the fluorescence spectrum[45]. The structure of the excited state of the complex is greatly influenced by the solvent. The excited complex is strongly polar, and the radical-ions formed may be stabilised in a medium of high dielectric constant. The whole process can be represented by the scheme

$$(D,\ A)_0 \xrightarrow{h\nu} (D^+,\ A^-)^*_S \xrightarrow{\text{solvent}} D^+_{\text{solvate}} + A^-_{\text{solvate}}\ .$$

If the complex does not dissociate, it is deactivated. The radiating transition to the ground state is registered as fluorescence of the complex:

$$(D^+,\ A^-)_S{}^* \longrightarrow (D,\ A)_0\ .$$

Intersystem conversion is possible with population of the lowest triplet level of one of the components of the complex, e.g. the donor:

$$(D^+,\ A^-)^* \longrightarrow (D_T{}^*,\ A).$$

Sometimes the lifetime of D_T is shorter in the complex than in the free molecule. Its values for naphthalene and its trinitrobenzene complex, for example, are respectively 20 and 2 s:[46] i.e. typical quenching occurs. The quantum yields of the phosphorescence of aromatic molecules may be increased by the presence of donor–acceptor interaction. Since acceptor molecules do not usually contain heavy atoms, the increase in the spin–orbital interaction, which increases the probability of a singlet–triplet transition, obviously originates in the bonding of the donor into a complex[46,47]. This involves deformation of the molecular orbitals, mixing of s- and p-orbitals, and increase in the spin–orbital interaction. The relative arrangement of energy levels in the complex that is necessary for fluorescence to occur has been analysed[48].

Conversion from the lowest singlet excited state of the complex can theoretically produce a triplet state of the complex itself (Fig. 2, curve $^3\epsilon$). After this, phosphorescence of the complex becomes possible:

$$(D^+,\ A^-)^*_S \rightarrow (D^+,\ A^-)^*_T \rightarrow (D,\ A)_0.$$

Such a process is still the least studied, and interpretation of the experimental results is not always unambiguous.

Great progress has recently been made in the experimental detection of excited states in donor–acceptor complexes. When complexes of tetracyanobenzene and pyromellitic dianhydride with aromatic compounds were illuminated in the charge-transfer band with laser light of wavelength 3371 Å, the absorption spectrum of the undissociated complex in an excited singlet state could be recorded for a few tens of nanoseconds[49]. Excited states have been studied also by the laser photolysis of complexes of tetracyanobenzene with toluene in acetonitrile. The absorption spectrum of the species obtained by exposure to a ruby laser is closely similar to that of the radical-anion of the acceptor. Kinetic analysis has established that the photoinduced species are formed within 10 ns.[50] Fluorescence of the excited singlet complex in solution is observed comparatively rarely. It has been studied in complexes of acid anhydrides with aromatic compounds[51,52] and of tetracyanobenzene with toluene[53]. A systematic investigation[54] of the spectral characteristics of the complexes of tetrachlorophthalic and pyromellitic anhydrides with hexamethylbenzene involved study of the absorption and fluorescence spectra, together with determination of the quantum efficiency of fluorescence in various solvents at room temperature.

Detection of the triplet state of a complex was first reported in 1967, when complexes of tetracyanobenzene with aromatic compounds were illuminated in frozen solutions: both phosphorescence of the complexes in the triplet state[55] and their triplet electron spin resonance signal[56,57] were claimed to have been observed. However, it has since been shown[58,59] that the observed phosphorescence was due to a triplet excited state of the acceptor (tetracyanobenzene). The role of the triplet state of the complex in photoionisation has been studied also by low-temperature flash photolysis: this provided the first experimental detection of the spontaneous ionisation of the triplet state of the complex of pyromellitic dianhydride with mesitylene[60]. It was also concluded that the triplet state may be populated by direct excitation of the complex in the ground state.

Strong attraction between an excited ion-pair and a donor molecule may lead to association (formation of an exciplex)

$$D \cdots (D^+,\ A^-)^*_S.$$

After intersystem conversion, phosphorescence of the triplet eximer is observed [61]:

$$D - - - (D^{+}, A^{-})_{S}^{\bullet} \rightarrow (D, D_{T}^{\bullet}A) \rightarrow D + .$$

With regard to the possibility of radical formation by thermal excitation of the complex, the lowest excited singlet state is energetically too high and is unattainable thermally. Theoretical examination of the energetics of complexes leads to the conclusion that, in the case of the uncharged ground state of the complex in systems comprising a donor of low ionisation potential and an acceptor having a positive electron affinity, the potential-energy curves of ground and triplet states of the complex may intersect [62,63]. If the point of intersection is sufficiently low energetically, thermal population of the triplet state of the complexes is possible (Fig. 2, passage from curve $^{1}\epsilon_{0}$ to curve $^{3}\epsilon$). In the case of a low-lying triplet state such electron transfer does not involve any considerable consumption of energy. Because of this, the thermal formation of radicals from molecular complexes can occur even when the charge-transfer band lies in the short-wavelength region.

III. RADICAL REACTIONS INVOLVING MOLECULAR COMPLEXES IN SOLUTION

Electron spin resonance can in many cases be conveniently used to demonstrate the radical nature of a reaction in solution. However, difficulties arise in assigning the e.s.r. signal to the complex itself. Formation of a triplet state, equivalent to a biradical, precedes the production of radicals by thermal or photoinduced electron transfer in the complex. After dissociation of the biradical, two e.s.r. spectra of equal intensity—due to donor and acceptor radicals—should both be present. Usually, however, only one radical is recorded in the e.s.r. spectrum after electron transfer in the complex and the formation of radical-ions [64]. This is probably due to dissociation of a radical-ion pair in solution into free radical-ions, one of which is more stable than the other. When e.s.r. spectra having a hyperfine structure are observed, they must evidently be assigned not to the complex but to radical electron-transfer reaction products; with a stable radical-ion pair, however, a wide signal should be observed, and at low temperatures the spectrum of the triplet state is registered [6]. The triplet state of a complex is in certain respects analogous to the radical pairs formed e.g. by solid-phase photolysis or radiolysis. The paramagnetism of such pairs has been studied quite thoroughly [65]. As already mentioned, the e.s.r. spectrum of the triplet state of a complex could be detected only in the solid phase. With regard to transitions having $\Delta m = 1$ and $\Delta m = 2$, exposure e.g. of complexes of tetracyanobenzene with methylated benzene derivatives at 77°K produces an e.s.r. signal in the region $g \simeq 4$. [56,57] An e.s.r. spectrum has been observed also in an analogous system on the irradiation of complexes placed in liquid crystals cooled to a vitreous state in a strong electric field. On excitation in the charge-transfer band, transitions were observed having $\Delta m = 1$ and $\Delta m = 2$. Each spectrum consisted of two groups of lines due to the triplet states of the donor and of the complex. This indicates the migration of energy from $(D, A)_{T}^{*}$ to D_{T}^{*}. The type of spectrum depends on the angle between the constant magnetic and electric fields; the method allows the orientation of complexes in the specimen to be studied [66]. The same paper reports observation of the e.s.r. spectrum of the triplet state of the complex in a tetracyanobenzene–naphthalene single crystal. At the same time both of the above transitions in the e.s.r. spectrum on the photochemical breakdown of the complex into radicals were detected also when the acridine–acridan system was illuminated in the charge-transfer band. Two types of radical pairs are formed in this system [67,68].

The use of electron spin resonance to investigate the radical reactions of complexes in solution is restricted by the low concentration and slow rates of conversion of complexes into radicals. The steady-state concentration of short-lived radical species in such reactions is often below the limit of sensitivity of the e.s.r. method.

1. Radicals with Electron Transfer from Donor to Acceptor in the Complex

In several cases increasing the polarity of the solvent does not produce the usual shift in the absorption band of neutral complexes in solution to lower frequencies, but a slight displacement in the opposite direction [69]. This effect is due to the influence of the solvent, which plays an extremely important part in reactions involving molecular complexes. Even in such solvents as hexane and carbon tetrachloride the reactant species which form the complex and the complex itself are in a state which is energetically greatly different from the gas phase [43,70]. The corresponding potential-energy curves will be found in Ref. 71, where the effect of the solvent on the thermodynamic characteristics of the complexes of tetracyanoethylene and iodine with several donors is discussed.

Dissociation of a neutral complex into radical-ions is facilitated by the lowering of the free energy of the latter state consequent on interaction with the solvent [72]. Solvation by a polar solvent makes dissociation into radical-ions energetically advantageous. If a complex is ionic in character in the ground state, a polar solvent tends to stabilise such state, and dissociation into radicals now occurs more easily in a non-polar solvent. This process can be represented as a chemical reaction involving the solvent S:

$$(D, A) + S \rightleftarrows D_{S}^{+} + A_{S}^{-} . \qquad (IV)$$

The equilibrium shifts to the right when the charge-transfer energy is less than the total energy of solvation of the two ions. The stability of the radical-ions towards recombination increases with the polarity of the solvent [73]. Thus it is important to know the energies of solvation of the species formed by dissociation in order to estimate the reactivity of complexes.

In solvents of low polarity the degree of charge transfer in most organic complexes, even those formed by strong donors and acceptors, is small. In polar solvents, however, ionic species may be formed. The reversibility of the process (IV) and the dependence of the position of equilibrium on the polarity of the solvent are supported by results reported in Ref. 74. The spectrum of an equimolecular mixture of tetramethyl-*p*-phenylenediamine and chloranil in acetonitrile exhibits bands corresponding to an anion (at 428 and 448 nm) and to a cation (568 and 618 nm) together with a band (843 nm) due to charge transfer in the complex. Addition of the non-polar carbon tetrachloride diminishes the absorption by the ionic species relative to that due to the complex. This change is reversible: addition of excess of acetonitrile again leads to a relatively greater intensity of absorption by the ions. Analogous results are obtained when the corresponding

ions—the perchlorate of the radical-cation of the amine (Wurster's salt) and the sodium salt of the radical-anion of chloranil—are taken as starting materials.

The effect of the solvent on a reaction may provide a definite criterion of a radical mechanism. With systems in which specific solvation is not of fundamental importance a weak solvent effect may indicate a reaction involving transfer of an atom, whereas a strong solvent effect usually indicates a reaction with transfer of an electron [75].

Electron spin resonance combined with ultraviolet spectroscopy will give a great deal of information on solvation effects in complexes. Taking the behaviour of the tetramethylhydrazine–iodine complex as example [76], we can divide the solvents investigated into three groups. In non-polar solvents (n-hexane, cyclohexane, carbon tetrachloride) there is no e.s.r. signal, but the ultraviolet spectrum contains a strong band due to the complex together with absorption by free and complexed iodine, the equilibrium constant being 450 ± 170 M^{-1} at 25°C. In solvents of intermediate polarity (chloroform, dichloromethane, isopropyl and isobutyl alcohols, dimethoxyethane) e.s.r. signals have already appeared with broad lines (1.7–4.4 G) due to the radical-cation of tetramethylhydrazine. In polar solvents (acetonitrile, acetone, methanol, water) fully resolved e.s.r. spectra are obtained with narrow lines (0.35 ± 0.03 G). In aqueous dioxan the e.s.r. spectral lines become narrower with increase in the radical concentration: i.e. the broadening is not due to spin–spin exchange, but results from electron exchange with tetramethylhydrazine not bound in the complex. The width of the e.s.r. spectral lines is constant in all polar solvents. In chloroform the e.s.r. signal slowly disappears, and the addition of polar solvents accelerates the destruction of radicals. No e.s.r. signal due to iodine is observed. When iodine is replaced by tetracyanoethylene the e.s.r. spectra of both radical-cation and radical-anion are observed in acetonitrile. From the results we arrive at the scheme

$$\begin{gathered}(CH_3)_2N{-}N(CH_3)_2 + I_2 \rightleftarrows (CH_3)_2N{-}N(CH_3)_2 \cdot I_2 \rightleftarrows \\ \rightleftarrows [(CH_3)_2N{-}\dot{N}(\overset{+}{C}H_3)_2\bar{I}\cdot]_S \rightarrow \\ \rightarrow [(CH_3)_2N{-}N(CH_3)_2]^+_S + [I_2]^-_S;\ [I_2]^-_S \rightarrow [I]_S + I^-\ .\end{gathered} \qquad (V)$$

In non-polar solvents the complex is undissociated. In solvents of moderate polarity the complex exists as solvated radical-ion pairs. In polar solvents the radicals are in the free form: the pairs are dissociated and the ions are solvated independently. The instability of the radical-anion of iodine makes the overall process irreversible.

Electron spin resonance spectra have been observed also in complex formation between iodine and tetraarylhydrazines in solution and in the solid state, each molecule of the complex being associated in the latter case with one unpaired electron [77]. Thus the e.s.r. method enables intermediate species to be studied in electron-transfer reactions, and free radical-ions to be distinguished from those combined in pairs.

Photochemical and kinetic studies provide valuable information on the mechanism of one-electron transfer in a complex with the formation of free radicals. When, for example, the tetracyanoethylene–oxolan complex was illuminated in its absorption band, the steady-state concentration of tetracyanoethylene radical-anions, with a characteristic nine-line spectrum, varied as the square root of the light intensity. The increase in the signal in the light was proportional to the square of the time, and the decay of the signal after the light had been switched off conformed to a second-order equation [78]. On the basis of the kinetic measurements it was suggested [78] that on the absorption of light the complex π is excited to a singlet state: $\pi \xrightarrow{I} \pi^S$, the rate of this process being proportional to the light intensity I. Transitions to the ground state $\pi^S \xrightarrow{k_2} \pi$ and to the triplet state $\pi^S \xrightarrow{k_3} \pi^T$ are unimolecular. However, the triplet state is converted into the ground state according to a first-order law: $\pi^T \xrightarrow{k_4} \pi$. If the singlet π^S had dissociated directly into radical-ions

$$\pi^S \longrightarrow D^+ + A^-,$$

solution of the corresponding kinetic equations would have led to a time dependence of the radical concentration involving a hyperbolic tangent. Such a relation was not observed experimentally. It was therefore concluded that the reaction proceeds through a triplet state:

$$\pi^T \xrightarrow{k_5} D^+ + A^-.$$

The most rapid among the various reactions of the radical-ions is recombination

$$D^+ + A^- \xrightarrow{k_6} \pi.$$

Solution of the kinetic equations with $[\pi^S]$ constant leads to direct proportionality between the observed steady-state concentration of radical-anions and the square root of the light intensity.

Photoinduced e.s.r. signals are detected in many complexes of acceptor molecules with donor solvents [79,80]. A more detailed study has been made of the chloranil–dioxan complex [79], on whose illumination the concentration of radicals reached its maximum value (10^{17} spins ml^{-1}) in 1–1.5 min, after which it decreased. This work is interesting also in the use of a rapid-response e.s.r. spectrometer (time constant ~0.03 s), in combination with a cumulative store to improve the signal noise ratio for the kinetic curves, in studying the kinetics of "rapid" e.s.r. signals (time to reach maximum concentration 0.1 s and time to die out after light switched off 0.05–0.15 s). The "rapid" e.s.r. signals are probably due to the primary products of photoexcitation of the complex. A more unambiguous interpretation is obtained in such cases e.g. by flash photolysis of the complex [29,60] or by investigations at low temperatures, when recombination of the radical-ions is much slower [80].

Electron transfer accompanying photolysis of a complex with formation of free radicals has been studied also in the reaction of amines with halogenated methanes [81] and with acid chlorides [27], oxolan with maleic anhydride [82], and ether with oxygen [83]. Detailed studies have been made of the low-temperature reactions of alcohols with halogens, which give radicals on photolysis of the unstable molecular complexes [84–86].

The spontaneous formation of radicals by thermal electron transfer in the complex is especially interesting. Thus on the dissolution of tetracyanoethylene in strong donors the e.s.r. signal of its radical-anions appears immediately, sometimes corresponding to up to 20% conversion of the original substance. An e.s.r. signal has been recorded on the dissolution of tetracyanoethylene in pyridine and its derivatives [87,88], in aromatic amines [28], dimethyl sulphoxide [73,89], *NN*-dimethylacetamide [73], and acetone [73,90], and also on its interaction with cyclopropylated ethylenes [91]. No e.s.r. signal appears in aprotic solvents [90], nor in the presence of oxygen [92]. The corresponding radical-cation is not usually observed, and the kinetics of the reaction can be followed conveniently

by means of the e.s.r. signal or the characteristic spectrum of the radical-anion of tetracyanoethylene in the ultraviolet and visible regions[28]. The formation of radicals depends on the polarity and the viscosity of the medium, since these factors influence the stabilisation of the resulting radical-ions and their rate of recombination[73,90]. In polar dimethyl sulphoxide, for example, tetracyanoethylene forms a strong 1 : 1 complex having an equilibrium constant of 95.4 ± 1.9 M^{-1} at 25°C and a heat of formation of $\Delta H = -11.3$ kcal $mole^{-1}$.[89] At low donor and acceptor concentrations the intensity of the e.s.r. signal is proportional to their concentration.

The following mechanism has been suggested for the formation of radicals[73]:

$$D + A \underset{k_2}{\overset{k_1}{\rightleftarrows}} \pi \overset{k_3}{\underset{k_3}{\rightleftarrows}} \pi^T \xrightarrow{k_4} D^+ + A^- \xrightarrow{k_5} \pi \ . \qquad \text{(VI)}$$

The complex is in a singlet ground state, but its formation involves partial thermal excitation to a triplet state. The singlet excited state is not formed, since it lies considerably above the ground state (3.34 eV); attempts to record fluorescence of the complex were unsuccessful. The triplet state either breaks down into radicals or returns to the ground state; the latter process involves a change in spin, and therefore occurs at a lower rate. With a large excess of the donor the recombination of radical-ions will also be a slow process. The absence of signals from the triplet state of the complex and from the radical-cation is explained by exchange broadening by collisions between π^T and π and also between $D^{\cdot+}$ and D.

The stability of the complexes formed by tetracyanoethylene varies in the sequence

dimethyl sulphoxide ($\Delta H = -11.3$ kcal $mole^{-1}$) > > *NN*-dimethylacetamide (−9.17) > acetone > > oxolan (−1.14).

In the first three solvents the formation of radical-anions is observed, a strong e.s.r. signal being obtained in dimethyl sulphoxide and dimethylacetamide ($[C_2(CN)_4^{\cdot-}] = 0.001$ M and $[C_2(CN)_4]_0 \simeq 0.0007$ M), in acetone the signal is weak, and in oxolan radicals are not detected. Thus a correlation exists between the stability of the complex, as measured by the change in enthalpy ΔH, and the e.s.r. signal. The high heat of formation of the complex with dimethyl sulphoxide displaces downwards all the levels in Fig. 3 due to the complex relative to the level of the free donor and acceptor molecules.

The triplet state of the complex is assumed to be populated thermally[73,89,90,92], which is confirmed by the proportionality of the e.s.r. signal intensity to $\exp(-\delta/kT)$. Calculation for the dimethyl sulphoxide complex with a Boltzmann distribution between the states (D + A) and $(D, A)^T$ gave $\delta \simeq 0.18$ eV and $J = 0.65$ eV, where $J = \delta + \Delta H$ is the singlet–triplet splitting. The corresponding energy diagrams for various solvents and a theoretical interpretation of the observed phenomena will be found in Refs. 73 and 89. According to the theory the rapid appearance of a dark e.s.r. signal is a general property of stable complexes. The signal intensity is closely connected with the heat of complex formation, which can thus be estimated. With ΔH determined by an independent method, the temperature dependence of the e.s.r. signal enables the activation energy δ to be found and hence J to be calculated. Because of the lack of convenient methods of measurement, the magnitude of this splitting is usually unknown for liquid-phase complexes.

Most complexes exhibit no electron spin resonance or else give only a very weak signal. In terms of the above scheme this is explained by the small heats of complex formation. The ground state of the complex is then close to the (D + A) level, and hence δ/kT is too large for appreciable thermal population of the $(D, A)^T$ level. It has been computed e.g. that the e.s.r. signal for the dimethyl sulphoxide–iodine complex ($\Delta H = -4.4$ kcal $mole^{-1}$) should be around 1% of that due to the dimethyl sulphoxide–tetracyanoethylene complex, and therefore is not observed.

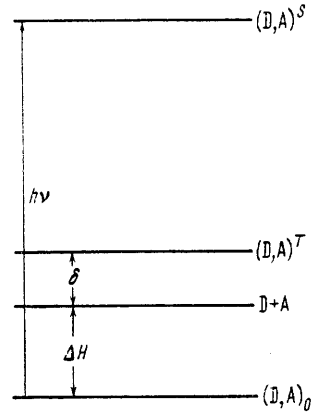
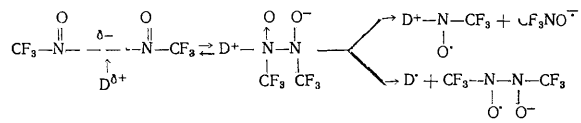


Figure 3. Energy diagram of various states of complex.

Thermal breakdown of a complex into radical-ions with transfer of an electron has been investigated in detail also in the reactions of nitroso-compounds with various electron donors[93–103]. The mechanism



(VII)

where D is a donor molecule, has been suggested e.g. for the dimer of trifluoronitrosomethane.

Electron transfer in a complex with the formation of radicals has been assumed also in the ozonisation of alkenes[104], the reaction of iodine with tertiary amines[105] and of tetranitromethane with tetra-alkyltetrazenes[106,107] and with 1,1-diphenylethylene[108], in the irradiation of the tetranitromethane–*N*-vinylcarbazole complex[26], and in the dissolution of chloroanil and benzoquinone in donor solvents[109]. An analogous mechanism of one-electron transfer in an intermediate complex probably operates in the reactions of peroxy-compounds with phosphites, sulphides, and aromatic amines. The kinetics and the mechanism of such processes have been discussed in a review[110]. The main part in the formation of peroxide complexes is played by hydrogen bonds[111]. Charge-transfer complexes may have an important role in biochemical processes[112]. Formation of free radicals from complexes takes place, for example, in the interaction of dihydroxyacetone with phenazine[113], of several medicinals (including antibiotics) with chloranil and other acceptors[114], and of flavins with phenols[115,116].

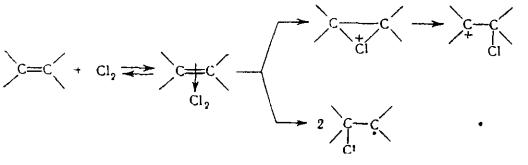
2. Radicals formed by Rupture of a Bond in One of the Components of the Complex

Free radicals are formed in several reactions of valency-saturated molecules at rates sometimes exceeding a hundredfold those calculated theoretically from the dissociation energy of the least stable bond. Such processes are sometimes termed *molecularly induced homolysis*, and their mechanism is not yet entirely clear [117,118]. In many cases such reactions have a radical-chain mechanism. A kind of feedback occurs in these processes: the energy required for dissociation of the molecule is partly or completely returned on the formation of new bonds after homolysis [2,119]. The solvent plays an important part in such reactions [120].

The formation of complexes in molecularly induced homolyses has been proved only in a series of reactions. In some cases their existence can be expected, since one of the reactants (often an alkene) has donor properties, while the other (e.g. a halogen) has acceptor properties. The formation of halogen–alkene complexes has been demonstrated experimentally [121,122].

Molecular complexes are probably involved in the formation of radicals in the liquid-phase chlorination of alkenes [119,123-128]. In the absence of light, oxygen, or a solvent the chlorination is a radical process with straight-chain alkenes and an ionic process with branched-chain alkenes. The radical reaction does not occur with tri- and tetra-alkylated alkenes. Oxygen strongly inhibits the radical reaction, which is then replaced by the slower ionic process. Dilution with a non-polar solvent also promotes the ionic reaction. Illumination increases the relative proportion of the radical reaction. The spontaneous formation of radicals in an alkene in the absence of a solvent and of oxygen is a rapid process unaffected by illumination. The reaction with cyclohexene goes readily even at −78°C. [119] The introduction of cyclohexane into the reacting mixture results in its chlorination, which proves the presence of chlorine atoms.

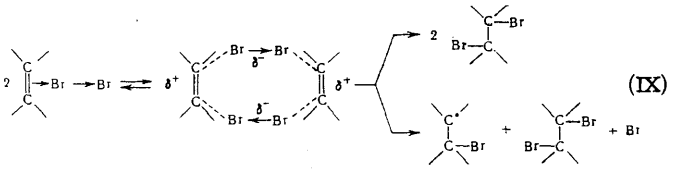
It is supposed that the reaction begins with the formation of an alkene–chlorine complex, which may either rearrange into ionic intermediate products or react with a second alkene molecule to form radicals:



(VIII)

Thus the classic scheme of the polar addition of chlorine to alkenes disregards all the specific features of the reaction. The low rate of initiation of free radicals is already sufficient for the radical-chain reaction to compete successfully with the ionic reaction [127].

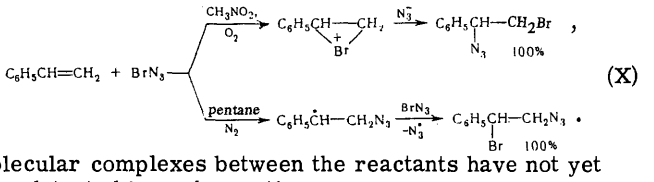
Schemes analogous to (VIII) have been suggested for the radical bromination [33] and nitration [86] of alkenes. A mechanism involving a complex containing two halogen molecules has been assumed [129] from kinetic results on the bromination of alkenes:



(IX)

Calculation shows that in this case the production of radicals is weakly endothermic ($q = -5$ kcal mole^{-1}), and therefore this mechanism has energetic advantages over the direct breakdown of a bromine molecule into atoms, which requires 46 kcal mole^{-1}. According to the above scheme polar and radical mechanisms of the halogenation of alkenes may involve closely similar transition states.

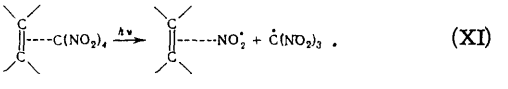
Complexes are probably involved also in the formation of radicals by the reaction of unsaturated compounds with iodine [130,131] alkyl hypohalites [120,132,133], halogen azides [134-137], peroxides [118], compounds containing a cyano-group [138], and ozone [104]. Spontaneous formation of radicals without initiation was observed in all these reactions. The possibility that molecular complexes are involved in directing the radical and ionic reactions is especially interesting. On the addition of bromine azide to alkenes, for example, theoretical yields of products of either the ionic or the radical reaction can be obtained depending on the conditions [135]. In the case of styrene, for example, the process can go according to the equations



(X)

Molecular complexes between the reactants have not yet been detected in such reactions.

The electronic rearrangement accompanying complex formation may tend to weaken a bond in one of the components [139]. In several cases the participation of complexes in the reaction is confirmed by combining photochemical decomposition with subsequent analysis of the resulting radicals by e.s.r. at low temperatures. In the photolysis of the complex of tetranitromethane with an alkene, for example, the energy of the quanta corresponding to the long-wavelength edge of the charge-transfer band is insufficient to rupture a bond in either component. In a mixture of the substances, however, tetranitromethane undergoes homolytic breakdown [25]. The latter is assumed to occur in conformity with the equation



(XI)

The free radicals formed by photolysis of the complex were identified by electron spin resonance at low temperatures. A similar reaction may occur even without illumination, obviously as a result of thermal excitation of the complex [140]. Under appropriate conditions the free radicals generated by the homolytic breakdown of tetranitromethane in the complex may lead to chain processes. The high quantum efficiency of the consumption of alkene and formation of a crystalline product on reaction with 1-phenylcyclohexene with illumination in the charge-transfer band, for example, indicates that the reaction has a chain mechanism [141].

Thus a detailed study of molecular complexes in such systems provides a deeper understanding of certain aspects of the mechanism of these reactions.

IV. RADICAL POLYMERISATION INVOLVING COMPLEXES

Many investigations have shown that a very promising method of polymerisation, besides the use of such

classical initiators as peroxides, diazo-compounds, etc., is the radical breakdown of molecular donor–acceptor complexes. Several facts indicate that complexes are involved in such reactions. Dilution of the reaction mixture with the solvent has been found to influence the composition of the polymer, a previously unknown effect. If the complex is responsible for the formation of a regular copolymer in the system, a diminution in this regularity is to be expected on dilution, which lowers the relative concentration of the complex. In the copolymerisation of divinyl ether with fumaronitrile, for example, dilution not only decreases the rate of polymerisation but also lowers the nitrile content of the copolymer [142].

If polymerisation takes place under the influence of active species formed by slow breakdown of a complex (e.g. according to scheme III), sigmoid kinetic curves should be obtained for the accumulation of the reaction product, as already mentioned. Such curves have been observed in several cases [143,144]. Finally, formation of a polymer having mainly a *cis*-1,4-microstructure by the interaction of butadiene with maleic anhydride confirms the involvement of a complex in the polymerisation [9,145]. The usual radical polymerisation of butadiene yields mainly the *trans*-1,4-microstructure. Thus the complexed diene—not the free compound—evidently takes part in the reaction, since precisely in the complex the strongest interaction with charge transfer should occur with a monomer having a *cis*-structure [145].

Complexes have a dual role in radical polymerisation: they are able firstly to initiate the reaction by breaking down into free radicals, and secondly to take part in chain growth by the bonding of free radicals into the complex. The Review considers mainly the process of initiation. The second aspect is also very interesting from both theoretical and practical points of view. The medium greatly affects the properties of free radicals, and solvation or bonding of the free radical into a complex may in considerable measure determine its reactivity in solution [8,11,146,147].

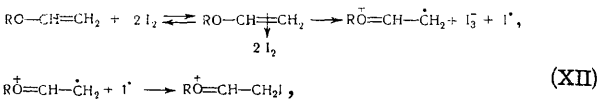
Examination of the literature reveals the following features of polymerisation initiated by molecular complexes. Such a reaction may occur at an extremely high rate, not attained with the usual initiators [148]. In some cases regular copolymers are formed, with a regular alternation of monomer units; independently of the proportions of the reactants, a 1 : 1 copolymer is usually obtained. The reaction mechanism cannot be described in terms of the laws of normal radical polymerisation. Sometimes the complex formed by the starting materials can be regarded as a monomer that is considerably more reactive than the usual monomers. Cases have been described in which neither component monomer of the complex is capable of polymerisation even in the presence of a radical initiator, whereas a mixture of the monomers is easily copolymerised even in the absence of an initiator [149]. On the other hand, the formation of a stable complex may so inactivate the monomer that polymerisation does not occur even in the presence of a radical initiator [150].

All cases of polymerisation initiated by the breakdown of a molecular complex into radicals can be divided into two groups. The complex may be a foreign reagent with respect to the monomers: i.e. its function is identical with that of the usual radical initiators. On the other hand, the initiating complex may include one or more monomer molecules. In the latter case the composition of the polymers can be varied by changing that of the complex, e.g. by the addition of various complexing agents [151,152].

The specific features of polymerisation initiated by a complex are due to the formation by electron transfer of two radical-ions

$$(A,\ D) \rightarrow A^{\cdot-} + D^{\cdot+},$$

which have different destinies. The ions may recombine, when it is supposed that polymerisation is begun by a biradical [148,153]. Recombination of the radicals yields a dipolar zwitterion $^{-}A-D^{+}$, which initiates ionic polymerisation [153]. Recombination of the radical centres may occur as a result of various secondary processes [143,149]. In the ionic polymerisation of vinyl ethers in the presence of iodine, for example, the reactions



(XII)

are possible [149].

Thus ionic and radical mechanism are closely connected, which explains the influence on radical polymerisation exerted by inhibitors of the ionic reaction [154]. When radical-ions are formed, ionic polymerisation is possible; this may be greatly accelerated by light, which facilitates electron transfer in the complex [155–157]. The mechanism of the conversion of radical-ions into carbonium ions has not yet been finally elucidated [158,159]. When one or both radical-ions obtained from the complex react with monomer molecules, the addition of the very first monomer molecule leads to the separation of ionic and radical centres, and here also both ionic and radical polymerisation is theoretically possible [153].

By no means all the above mechanisms are realised in practice. Thus the monomeric radical-cations studied hitherto do not exhibit simultaneous cationic and free-radical activity during polymerisation; no examples have yet been found of the formation from $D^{\cdot+}$ of bications $^{+}D-D^{+}$ to lengthen the chain. Many electron acceptors present in a complex are inhibitors of free-radical reactions, and perhaps suppress the radical activity of $D^{\cdot+}$. [149]

The dissociation of weak complexes into radicals cannot be detected experimentally by electron spin resonance, but the concentration of radicals is nevertheless sufficient for polymerisation to occur [160]. Examination of the kinetics of polymerisation is then a convenient method for studying the rate of breakdown of the initiating complex. In many cases in which the complex served merely to generate radicals, for example, the reaction velocity was proportional to the square root of the concentration of the complex [161–164]. The simplest explanation of this relation is the formation of an equilibrium complex, whose consumption is accompanied by the appearance of free radicals that react with the monomer [161]. More complicated mechanisms have also been suggested [163,165].

The most detailed study has been made of the initiation of polymerisation by complexes of aromatic amines with carboxylic acids and their derivatives. A relation has been established between the energetics of formation of the complexes and the kinetic parameters of the polymerisation initiated by them. The results are presented in Table 2.

The reactions between amines and acid chlorides are rapid. With an initial concentration of 0.1 M, for example, the half-conversion time is of the order of milliseconds [167]. A low-temperature technique is used [168] to study such complexes and their reactions. Bands due to complexes of anhydrides with amines have been detected at –196°C.

When the temperature rises by a few tens of degrees, chemical reaction occurs with disappearance of the complex. The infrared spectra indicate a decrease in the concentration of anhydride and amine groups, together with the formation at low temperatures of an ammonium salt [168].

Table 2. Influence of reaction conditions on the activation energy E_a for the polymerisation of methyl methacrylate initiated by the complexes of dimethylaniline with various acceptors.

Acceptor*	Parameters of complex			E_a, kcal mole^{-1}				Ref.
				no solvent		in acetonitrile		
	$h\nu_{max}$, kcal mole^{-1}	K_{eq} (25°C)	$-\Delta H$, kcal mole^{-1}	dark reaction	photochemical reaction	dark reaction	photochemical reaction	
TCPA	62.3	10.85	3.6	—	—	7.2	—	164
PA	76.2	4	2.0	—	12.0	11.5	11.5	164, 166
IPC	79.5	6.65	1.8	—	—	8.8	—	164
BAn	84.5	3.51	1.2	—	13.2	11.0	11.0	164, 166
BC	84.6	9.5	1.1	13.5	—	7.0	—	162, 164
BAc	—	—	—	13.2	6.4	—	—	161

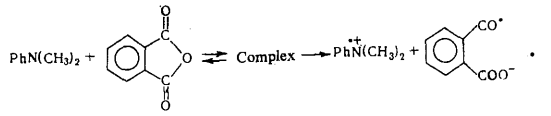
*TCPA = tetrachlorophthalic anhydride
PA = phthalic anhydride
IPC = isophthaloyl chloride
BAn = benzoic anhydride
BC = benzoyl chloride
BAc = benzoic acid

The following schemes have been suggested for the formation of radicals by electron transfer in complexes of aromatic amines [161,169]:

$$PhN(CH_3)_2 + PhCOOH \rightleftarrows \text{Complex} \longrightarrow Ph\overset{\cdot+}{N}(CH_3)_2 + PhCO^{\cdot} + OH^-,$$

$$PhN(CH_3)_2 + PhCOCl \rightleftarrows \text{Complex} \longrightarrow Ph\overset{\cdot+}{N}(CH_3)_2 + PhCO^{\cdot} + Cl^-,$$

$$PhN(CH_3)_2 + (PhCO)_2O \rightleftarrows \text{Complex} \longrightarrow Ph\overset{\cdot+}{N}(CH_3)_2 + PhCO^{\cdot} + PhCOO^-,$$



Breakdown of the complex is facilitated by ionic solvation, the effect being most strongly developed when the chloride ion is formed, and weakest with the radical-anion from phthalic anhydride. With strong complexes in a polar solvent it is sometimes possible to record the e.s.r. spectrum of the radical-cation of the amine [170,171]. However, it has been shown that polymerisation is initiated by the hydrocarbon radicals [172]. The rate of breakdown of the complex is strongly affected by light and the presence of oxygen, as well as the polarity of the medium [160,170,171,173-175].

As well as the complexes of amines with acid derivatives, polymerisation has been initiated by the use of complexes of nitrogen heterocycles with sulphur dioxide and with halogenated methanes [150], complexes of polymers with sulphur dioxide and carbon tetrachloride [150,185], and previously illuminated complexes of maleic anhydride with amides [176-178] and oxolan [179,180].

The mechanism of polymerisation initiated by complexes containing monomers has not yet been finally elucidated. Several authors hold the view that the determining factor is radical–monomer interaction in the transition state: others consider that the formation of copolymers of alternating structure is due to the involvement of molecular donor–acceptor complexes in initiation and chain growth [9]. Only one monomer—the donor—can enter the complex, and the second component is then an acceptor of electrons [149,181]. It is usually supposed that such a mechanism applies e.g. to the polymerisation of *N*-vinylindole and *N*-vinylpyrrole under the influence of chloranil, tetracyanoethylene, and other acceptors [182], and also the polymerisation of *N*-vinylcarbazole in the presence of chloranil and tetranitromethane [143,183]. In some cases initiation has been effected by illuminating the complex in the charge-transfer band [184].

The complex may also consist of two monomers, one with donor properties and the other with acceptor properties. Examples of reactions of this type that have been investigated are the copolymerisation of dioxen with maleic anhydride [185-187], of 1,2-dimethoxyethylene with maleic anhydride [187], of styrene and butyl vinyl ether with maleic anhydride [188], of butyl vinyl ether with acrylonitrile and maleic anhydride [189,190], of methyl methacrylate with the dimer of methyl vinyl ketone [191] and with *N*-vinylpyrrolidone [192], and also of sulphur dioxide with several olefinic compounds—1-methylcyclopropene [144], cyclopentene [193], bicyclo[2,2,1]hept-2-ene [148], styrene, and methyl methacrylate [194].

The possibility of polymerisation with weak complexes, incapable of complete electron transfer with dissociation into radicals, is explained on the assumption of mutual activation of donor and acceptor in the complex [149].

Valuable information on the reactivity of the complex is obtained from a study of ternary copolymerisation. In several cases the reaction in which donor and acceptor monomers enter the polymer chain alternately can be regarded as the binary copolymerisation of the complex formed by these monomers with a molecule of the third monomer [195]. Ternary copolymerisation has been studied on the systems

- styrene–maleic anhydride–sulphur dioxide [151]
- 2-chloroethyl vinyl ether–maleic anhydride–acrylonitrile, dioxen [145,196,197]
- methyl methacrylate–methyl vinyl ketone dimer–styrene, acrylonitrile [191]
- methyl methacrylate–maleic anhydride–*N*-vinylpyrrolidone [198]
- cyclopropene–acrylonitrile–sulphur dioxide [199]
- dioxen–maleic anhydride–2-chloroethyl acrylate [200]
- anethole–maleic anhydride–2-chloroethyl methacrylate, methacrylonitrile, acrylonitrile [195]

in the last three of which a kinetic study was made.

An interesting investigation has recently been made of the relation between the thermodynamic constants of the complexes formed by two monomers in various solvents and the reactivity of these complexes [197]. Increase in the equilibrium constant of the complex as the solvent is changed leads to an increase in the reaction velocity. When different complexes are compared, however, the main factor is not the concentration but their reactivity. For example, 1,4-dioxen and 2-chloroethyl vinyl ether become more reactive by factors of 31 and 11 respectively when they enter a complex with maleic anhydride. The same paper proposes a classification according to which all polymerisation reactions involving complexes are divided into several classes according to the equilibrium constant K_{eq} of the complex. When $K_{eq} \simeq 0.01$, reaction either does not take place at all or occurs only in the presence of an initiator. When K_{eq} increases to 0.1–1, the radical or

ionic reaction may occur spontaneously. A stable complex ($K_{eq} \to \infty$) is unable to initiate polymerisation.

Thus the above results indicate the wide possibilities for varying the rate and the selectivity of polymerisation processes and the structure of the polymers by combining the initial monomers into complexes.

Examination of the literature thus reveals only a small number of investigations, based on kinetic results, of the conversion of molecular complexes into free radicals. The mechanism of the process, especially in the absence of light, is still obscure. Rearrangement of the electronic structure accompanying complex formation may obviously weaken a bond in one of the components. In several cases a correlation has been established between the e.s.r. signal and the enthalpy of formation of the complex. Investigation of the entropy contributions in such processes is extremely important.

The high rate and the reversibility of complex formation often lead to ambiguity in the kinetic results. Processing the experimental data on electronic computers would enable the reliability of the proposed mechanisms to be assessed.

Fresh correlations must be sought between the thermodynamic characteristics of complex formation (K_{eq}, ΔH, ΔS) and the reactivity of the molecular complexes. In our view, a promising line of research would be the kinetic investigation of systems in which several complexing processes are competing (e.g. the interaction of reactant molecules with themselves and the solvent). Knowledge of the energies of solvation of the species formed from the complex would facilitate a quantitative estimate of the reactivity of the complexes. Such data could usefully be obtained by means of nuclear magnetic resonance, a method which in several cases gives reliable information also on the thermodynamic characteristics of molecular complexes. Thus the most effective way of solving the problem discussed in the Review, is to combine various methods of investigation (kinetic, photochemistry, in particular flash, e.s.r., and n.m.r.). When analysing the mechanism of the formation of radicals from valency-saturated molecules, we must take into account the possibility of competition between the appearance of radicals by electron transfer in the complex and directly from the original molecules under the influence of the solvent.

Examination of the role of molecular complexes in the formation of free radicals, especially in the case of polymerisation processes, shows that radical and ionic mechanisms are more closely connected than had been assumed. This connection is understandable if the initial stage is electron transfer in the molecular complex with the formation of radical-ions. Study of the laws of the conversion of molecular complexes into other active intermediate products will permit control of the rate and the selectivity of the most diverse processes.

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Preparation of Vicinal Difunctional Compounds by the Converted Electrophilic Halogenation of Multiple Bonds

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The halogenation of unsaturated compounds in various reactive solvents (water, mineral acids, lower aliphatic alcohols and acids, etc.), involving the addition of halogen and a solvent fragment at the multiple bond, is discussed. The reasons for the varying orientation in the addition of unlike species at the multiple bond, as a function of the structure of the unsaturated compound, the type of electrophilic halogen, and the nucleophile, are considered in terms of the theory of halogenonium ions. The list of references contains 132 items.

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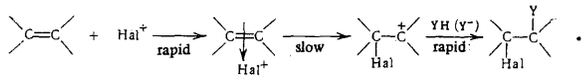
1. INTRODUCTION

Consideration is given to electrophilic additions to unsaturated compounds, in which the electrophilic species is a positively charged halogen, and the nucleophilic species either a different halogen ion or a neutral molecule. These reactions can be represented by the general scheme



The interest of such processes is that they provide convenient methods for obtaining in a single stage saturated compounds with different substituents in vicinal positions, providing a route to further syntheses. Furthermore, such reactions enable us to establish the sequence of attack by reagents at a double bond and the orientation of the addition of the attacking species to unsymmetrical unsaturated compounds, which makes it possible to assess the mechanism of the processes quite objectively.

Among the immense number of studies on electrophilic addition the least attention has been paid to these reactions[1-4]. The reason is that until recently methods for the quantitative determination of structural isomers were lacking, and therefore great difficulties arose in determining the direction of the addition of unlike species at the double bond in an unsymmetrical unsaturated compound. With the appearance of new methods of analysis (gas–liquid chromatography, nuclear magnetic resonance) interest in concerted additions grew considerably. Several products that had previously been regarded as pure compounds were found to be mixtures of isomers[3].

The selectivity of additions is the most important factor determining the subsequent preparative utilisation of the products. In planning a synthesis it is necessary to know the orientation of addition to be expected from an unsaturated compound of specified structure with a particular electrophilic halogen and nucleophile. Summarising available information on reactions of this type has revealed several of their general features, which can serve as a guide in the development of methods of synthesis. The experimental results have been interpreted in terms of the theory of halogenonium ions[3].

2. ADDITION OF ELEMENTS OF HYPOHALOUS ACIDS

These reactions constitute the most thoroughly studied class of concerted halogenations[3,5]. The hypochlorination of ethylene forms the basis of the hitherto industrially important method of obtaining oxiran via 2-chloroethanol[6]:

$$CH_2{=}CH_2 + Cl_2 + H_2O \rightarrow \underset{85\%}{ClCH_2CH_2OH} + \underset{10\%}{ClCH_2CH_2Cl} + \underset{1\%}{ClCH_2CH_2OCH_2CH_2Cl}\ ,$$

$$ClCH_2CH_2OH \xrightarrow{-HCl} CH_2{-}CH_2 \quad (O)$$

Analogous methods give high yields of propylene chlorohydrin[7], glycerol chlorohydrins from allyl chloride[8], and butylene chlorohydrins from a mixture of butenes[9].

Vinyl chloride adds the elements of hypochlorous acid in conformity with Markovnikov's rule to form the unstable intermediate 1,2-dichloroethanol, which is dehydrochlorinated to give a high yield of chloroacetaldehyde[10]:

$$CH_2{=}CHCl \xrightarrow{HOCl} ClCH_2CH(Cl)OH \xrightarrow{-HCl} \underset{96\%}{ClCH_2CHO}\ .$$

Cyclohexene reacts with an equimolecular quantity of hypochlorous acid in the presence of mercuric oxide in water to give a 70% yield of 2-chlorocyclohexanol[11]. The action of t-butyl hypochlorite on styrene in aqueous acetic acid at room temperature yields 2-chloro-1-phenylethanol, but in the absence of acetic acid the t-butyl ether of this alcohol is obtained[12] (addition products conforming to Markovnikov's rule):

$$C_6H_5CH{=}CH_2 \xrightarrow[H_2O,\ CH_3CO_2H]{t\text{-}BuOCl} \underset{84\%}{C_6H_5CH(OH)CH_2Cl}\ .$$

Diallyl ether reacts with an aqueous solution of bleaching powder to give an almost theoretical yield of 1,7-dichloro-4-oxaheptane-2,6-diol[13]:

$$(CH_2{=}CHCH_2)_2O \xrightarrow{HOCl} [ClCH_2CH(OH)CH_2]_2O\ .$$

$\alpha\beta$-Unsaturated acids (or their esters), nitriles, aldehydes, and ketones containing an unsubstituted hydrogen atom in the α-position relative to the functional group add hypohalous acids predominantly (but not exclusively) with

the halogen becoming attached to the α-carbon atom, and the hydroxyl to the β-carbon atom[14-27]:

$$CH_2{=}CHCO_2H \xrightarrow{HOCl} HOCH_2CHClCO_2H^{15-17}$$

$$CH_3CH{=}CHCO_2H \xrightarrow{HOCl} \underset{74\%}{CH_3CH(OH)CHClCO_2H} + \underset{26\%}{CH_3CHClCH(OH)CO_2H^{20}}$$

$$CH_2{=}CH{-}CN \xrightarrow{HOCl} \underset{79\%}{HOCH_2CH(Cl)CN} + \underset{21\%}{ClCH_2CH(OH)CN^{27}}.$$

The yields in such reactions are usually 40–67%[22-27], but may reach 90–95% in individual cases (e.g. in the hypochlorination of certain β-substituted $\alpha\beta$-unsaturated acids and their salts)[23].

The orientation of addition changes when a methyl substituent is present at the double bond in the α-position with respect to an electron-accepting functional group: the halogen goes mainly to the β-carbon atom and the hydroxyl to the α-carbon atom[23,27]. The yields (%) are respectively

$$\underset{CH_2=CY}{\overset{CH_3}{|}} \xrightarrow{HOCl} \underset{ClCH_2C(OH)Y}{\overset{CH_3}{|}} + \underset{HOCH_2CClY}{\overset{CH_3}{|}}$$

(Y=COOH 90 and 10; Y=$COOC_2H_5$ 70 and 30; Y=CN 58 and 42).

The direction of the addition of hypochlorous acid to hexenoic acids has been studied as a function of the position of the double bond relative to the carboxyl[22]. Hex-2-enoic acid reacts so slowly that a considerable proportion of the hypochlorous acid decomposes, and a single product—2-chloro-3-hydroxyhexanoic acid—is formed in low yield (15%). Hex-3-enoic acid reacts considerably more readily and gives a good yield of a mixture of addition products—3-chlorohexan-4-olide and 4-chloro-3-hydroxyhexanoic acid:

$$CH_3CH_2CH{=}CHCH_2CO_2H \xrightarrow{HOCl} \underset{80\%}{CH_3CH_2CH(O{-}CHClCH_2CO)} + \underset{20\%}{CH_3CH_2CHClCH(OH)CH_2CO_2H}.$$

Hex-4-enoic acid on hypochlorination gives an almost theoretical yield of 5-chlorohexan-4-olide, with a less than 5% yield of the addition product of opposite orientation:

$$CH_3CH{=}CHCH_2CH_2CO_2H \xrightarrow{HOCl} \underset{95\%}{CH_3CHClCH(O{-}CH_2CH_2CO)}.$$

Hypohalous acids add to butadiene preferentially at the 1,2-position[28,29]:

$$CH_2{=}CH{-}CH{=}CH_2 \xrightarrow[H_2O,CH_3CO_2H]{t\text{-}BuOCl} \underset{20\%}{ClCH_2CH(OH){-}CH{=}CH_2} + \underset{14\%}{ClCH_2CH{=}CHCH_2OH}.$$

Aqueous bromoacetamide acts on chloroprene and bromoprene to give 30–35% yields of products exclusively of 3,4-addition[30-32]:

$$CH_2{=}CCl(Br){-}CH{=}CH_2 \xrightarrow{HOBr} CH_2{=}CCl(Br){-}CH(OH)CH_2Br.$$

1-Bromobutadiene and 1,2-dichlorobutadiene also add hypobromous acid at the unsubstituted double bond[32,33]. 1,4-Addition products to halogenated butadienes have not been detected. This was explained by steric hindrance by the halogen substituent to the approach of the attacking electrophilic halogen[34].

Fundamental researches on the addition of hypohalous (hypochlorous, hypobromous, and hypoiodous) acids to unsaturated compounds have been undertaken by the English school of chemists[3]. As will be shown below, the main features discovered in the study of these reactions are of general significance. An immense volume of data have been obtained on the direction of the addition of hypochlorous acid to propene compounds in dilute aqueous solutions of perchloric acid and silver perchlorate (to combine with the chloride anion) in conformity with scheme 1 (Table 1).

Table 1. Products of the hypochlorination of propene derivatives according to scheme 1.

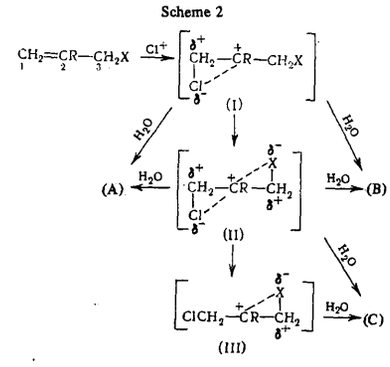
R	X	Products, % (A)	(B)	(C)	Ref.
H	H	91	9	0	15, 36
H	OH	73	27	0	37, 39
H	^{36}Cl	30	66	4	38, 40
H	Br	32	40	28	41
H	I	30	22	48	42
CH_3	H	100	0	0	35
Cl	^{36}Cl	96	4	0	43, 44
CH_3	^{36}Cl	94	4	2	40

The chlorine cation is found to add either at $C_{(1)}$ or at $C_{(2)}$, the selectivity of the reaction depending on the presence of substituents at $C_{(2)}$ and $C_{(3)}$. Migration of halogen from $C_{(3)}$ to $C_{(2)}$ is observed in allyl halides. The percentage of the product of migration increases in the sequence Cl < Br < I; the hydroxy-group at $C_{(3)}$ does not migrate. The presence of methyl or halogen at $C_{(2)}$ favours preferential addition in conformity with Markovnikov's rule.

Scheme 1

$$CH_2{=}\overset{1}{C}(R){-}\overset{2}{C}H_2\overset{3}{C}H_2X + HOCl \longrightarrow \underset{\text{(A) according to Markovnikov's rule}}{ClCH_2\overset{OH}{\overset{|}{C}}(R)CH_2X} + \underset{\text{(B) contrary to Markovnikov's rule}}{CH_2(R){-}\overset{OH}{\overset{|}{C}}ClCH_2X} + \underset{\text{(C) formally contrary to rule (with 3 → 2 migration of substituent X)}}{ClCH_2\overset{X}{\overset{|}{C}}(R)CH_2OH}$$

Scheme 2

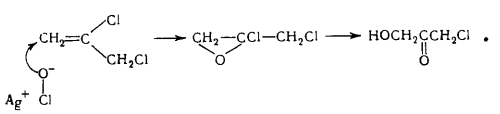


The results suggest a reaction mechanism (scheme 2) in which the chlorine cation, added at the site of highest electron density in the unsaturated compound, forms a chloronium cation (I) by coordination of its lone pairs of electrons with the cationic carbon centre. This stage determines the rate of the reaction. If the substituent X is likewise capable of such coordination, structures (II) and (III) are also possible. Further reaction of these ions

with water yields the adducts (A) (in conformity with Markovnikov's rule), (B) (unrearranged adduct contrary to the rule), and (C) (rearranged adduct contrary to the rule). A methyl group at the cationic carbon centre stabilises the intermediate cation and favours orientation of addition according to rule[35,45,46]: with 3-chloro-2-methylpropene 2% of the 6% of adduct formed contrary to Markovnikov's rule corresponds to the rearranged product (C).[40] A chlorine atom at the cationic carbon centre also promotes orientation according to the rule[43,45], but 3 → 2 migration of the allyl halogen does not occur[43].

Polar solvents stabilise the intermediate carbon cation and thereby promote the 3 → 2 displacement of the allylic halogen. Thus in the hypochlorination of allyl bromide not in water but in a less ionised solvent—40% and 70% aqueous dioxan[41]—the quantity of rearranged adduct has fallen from 28% to 18% and 11% respectively. A similar phenomenon has been observed with allyl iodide[42].

When 2,3-dichloropropene undergoes hypochlorination in the presence of silver perchlorate, the yield of normal addition products (Table 1) decreases, and a new product, 1-chloro-3-hydroxyacetone, appears[44,48,49]. When an alkene labelled with chlorine-36 at position 3 was used, 1-chloro-3-hydroxyacetone was obtained containing all the labelled chlorine. Kinetic measurements in the presence of excess of silver ions and of the alkene showed the occurrence of autocatalysis, which is promoted by increasing the concentration of hypochlorous acid and of the alkene together with low concentrations (preferably the absence) of mineral acid. Analysis of the products under kinetically controlled conditions showed that the autocatalysis was due to the formation of 1-chloro-3-hydroxyacetone. The explanation offered[49] for these results was that, in the presence of silver ions, the usual electrophilic addition was accompanied by nucleophilic attack on the double bond by the hypochlorite anion with subsequent formation of an epoxide. Under the reaction conditions the epoxide ring was opened with formation of the hydroxyketone:



This reaction is favoured by the presence of electron-accepting substituents attached at the double bond.

Orientation contrary to Markovnikov's rule occurs to a greater extent with electrophilic bromine and iodine than with electrophilic chlorine[41,42,50-52] (cf. Table 1):

$$CH_3{=}CH{-}CH_3 \xrightarrow[Cl^-]{Br^+} \underset{54\%}{BrCH_2CHClCH_3} + \underset{46\%}{ClCH_2CHBrCH_3}\ .$$

The presence of strongly electron-donating or electron-accepting groups at the double bond promotes the selective occurrence of concerted addition[50-52]:

$$C_6H_5CH{=}CH_2 \xrightarrow[Cl^-]{I^+} C_6H_5CHClCH_2I \quad (95\%)$$

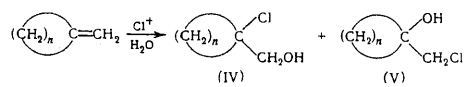
$$CH_3CH{=}CHSO_3H \xrightarrow[Cl^-]{I^+} CH_3CHClCHISO_3H \quad (90\%)\ .$$

The addition of hypobromous acid to 3,3,3-trichloropropene takes place selectively contrary to the rule[53]:

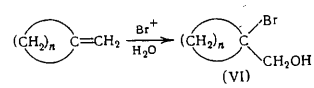
$$CH_2{=}CHCCl_3 \xrightarrow[H_2O]{Br^+} HOCH_2CHBrCCl_3\ .$$

The orientation of addition is similar in the hypochlorination of 3,3-di- and 3,3,3-tri-chloropropenes[54].

The addition of hypochlorous acid to methylenecycloalkanes yields two structural isomers, whereas the addition of hypobromous acid gives almost entirely a single isomer formed contrary to Markovnikov's rule[45,55,56]:



with n = 4–7 the respective percentages of (IV) are 60, 41, 67, and 35, accompanied by (V)—40, 50, 32, and 64;



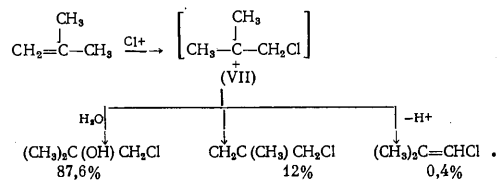
the percentages of (VI) with n = 4–7 are respectively 99, 91, 98, and 87. The predominance of the anomalous orientation in the case of the cyclopentane and cycloheptane rings is attributed[55] to steric hindrance of the trigonal carbon atom in these rings, but it is acknowledged that such an explanation does not completely account for the influence of the ring on the orientation in this reaction, since the addition of hydrogen bromide to such compounds yields an adduct strictly according to Markovnikov's rule[57].

When allene hydrocarbons react with an aqueous suspension of calcium hypochlorite in an atmosphere of carbon dioxide, addition takes place with the chlorine cation going to the central carbon atom, and the hydroxyl to the adjacent atom having the largest number of alkyl substituents[58]:

$$CH_2{=}C{=}CH{-}C_2H_5 \xrightarrow[H_2O]{Cl^+} \underset{\substack{OH\\63\%}}{CH_2{=}CClCHC_2H_5} + \underset{\substack{OH\\7\%}}{CH_2CCl{=}CHC_2H_5}\ .$$

In no case was the formation of α-chloro-ketones observed, which should have been obtained with the opposite orientation of addition. An earlier publication[59] had reported that chloroacetone was obtained by the action of hypochlorous acid on allene.

Concerted addition to unsaturated compounds having a quaternary carbon atom at the double bond is accompanied by the formation of small amounts of unsaturated substitution products[4,43,44,46,47]:



Possible reasons why particularly ions of type (VII), having electron-donating substituents at the cationic carbon centre, tend to undergo the competing loss of a proton have been discussed[4,60-62].

3. ADDITION OF HALOGENS IN ORGANIC SOLVENTS

The reaction of unsaturated compounds with molecular halogens, N-halogeno-amides, or t-butyl hypochlorite in certain organic solvents (alcohols, acids, acid anhydrides) or mineral acids (sulphuric, phosphoric, etc.) results in concerted addition of halogen and a solvent fragment at the multiple bond. Comprehensive investigations on the halogenoalkoxylation of ethylenic, diene, and enyne hydrocarbons and the properties of the resulting ethers of β-halogeno-alcohols have been reported in detail in a monograph[63].

When ethylene and chlorine are passed simultaneously into a solution of sodium acetate in acetic acid, a mixture of dichloroethane and 2-chloroethyl acetate is obtained[64]:

$$CH_2=CH_2 \xrightarrow[CH_3CO_2H,\ CH_3CO_2Na]{Cl_2} \underset{47\%}{ClCH_2CH_2OCOCH_3} + \underset{45\%}{ClCH_2CH_2Cl}\ .$$

Conducting this reaction in acetic anhydride increases the yield of the chloro-ester to 87%. The use of methyl acetate as solvent raises the yield of dichloroethane. Chlorination (or bromination) of ethylene in the presence of mercuric acetate in formic, acetic, and chloroacetic acids also leads to the formation of 2-halogenoalkyl esters[65].

The action of *NN*-dichlorobenzenesulphonamide in methanol on but-2-ene gives 2-chloro-3-methoxybutane together with a small quantity of 2,3-dichlorobutane[66]:

$$CH_3CH=CHCH_3 \xrightarrow[CH_3OH]{Cl^+} \underset{70-80\%}{CH_3CHClCH(OCH_3)CH_3} + CH_3CHClCHClCH_3\ .$$

The same reaction with but-1-ene probably leads to a mixture of isomers with the substituents in the 1,2-positions[66,67].

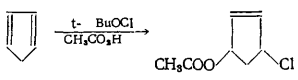
t-Butyl hypochlorite acts on alkenes (ethylene, propene, pent-2-ene, hex-3-ene, hept-1-ene, cyclohexene) in methanol, ethanol, phenol, and acetic acid in the presence of catalytic quantities of toluene-*p*-sulphonic acid to give satisfactory yields (from 30–40% to 60–70%) of the corresponding β-chlorinated ethers and esters[68]. It must be supposed that, in the case of unsymmetrical alkenes, the products are mixtures of isomers. The preparation of β-halogeno-esters of strong acids by the concerted halogenation of alkenes in these acids has been reported[69,70].

The addition of methyl hypochlorite to buta-1,3-diene by the action of *NN*-dichlorobenzenesulphonamide in methanol gives a total yield of 46% of 1,2- and 1,4-addition products, in which the former strongly predominates[71]:

$$CH_2=CH-CH=CH_2 \xrightarrow{ClOCH_3} \underset{OCH_3\quad 83\%}{ClCH_2CH(OCH_3)-CH=CH_2} + \underset{17\%}{ClCH_2CH=CHCH_2OCH_3}\ .$$

The bromo- and iodo-alkoxylation of butadiene yields almost exclusively 1,2-addition products[28,71-73]. Thus the action of a methanolic solution of bromine on butadiene forms 4-bromo-3-methoxybut-1-ene (63%) slightly contaminated with 1-bromo-4-methoxybut-2-ene (4%) and products of the addition of two bromine atoms[73].

The chloro-acetoxylation of cyclopentadiene by the action of t-butyl hypochlorite dissolved in acetic acid gives a 47% yield of a conjugate 1,4-addition product—*trans*-5-chlorocyclopenten-3-yl acetate[74]:



The chloro- and bromo-methoxylation of isoprene always involves the attachment of halogen at position 1. In the case of chloro-alkoxylation this leads to 1,2- and 1,4-addition products in the proportions 2 : 1:[75,76]

$$\overset{1}{CH_2}=\overset{2}{C}(CH_3)-\overset{3}{CH}=\overset{4}{CH_2} \xrightarrow{ClOR} \underset{OR}{ClCH_2C(CH_3)=CH_2} + \underset{CH_3}{ClCH_2C(OR)=CH-CH_3}\ .$$

Only 1,2-addition products—3-alkoxy-4-bromo-3-methylbut-1-enes—have been identified on bromo-alkoxylation[63,75]. The bromo- and iodo-alkoxylation of chloroprene and bromoprene, unlike those of isoprene, take place mainly at the 3,4-positions[77-79]:

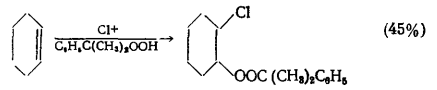
$$\overset{1}{CH_2}=\overset{2}{C}(Cl)-\overset{3}{CH}=\overset{4}{CH_2} \xrightarrow{BrOR} CH_2=C(Cl)-CH(OR)-CH_2Br$$

The chloro-alkoxylation of the same compounds yields 1,4- and 3,4-addition products in the proportions 4 : 1.[80] Thus in isoprene the substituted double bond is the more reactive, whereas in halogenoprenes this applies to the unsubstituted double bond.

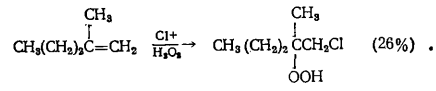
The halogeno-alkoxylation of butenyne and its homologues takes place mainly in the vinyl group[81,82]:

$$CH_2=CH-C\equiv CH \xrightarrow{HalOR} HalCH_2-\underset{OR}{CH}-C\equiv CH\ .$$

The action of t-butyl hypochlorite and alkyl hydroperoxides or hydrogen peroxide on certain ethylenic compounds (2-methylpent-1-ene, hex-3-ene, cyclohexene, etc.) forms β-chlorinated peroxides in 20–50% yields[83]:



(45%) ;

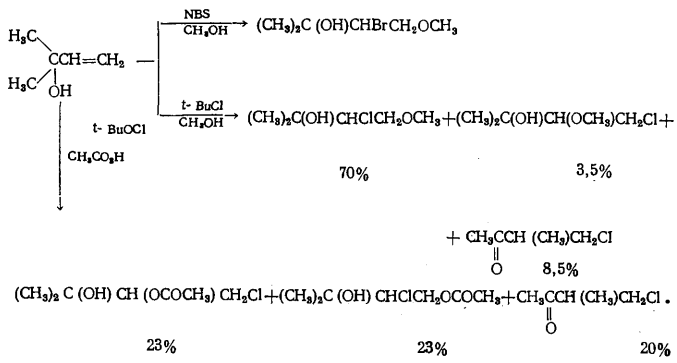


(26%) .

Vinyl ethers react with t-butyl hypochlorite in the presence of primary or secondary alcohols, alkyl hydroperoxides, or hydrogen peroxide to give moderate yields of chlorinated acetals, peroxy-acetals, and hydroperoxy-acetals respectively[83].

The chloro-methoxylation of allyl alcohol with methanolic molecular chlorine[84] or hexachloromelamine[85] yields a mixture of isomeric methoxychloropropanols together with 2,3-dichloropropan-1-ol. The addition product conforming to Markovnikov's rule predominates in the isomeric mixture.

The bromo-methoxylation of 1,1-dimethylpropanol with methanolic *N*-bromosuccinimide (NBS)[86] gives a 46% yield of the non-Markovnikov selective addition product. The chloro-methoxylation of this compound with t-butyl hypochlorite in methanol[86] gives a mixture of structural isomers with the same isomer strongly predominating. The addition of chlorine acetate $ClOCOCH_3$ gives a mixture of equal quantities of structural isomers, accompanied by β-chloro-ketones resulting from a pinacoline type of rearrangement[87]:



The chloro- and bromo-methoxylation of 1,1,2-trimethylpropenol also gives a mixture of the two isomeric addition products, together with considerable quantities of β-halogeno-ketones[87-92]. Rearrangement with the formation of β-halogeno-ketones becomes the main reaction of this propenol and of 1-aryl-1,2-dimethylpropenols with t-butyl hypochlorite when protic are replaced by aprotic solvents (dichloromethane, nitromethane)[93-97].

3,3,3-Trifluoropropene reacts readily with an acetic-acid solution of bromine in the presence of mercuric acetate or sulphate to give a high (78%) yield of the non-Markovnikov concerted addition product[98]:

$$CF_3CH{=}CH_2 \xrightarrow[CH_3CO_2H,\,Hg(OCOCH_3)_2]{Br^+} CF_3CHBrCH_2OCOCH_3 .$$

The dibromide is the main product in the absence of mercury salts. An analogous orientation of electrophilic addition is found in the concerted chlorination of 3,3,3-trichloropropene[99] and 3,3,3-trichloro-2-methylpropene[100].

The chlorination of compounds containing a 2,2-dichlorovinyl group, in mixtures of acetic acid and mercuric acetate, formic and concentrated sulphuric acids, gives high yields of α-chlorinated carboxylic acids[101]:

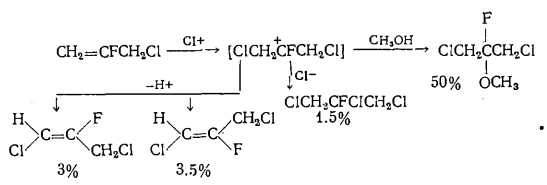
$$R(CH_2)_nCH{=}CCl_2 \xrightarrow[HCO_2H]{Cl^+} [R(CH_2)_nCHClCCl_2OCOH] \xrightarrow[(60-80\%)]{H_2O} R(CH_2)_nCHClCO_2H .$$

Thus the presence of three fluorine or chlorine atoms in the allyl position promotes non-Markovnikov addition. The presence of two halogen atoms in the 1-vinyl position favours the addition of halogen at the adjacent carbon atom forming the double bond[98,101].

Allyl chloride and bromide with methyl hypochlorite form every possible addition product, with the non-Markovnikov products predominating[102]: e.g.

$$CH_2{=}CHCH_2Cl \xrightarrow[CH_3OH]{Cl^+} \underset{12.5\%}{ClCH_2CH(OCH_3)CH_2Cl} + \underset{18.5\%}{CH_3OCH_2CHClCH_2Cl} .$$

The chloro-methoxylation of 2-halogenoallyl chlorides conforms to Markovnikov's rule[103], as was to be expected by analogy with the hypochlorination of 2-chloroallyl chloride[43,44]; unsaturated substitution products are also formed:



The concerted halogenation of double bonds in cholesterol[104,105] and in corticosteroids[106] provides an example of selective addition contrary to Markovnikov's rule.

4. HALOGENOFLUORINATION

In 1959 the first papers were published on the concerted halogeno-fluorination of steroids by *N*-halogeno-amides and anhydrous hydrogen fluoride in the presence of organic acceptors of protons (alcohols or ethers) in chloroform[107–110]. The bromo-fluorination of Δ^5-steroids with *N*-bromoacetamide and hydrogen fluoride forms 5α-bromo-6β-fluorosteroids (contrary to Markovnikov's rule), whereas iodo-fluorination with *N*-iodosuccinimide and hydrogen fluoride gives 5α-fluoro-6β-iodosteroids[110]. Halogeno-fluorination involves *trans*-addition[106,108,109]. Thus vicinal *trans*-bromofluoro- and *trans*-fluoroiodo-cyclohexanes are obtained in satisfactory yields from cyclohexene under the above conditions[109].

This method has since been used to prepare simpler bromofluoro- and chlorofluoro-derivatives. The bromo-fluorination of esters of $\alpha\beta$-unsaturated carboxylic acids unsubstituted in the α-position gives 50–70% yields of 2-bromo-3-fluoroalkanoic esters[111,112]:

$$CH_2{=}CHCO_2CH_3 \xrightarrow[F^-]{Br^+} FCH_2CHBrCO_2CH_3 .$$

The chloro-fluorination of ethylene, propene, vinylidene chloride and fluoride, and methyl acrylate has been accomplished with moderate (30–60%) yields by chlorinating these compounds with gaseous chlorine in liquid hydrogen fluoride or with hexachloromelamine and hydrogen fluoride in ether[113]: e.g.

$$CH_2{=}CHCO_2CH_3 \xrightarrow[F^-]{Cl^+} FCH_2CHClCO_2CH_3 .$$

The intermediate formation of a β-chloro-cation in the concerted addition of chlorine and fluorine to alkenes has been proved[113] in the case of the chloro-fluorination of ethylene in the presence of benzene. Formation of 1-chloro-2-fluoroethane and mono- and dichlorobenzenes is then accompanied by an 8% yield of phenethyl chloride:

$$CH_2{=}CH_2 \xrightarrow{Cl^+} [ClCH_2\overset{+}{C}H_2] \begin{cases} \xrightarrow{F^-} ClCH_2CH_2F , \\ \xrightarrow{C_6H_6} ClCH_2CH_2C_6H_5 . \end{cases}$$

The bromo-fluorination of C_2–C_{18} alk-1-enes by means of *N*-bromoacetamide and hydrogen fluoride in an ether–chloroform mixture gives good (up to 60–70%) yields of 1-bromo-2-fluoroalkanes, together with a certain amount (3–8%) of the isomeric 2-bromo-1-fluoroalkanes[114]. In some cases the addition of pyridine to the solvent increases the yield of the addition product. Thus the bromo-fluorination of styrene in ether produces a 25% yield of β-bromo-α-fluoroethylbenzene, but in a 4 : 1 ether–pyridine mixture the yield rises to 68%. The bromo-fluorination of allyl bromide gives both isomeric dibromofluoropropanes, with the addition product contrary to Markovnikov's rule predominating:

$$CH_2{=}CHCH_2Br \xrightarrow[F^-]{Br^+} \underset{22\%}{BrCH_2CHFCH_2Br} + \underset{32\%}{FCH_2CHBrCH_2Br} .$$

When methyl acrylate undergoes bromo-fluorination by the above method in ethereal pyridine, the expected methyl α-bromo-β-fluoropropionate is accompanied by small quantities of methyl β-bromo-α-fluoropropionate and methyl β-bromo-α-ethoxypropionate[112]. The bromo-fluorination of methyl methacrylate yields the single addition product—methyl β-bromo-α-fluoro-α-methylpropionate[115]:

$$CH_2{=}C(CH_3)CO_2CH_3 \xrightarrow[F^-]{Br^+} BrCH_2\overset{CH_3}{\overset{|}{C}}FCO_2CH_3 .$$

The chloro-fluorination of methyl α-methoxyacrylate by hexachloromelamine and hydrogen fluoride goes similarly[116].

The bromo-fluorination of allyl acetate by means of *N*-bromoacetamide and hydrogen fluoride gives 3-bromo-2-fluoropropyl acetate in low yield. The presence of the isomeric product formed contrary to Markovnikov's rule was not established[115].

The chloro-fluorination of allyl alcohol by hexachloromelamine and hydrogen fluoride in methanolic chloroform yields both possible isomers[85]:

$$CH_2{=}CHCH_2OH \xrightarrow[F^-]{Cl^+} \underset{45\%}{ClCH_2CHFCH_2OH} + \underset{5\%}{FCH_2CHClCH_2OH} .$$

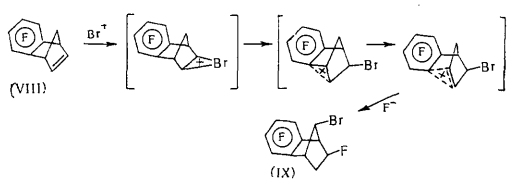
The chloro-fluorination of 2-fluoro- and 2-chloro-allyl alcohols, as well as that of the corresponding chlorides, leads to selective addition of chlorine fluoride in conformity with the Markovnikov rule[103,117]:

$$CH_2{=}CHalCH_2OH \xrightarrow[F^-]{Cl^+} ClCH_2CFHalCH_2OH$$

Hal=F (yield 76%), Cl (50%) .

In the case of the allyl chlorides this is accompanied by small quantities of products of substitution and of the addition of two chlorine atoms[103]. Allyl chloride and bromide are chloro-fluorinated with the formation of every possible addition product; in the case of allyl bromide a product is also detected in which the bromine atom has migrated. Products of substitution by chlorine were not found[102].

Several specific aspects of the addition to fluoroalkenes of interhalogen compounds, and in particular of halogens, have been discussed in review papers[118,119]. The bromofluorination of (VIII) by *N*-bromosuccinimide and hydrogen fluoride in ether yields the Wagner–Meerwein rearrangement product (IX):



(VIII) (IX)

Rearrangement takes place also on the addition of bromine chloride and methyl hypochlorite to (VIII); the addition of iodine chloride, however, is not accompanied by rearrangement[120].

5. MECHANISM OF CONCERTED ELECTROPHILIC HALOGENATION

Examination of the experimental work surveyed in Sections 1–3 shows that the observed orientation of concerted addition at a multiple bond can in most cases be explained satisfactorily by scheme 2 (Section 2). Summarising the experimental results on various reactions involving the concerted electrophilic chlorination of allylic systems makes it possible to elucidate the influence of the nucleophile and the structure of the original unsaturated compound on the orientation of addition.

When position 2 in the initial alkene is unsubstituted, addition of a nucleophile Y is preceded by an intermediate halogenonium cation, the structure of which (I–III in scheme 2) is influenced by neighbouring groups (in particular the substituent X in the compounds surveyed in Table 2).

Attack by the nucleophile Y on the cations results in the formation of—(A) a product of addition according to Markovnikov's rule, (B) an unrearranged product of addition contrary to this rule, and (C) a rearranged product of addition contrary to the rule. When X = H addition both of hypochlorous acid and of chlorine fluoride takes place almost entirely according to rule. When X = OH, Cl, Br, the quantity of anomalous products (B) + (C) increases with increase in the relative participation of the groups X in the formation of onium structures of types (II) and (III). This regularity is observed with all three reactions examined (hypochlorination, chloro-methoxylation, and chloro-fluorination).

In comparison with methanol and water molecules, the fluoride anion, acting as a nucleophile, enhances the selectivity of addition in favour of the adduct (A). This is probably due to the high nucleophilic activity and small size of the fluoride anion, as a consequence of which it is less subject to steric hindrance than are neutral methanol and water molecules, and easily penetrates the shielded cationic carbon centre situated at the central carbon atom.

Nevertheless, in the presence of bulky electronegative substituents (Cl, Br) the proportional attack by the fluoride anion at the less hindered 1-carbon atom (cations I and II) and the 3-carbon atom (cations II and III) increases, and the relative quantity of non-Markovnikov adducts becomes larger. It is noteworthy that the ratio of rearranged to unrearranged adduct is considerably larger in the chloro-fluorination than in the hypochlorination of allyl bromide (C/B = 1.6 and 0.7), which is probably due to the higher polarity of the environment produced by liquid hydrogen fluoride. When the nucleophiles are bulky and possess less nucleophilic activity than methanol and water molecules, attack on the intermediate cation is more intense at the less hindered 1,3-carbon atoms. For these nucleophiles with X = Cl, Br the non-Markovnikov isomers predominate.

Table 2. Concerted electrophilic chlorination of allylic derivatives according to scheme 2:

$CH_2{=}CHCH_2X + Cl^+ + Y \rightarrow (A) + (B) + (C)$

X	Y	Products, % (A)	(B)	(C)	Ref.
H	H_2O	91	9	0	35–37
H	F^-	100	—	—	113
OH	H_2O	73	27	0	39
OH	CH_3OH	71	29	0	102
OH	F^-	90	10	0	84, 102
^{36}Cl	H_2O	30	66	4	38, 40
Cl	CH_3OH	41	—	59*	85, 102
Cl	F^-	68	—	32*	102
Br	H_2O	32	40	28	41
Br	CH_3OH	26	—	74*	102
Br	F^-	60	15	25	102

* Sum of (B) + (C).

These ideas suggest that passing from allyl alcohol to the acetate and especially the trihalogenoacetates will produce a change in the orientation of concerted addition in favour of the non-Markovnikov adduct. The expected effect has in fact been observed[121] in the chloro-fluorination and chloro-methoxylation of these derivatives (Table 3). For the addition of chlorine fluoride the relative quantity of the non-Markovnikov adduct 2-chloro-3-fluoropropan-1-ol increases in the sequence

$$OH < OCOCH_3 < OCOCCl_3 < OCOCF_3,$$

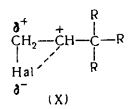
for the addition of methyl hypochlorite the quantity of the corresponding adduct 2-chloro-3-methoxypropan-1-ol increases in the sequence

$$OH < OCOCH_3 < OCOCF_3 < OCOCCl_3.$$

This fact is consistent with the concept of steric hindrance to attack by the nucleophile. The bulky trichloroacetate group proves a greater obstacle than the trifluoroacetate group to the electrically neutral nucleophilic methanol molecule. The small, negatively charged fluoride ion is probably more subject to electrostatic repulsion than to actual steric hindrance, so that the trifluoroacetate group then exerts a stronger orienting influence than does the trichloroacetate group.

It is probable that the role of steric factors is in general large in electrophilic halogenation. This principle is illustrated by the preferential non-Markovnikov halogenation of propene derivatives in which all the allylic hydrogen

atoms have been replaced by other groups— $CH_2:CH.C(CH_3)_3$,[122] $CH_2:CH.CCl_3$,[53,54] $CH_2:CH.CF_3$,[98] and $CH_2:CH.COOR$.[111-113] These results cannot be explained solely by the distribution of electron density in the ground state of the unsaturated compounds, for otherwise the opposite orientation would have been expected with t-butylethylene (n-butylethylene gives 80% of the Markovnikov addition product[122]). It must be assumed that the most important factor here is the shielding effect of β-substituents, which block the cationic carbon centre in the ion



(X)

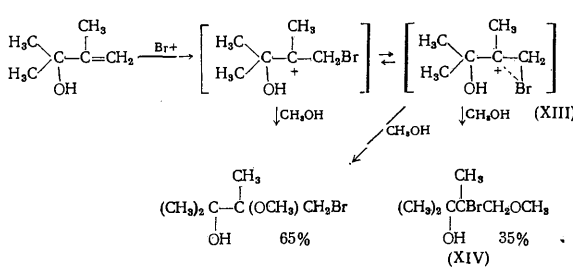
leaving the terminal carbon atom more accessible to attack by the nucleophile[122,123].

Table 3. Concerted chlorination of allyl acetates[121].

Initial compound	Addition products, %	
	according to Markovnikov	contrary to Markovnikov
Chloro-fluorination	$ClCH_2CHFCH_2OH$	$FCH_2CHClCH_2OH$
$CH_2=CHCH_2OH$	90	10
$CH_2=CHCH_2OCOCH_3$	82	18
$CH_2=CHCH_2OCOCCl_3$	74	26
$CH_2=CHCH_2OCOCF_3$	67	33
Chloro-methoxylation	$ClCH_2CH(OCH_3)CH_2OH$	$CH_3OCH_2CHClCH_2OH$
$CH_2=CHCH_2OH$	71	29
$CH_2=CHCH_2OCOCH_3$	54	46
$CH_2=CHCH_2OCOCCl_3$	36	64
$CH_2=CHCH_2OCOCF_3$	50	50

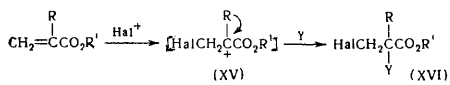
The concerted chlorination of 2-methyl- and 2-halogeno-allyl compounds takes place almost entirely according to Markovnikov's rule (Table 4). With an electron-donating substituent (α-substituent) present in the resulting cationic carbon centre, both addition of the nucleophile and detachment of a proton are probably preceded by a classic carbonium ion (XI) [scheme 3]. The decrease in the positive charge in the cationic carbon centre due to the electron-donating influence of the substituent R prevents formation of the halogenonium cation (XII) by coordination of the p-electrons of the β-halogen (this applies mainly to chlorine, which interacts feebly with the cationic carbon centre[3]). However, the intermediate state (XII) is not excluded in chlorination, since small quantities (4–6%) of non-Markovnikov adducts are nevertheless formed (Table 4 and also Refs. 84–89).

In the concerted bromination of 1,1,2-trimethylpropenol the equilibrium is already considerably displaced towards the halogenonium ion (XIII), and the quantity of non-Markovnikov adduct (XIV) is large[87-89]:



(XIV)

In this case the β-substituents also favour orientation contrary to Markovnikov's rule. The strong orienting influence of α-substituents capable of donating electrons to the cationic carbon centre is apparent in electrophilic addition to α-substituted acrylaldehydes[124] and acrylates[23,115,116], which in the absence of an α-substituent tend to add contrary to the rule[5,15-17,22,23,111-113].



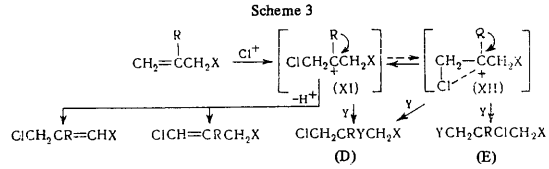
(XV) (XVI)

Table 4. Concerted chlorination of 2-substituted allylic derivatives according to scheme 3:

$CH_2=CRCH_2X+Cl^++Y\rightarrow(D)+(E)$

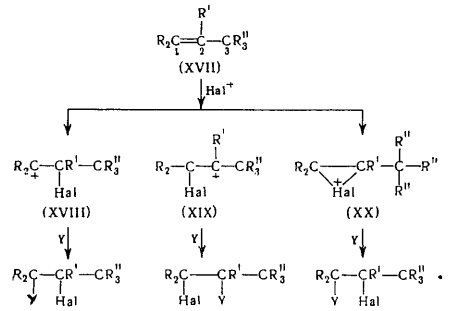
R	X	Y	Products, % (D)	Products, % (E)	Ref.
CH_3	H	H_2O	100	0	35
CH_3	Cl	H_2O	94	6	40
F	OH	F^-	100	0	117
Cl	OH	F^-	100	0	117
F	Cl	CH_3OH	100	0	103
F	Cl	F^-	100	0	103
Cl	Cl	H_2O	96	4	43, 44
Cl	Cl	CH_3OH	>96	<4	103
Cl	Cl	F^-	100	0	103

Scheme 3



The substituents (methyl[14,15,23,115], methoxyl[116,124,125], and probably halogen[126]) enhance the nucleophilic character of the double bond in acrylates and thereby promote formation of a stable carbonium ion (XV) and hence the Markovnikov adduct (XVI). Thus the distribution of electron density in the ground state of the unsaturated molecule is not the dominant factor determining the direction of concerted electrophilic addition[2]. The orientation of addition obviously depends mainly on the structure of the transitional cation, in which an important part is played by the electronic and steric effects of substituents in α- and β-positions relative to the cationic carbon centre[3,61,102,103].

Let us consider as unsaturated compound the propene system (XVII) (in which R and R′ are substituents capable of donating electrons to the cationic carbon centre). Three main types of intermediate carbon cations (XVIII)–(XX) may be formed as a result of electrophilic attack by the halogen:



The presence of 1-vinyl substituents R favours formation of the stable classic ion (XVIII) and hence addition of halogen to $C_{(2)}$ while the nucleophile Y goes to $C_{(1)}$. The presence of a 2-vinyl substituent R′ favours the classic ion (XIX) with addition of halogen to $C_{(1)}$ and the nucleophile Y to $C_{(2)}$. Allylic substituents R″ shield the central carbon atom in the cation (XX) and promote attack by the nucleophile at $C_{(1)}$ with addition of halogen at $C_{(2)}$†. Which addition product predominates depends also on the nucleophilic activity and the steric radius of the attacking reagent Y. This effect is most strongly developed when R = R″ = H, i.e. when an intermediate cation of halogenonium type (XX) is dominant.

In the simple cases discussed above we observe selective addition either according or contrary to Markovnikov's rule. There are other views on the mechanism of the electrophilic halogenation of unsaturated compounds, developed by Shilov[127-131], which envisage the formation of a different type of donor–acceptor complexes of the substrate with the attacking molecules. However, the suggested schemes cannot explain the varying orientation of the addition of unlike species at a double bond, nor the rearrangement usually observed in such reactions.

Theoretical aspects of the electrophilic halogenation of diene hydrocarbons with conjugated multiple bonds have been considered[3,72,132]. There is insufficient clarity in this question[3,132], and the problem requires further study.

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† We have already mentioned a possible migration of allylic substituents R″ to $C_{(2)}$ when R″ = Cl, Br, I, and also rearrangements of the pinacoline type in the halogenation of vinylalkyl(aryl)carbinols (Sections 2, 3, and 5).

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Intramolecular Rearrangements of Hydrocarbon Radicals in the Gas Phase

A.D.Stepukhovich and V.I.Babayan

The review deals with the rearrangements of alkyl radicals occurring in various gas-phase processes. Intramolecular isomerisations involving the migration of a hydrogen atom with formation of three-, four-, five-, and six-membered transition states are examined. The possibility of the isomerisation of small alkyl radicals (ethyl and propyl radicals) and of the transfer of hydrogen to a neighbouring carbon atom in long-chain radicals is discussed. The process mechanism is considered. The bibliography includes 82 references.

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I. INTRODUCTION

Among reactions of free radicals, those involving their intramolecular isomerisation and leading to the migration of the free valence along the carbon skeleton of the species from one carbon atom to another are of special interest. Owing to isomerisation, the structure of the products of reactions involving free radicals can differ appreciably from that of the products which might have been expected in the absence of radical rearrangements. In many chain processes the isomerisation of the initially formed radicals can lead to the replacement of less active intermediate centres by more active ones. In polymerisation processes such rearrangements result in branching and cross-linking of the polymer chains.

The concept of radical isomerisation arose and began to be developed immediately after the discovery of free radicals and the elucidation of the role which they may play in various chemical reactions. In the 1940's–1950's, radical isomerisation was already adduced to explain experimental data for the thermal decomposition[1,2], isomerisation[3], oxidation[4-6], and other reactions[7,8] of organic compounds involving free radicals. However, one should note that at that time there was in fact no proof of the reality of processes of this kind.

This deficiency was eliminated to a considerable degree in the 1960's when studies on radical isomerisation were directed to the identification of radical centres. The first quantitative data for the kinetic characteristics of isomerisation processes have now also been obtained. In thermal or photolytic decomposition of various organic compounds, two or more isomeric radicals are formed via almost equally probable independent pathways and even the identification of the radicals and the use of tracer atoms do not always make it possible to state unambiguously whether radical rearrangements occur in the system. The fairly frequent formation in the system of structurally isomeric radicals can be explained by a sequence of bimolecular radical substitution, addition, and decomposition reactions without resorting to the hypothesis of radical isomerisation. Therefore numerous contradictory data and conclusions concerning the possible isomerisation of alkyl radicals by the migration of hydrogen atoms have accumulated in the literature dealing with gas-phase free-radical processes.

The present review is concerned with rearrangements of alkyl radicals in the gas phase. The review literature on this question is scanty. We can only point to one review in Czech[9] and a brief description of gas-phase radical rearrangements in monographs by Semenov[10], Pryor[11], Magaril[12], and Freidlina et al.[13] The well tested structural chemical principle of 1 — 2, 1 — 3, 1 — 4, 1 — 5, ... migrations of hydrogen atoms has been adopted in the present review for the classification of rearrangements. The numerical values indicate the relative positions of two rearrangement centres. However, wherever convenient, we have employed the approach of Rabinovitch and coworkers[14], designating the hydrogen atom shift as an *Nab* process, where *N* is the number of units in the ring of the cyclic transition state equal to 3, 4, 5, ..., *a* = *p*, *s*, or *t* refers to primary, secondary or tertiary C — H bonds undergoing dissociation, and *b* = *p*, *s*, or *t* refers to C — H bonds being formed.

Thus the isomerisation

$$CH_3-CH_2-CH_2-CH_2-\dot{C}H-CH_3 \rightarrow \dot{C}H_2-CH_2-CH_2-CH_2-CH_2-CH_3$$

will be designated as a 6*ps* reaction, which corresponds to a 1 — 5 migration of hydrogen according to the first classification. The Rabinovitch notation has the advantage that it reflects two important factors responsible for the occurrence of the rearrangement: the ring size of the transition state and the thermochemistry of the process, i.e. the conversion of less stable radicals into more stable radicals (the conversion of a primary into a secondary or tertiary radical) or conversely.

Intramolecular rearrangements of radicals are usually regarded as reactions of the radical with itself. Accordingly, the present review deals with intramolecular substitution reactions of alkyl radicals which can be represented schematically in the following way:

$$R-\dot{C}H-(CH_2)_n-\overset{H}{\underset{|}{C}}H-R' \rightarrow R-\overset{H}{\underset{|}{C}}H-(CH_2)_n-\dot{C}H-R',$$

where R, R′ is either a hydrogen atom or a hydrocarbon group.

II. 1 — 2 MIGRATION OF A HYDROGEN ATOM

Contradictory views have been expressed in the literature concerning the possibility that alkyl radicals can rearrange by the transfer of a hydrogen atom from a carbon atom adjoining the atom with an unpaired electron.

In order to account for the reaction products, many investigators had to resort to the hypothesis of 1 — 2 migration of a hydrogen atom; however, no one has succeeded in justifying rigorously a rearrangement of this type.

Glazebrook and Pearson[1] investigated the photolysis of di-isopropyl ketone, trapping the radicals formed with metallic mercury. When mercury iodide was added to the system, *n*-propylmercury iodide was obtained unexpectedly. This led the investigators to the conclusion that the isopropyl radicals formed in the primary photolytic step isomerise via a 3*ps* reaction into n-propyl radicals, the isomerisation probably occurring at the instant of the combination of the radical with mercury, since in the absence of the latter the rearrangement does not occur:

$$CH_3\dot{C}HCH_3 \rightarrow \dot{C}H_2CH_2CH_3\,. \qquad (1)$$

This conclusion was questioned by Kharasch and coworkers[15,16], who investigated the thermal decomposition of n-propyl and isopropyl peroxides in carbon tetrachloride but failed to detect rearrangements of the alkyl radicals formed and concluded that there is no isomerisation in the gas-phase reactions either.

The decomposition of alkyl radicals is known to involve bonds in the β-position relative to the free valence[17] (the β-rule). In the presence of radical isomerisation, apparent deviations from this rule should be observed. Thus in the decomposition of isopropyl radicals, ethylene and a methyl radical should be formed, in the decomposition of n-butyl radicals—a methyl radical and propene, etc. The detection in the system of products of such "anomalous" decomposition might constitute serious evidence in support of the occurrence of radical rearrangements in the system.

Heller and Gordon[18] studied the photolysis of [D_2]di-isopropyl ketone at temperatures in the range 200 — 500°C and pressures of 14 — 16 mmHg. In the high-temperature range (407 — 504°C), they detected ethylene and methane in proportions close to 1 : 1. They suggested that under these conditions the anomalous decomposition of the isopropyl radical

$$CH_3\dot{C}DCH_3 \rightarrow CH_3CDH\dot{C}H_2 \rightarrow CH_2{=}CHD + \dot{C}H_3 \qquad (2)$$

plays an important role.

The presence in the system of n-propyl radicals is also indicated by the appearance on the chromatogram of a peak corresponding to 2-methylpentane, which is a product resulting from the combination of n-propyl and isopropyl radicals. The formation of the n-propyl radical via other pathways, namely by the attachment of H· to propene or the intermolecular isomerisation

$$CH_3\dot{C}DCH_3 + CH_3CH_2CH_3 \rightarrow CH_3CDHCH_3 + CH_2\dot{C}H_2CH_3$$

and "atomic cracking", did not occur under these conditions. If reaction (2) proceeds via two stages (rearrangement and decomposition), then, according to the authors, isomerisation is rate-limiting.

The anomalous decomposition of isopropyl radicals, $CH_3\dot{C}HCH_3 \rightarrow \dot{C}H_3 + CH_2 = CH_2$, is believed[18] to be responsible for the formation of part of the ethylene which is a side product in the pyrolysis of isobutane. The rate constant obtained for this reaction in the temperature range 440 — 541°C and in the pressure range 50 — 150 mmHg agrees to some extent with Heller's results[18] (Table 1). A somewhat different value of the rate constant for this reaction in the temperature range 417 — 493°C was obtained by Kerr and Trotman-Dickenson[20] in the photolysis of isobutyraldehyde.

The β-rule breaks down similarly in the decomposition of butyl radicals. In a study of the photolysis of n-valeraldehyde at 300 — 416°C, the same workers[21] observed a rapid increase of the amount of methane and propene with retention of the ratio [methane]/[propene] ≃ 1. An anomalous decomposition reaction consisting of 1 — 3 migration of hydrogen and the dissociation of the C — C bond,

$$CH_3CH_2CH_2\dot{C}H_2 \rightarrow CH_3\dot{C}HCH_2CH_3 \rightarrow CH_3CH{=}CH_2 + \dot{C}H_3\,, \qquad (3)$$

was stated to be the cause of this behaviour.

Table 1. Kinetic parameters of the anomalous decomposition of alkyl radicals.

Reaction	T, °K	$\lg A$ (s^{-1})	E, kcal mole^{-1}	References
$CH_3\dot{C}DCH_3 \rightarrow CH_2CHD + \dot{C}H_3$	686—777	15.05	32.5±2.0	18
iso-$\dot{C}_3H_7 \rightarrow C_2H_4 + \dot{C}H_3$	690—770	10.6	29.5	20
	713—814	12.0±0.2	34.5±0.5	19
	690—814	11.28±0.68	31.88±2.36	25
n-$\dot{C}_4H_9 \rightarrow C_3H_6 + \dot{C}H_3$	523—650	11.0	23	22, 26, 27
	571—689	12.1	27.1	21, 26, 27
n-$\dot{C}_4H_9 \rightarrow$ s-$\dot{C}_4H_9 \rightarrow \dot{C}H_3 + C_3H_6$	913—933	14.71	41.0	23
t-$\dot{C}_4H_9 - C_3H_6 + \dot{C}H_3$	742—797	16.0	46.3	24, 27
	—	8.5	18.5	26

As in the work of Heller and Gordon[18], it remained obscure whether the rearrangement occurs before the decomposition or simultaneously with it. The authors believe that isomerisation precedes decomposition: the first reaction stage is exothermic and the s-butyl radical formed has a larger store of energy than is required for decomposition. If such a radical is not deactivated by a collision (the probability of which is small at low pressures), then it will of course decompose.

A reaction similar to reaction (3) was invoked still earlier by Bywater and Steacie[22] to explain the approximate equality of the rates of formation of methane and propene in the photolytic decomposition of n-butane (250 — 400°C, 200 mmHg) sensitised by mercury. A reaction of this kind should be accompanied by 1 — 2 or 1 — 3 migration of hydrogen.

The conclusion that the n-butyl radical isomerises to the s-butyl radical with subsequent decomposition into a methyl radical was also reached by Lin and Back[23] using results on the kinetics of the secondary formation of methane in the thermal decomposition of ethane (550 — 726°C, 10 — 600 mmHg). Probably the reaction does indeed occur in two stages, since for high degrees of conversion the presence of *cis*- and *trans*-but-2-enes in the system may be evidence of the existence of s-butyl radicals.

The isomerisation of t-butyl radicals was studied by Birrell and Trotman-Dickenson[24] in the photoinitiated decomposition of trimethylacetaldehyde. Above 470°C, they obtained considerable amounts of propene and methane. The authors explain this by isomerisation reactions followed by the decomposition of the t-butyl radical:

$$(CH_3)_2\dot{C}CH_3 \rightarrow (CH_3)_2CH\dot{C}H_2 \rightarrow CH_3CH{=}CH_2 + \dot{C}H_3\,. \qquad (4)$$

Thus it is evident that a number of studies appear to indicate the possibility of hydrogen shifts via a three-membered cyclic transition state under the usual experimental conditions of cracking and photolysis reactions. Table 1 lists the kinetic parameters of such reactions.

However, there exists no less convincing evidence that the decomposition of hydrocarbon radicals takes place always in accordance with the β-rule. Thus Jackson and McNesby[28] studied the thermal decomposition of [1,1,1-D_3]propane at 472 — 553°C and a pressure of about 50 mmHg. Under these conditions, the n-propyl radical decomposes rapidly into ethylene and a methyl radical, while for the isopropyl radical four possible decomposition pathways were suggested:

$$CD_3\dot{C}HCH_3 \rightarrow [\dot{C}D_2CHDCH_3] \rightarrow CD_2{=}CDH + \dot{C}H_3, \quad (5)$$

$$CD_3\dot{C}HCH_3 \rightarrow [CD_3CH_2\dot{C}H_2] \rightarrow \dot{C}D_3 + C_2H_4, \quad (6)$$

$$CD_3\dot{C}HCH_3 \rightarrow \dot{D} + CD_2{=}CH{-}CH_3, \quad (7)$$

$$CD_3\dot{C}HCH_3 \rightarrow \dot{H} + CD_3{-}CH{=}CH_2. \quad (8)$$

The authors detected 3% of C_2H_3D which they believe to have been formed via reaction (5). The ratio of the yield of ethylene formed as a result of isomerisation to the yield of propene is given by the ratio $(k_5 + k_6)/(k_7 + k_8)$ and corresponds to k_9/k_{10} for the reactions

$$CH_3\dot{C}HCH_3 \rightarrow [CH_3CH_2\dot{C}H_2] \rightarrow \dot{C}H_3 + C_2H_4, \quad (9)$$

$$CH_3\dot{C}HCH_3 \rightarrow \dot{H} + C_3H_6. \quad (10)$$

In the above temperature range, the ratio is on average 0.88. In general, this value increases with temperature, although some investigators[18,29] noted the opposite behaviour. Thus, despite the fact that the above investigation does not involve the rejection, in principle, of the possibility of the 3*ps* isomerisation of a small radical, under the usual cracking conditions this process takes place to only a small extent and can hardly compete with other reactions of the isopropyl radical.

The photolysis of di-isopropylmercury in a flow system at 150 — 300°C and a pressure of about 4 mmHg has been investigated[30]. Only one C_6 hydrocarbon (2,3-dimethylbutane, formed by the recombination if isopropyl radicals) was obtained. There is no isomerisation of iso-$\dot{C}_3H_7$ to n-$\dot{C}_3H_7$. However, the presence in the reaction products of isobutane and ethylene suggests the reaction

$$CH_3\dot{C}HCH_3 \rightarrow \dot{C}H_3 + CH_2{=}CH_2,$$

which is fully in agreement with the data of Heller and Gordon[18]. The results of a study by Billinge and Gowenlock[30] suggest that the decomposition and isomerisation stages take place simultaneously. This is indicated by the absence from the system of other isomeric hexanes following the addition of perfluorocyclohexane. Since even in the presence of the additive the pressure in the system did not exceed about 4.5 mmHg, deactivation due to perfluorocyclohexane is unlikely.

McNesby et al.[31] studied the pyrolysis of acetone in the presence of n-[2,2,3,3-D_4]butane at 365 — 506°C and 32 mmHg. Two decomposition pathways were suggested for each butyl radical:

$$\dot{C}H_2CD_2CD_2CH_3 \rightarrow \left[\begin{array}{c} D \\ \diagup \\ CH_2{-}CDCD_2CH_3 \end{array}\right] \rightarrow CH_2DCD{=}CD_2 + \dot{C}H_3, \quad (11)$$

$$\dot{C}H_2CD_2CD_2CH_3 \rightarrow CH_2{=}CD_2 + CD_2CH_3\dot{}, \quad (12)$$

$$CH_3\dot{C}DCD_2CH_3 \rightarrow \left[\begin{array}{c} CH_2{-}CDCD_2CH_3 \\ \diagdown \\ H \end{array}\right] \rightarrow CH_2{=}CDH + CD_2CH_3\dot{}, \quad (13)$$

$$CH_3\dot{C}DCD_2CH_3 \rightarrow CH_3CD{=}CD_2 + \dot{C}H_3. \quad (14)$$

The study of the mass spectra of the ethylene (mainly $CH_2 = CD_2$) and propene fractions led to the conclusion that reactions (12) and (14) predominate. Reaction (11), the 1 — 2 migration of deuterium, is not particularly important, since the amount of [D_4]-propene is not more than 1% of the main product—[D_3]propene. [D]ethylene is formed to a very slight extent or not at all. Thus isomerisations of the 3*sp* and 3*ps* types occur to an insignificant extent under the above experimental conditions.

Nevertheless the formation of [D_3]propene as the main product does not always imply a low degree of isomerisation of the butyl radical[21,24]. The formation of such propene can be accounted for also by the 1 — 3 migration of deuterium followed by decomposition via a reaction analogous to reaction (3):

$$\dot{C}H_2CD_2CD_2CH_3 \rightarrow CH_2DCD_2\dot{C}DCH_3 \rightarrow CH_3CD{=}CD_2 + \dot{C}H_2D.$$

In their study of the isotope composition of the methane fraction, Gordon and McNesby[32] did not detect dideuteriomethane, which should have been formed since under these conditions (400 — 450°) methyl radicals abstract deuterium more than twice as readily as hydrogen. However, the yields of methane and propene in the study by Kerr and Trotman-Dickenson[21] can be accounted for by the abstraction by free radicals of equivalent hydrogen atoms from n-valeraldehyde at the β- and γ-carbon atoms with subsequent decomposition of the large radicals:

$$\dot{R} + CH_3CH_2CH_2CH_2CHO \rightarrow RH + CH_3\dot{C}HCH_2CH_2CHO \rightarrow CH_3CHCH_2 + \dot{C}H_2CHO,$$
$$\dot{R} + CH_3CH_2CH_2CH_2CHO \rightarrow RH + CH_3CH_2\dot{C}HCH_2CHO \rightarrow \dot{C}H_3 + CH_2CHCH_2CHO.$$

Frey and Hepp[33], who studied the decomposition of di-n- and di-s-butylmercury at 490°C and 1 — 5 mmHg, also found that the decomposition of the n- and s-butyl radicals takes place in accordance with the β-rule and the isomerisation n-$C_4H_9 \rightleftharpoons$ s-C_4H_9 with subsequent decomposition takes place to only a very slight extent (about 0.1%) under these conditions if at all. It was also shown[34] that, at low pressures and at 350 — 525°C, the n-butyl radical decomposes only into ethylene and an ethyl radical and the s-butyl radical decomposes only into propene and a methyl radical. The decompositions of n-butyl and t-isobutyl radicals take place in accordance with the β-rule.

The isomerisations of isobutyl radicals were also studied by McNesby and Jackson in the thermal decomposition of [2-D]isobutane at 45 — 56 mmHg.[35] At 540°C the rate of the isomerisation reaction

$$(CH_3)_2CD\dot{C}H_2 \rightarrow (CH_3)_2\dot{C}CH_2D$$

is only one hundredth of the rate of the direct decomposition

$$(CH_3)_2CD\dot{C}H_2 \rightarrow \dot{C}H_3 + CH_3CD{=}CH_2.$$

Thus the results quoted show that the usual experimental technique and method do not allow a solution of the problem of the possible 1 — 2 or 1 — 3 migration of hydrogen in alkyl radicals and indicate only an unimportant role of these processes in the cracking and photolysis of many organic compounds. In particular, the β-rule holds with a high degree of precision for the decomposition of alkyl radicals.

The 3*sp* isomerisation of n-$\dot{C}_3H_7$ and iso-$\dot{C}_3H_7$ is also insignificant. In the study already discussed[30], the only hexane obtained in the photolysis of di-n-propylmercury at 380 — 460°C was n-hexane. Similarly in the photolysis of di-n-propyl ketone (55 — 357°C, 8 — 115 mmHg), 98% of the C_6 fraction consisted of n-hexane[36]. Lossing and de Sousa[34] also showed that the decomposition products of n-propyl radicals are ethylene and methyl radicals.

The most accurate results, whereby it is possible to infer the occurrence of 1 — 2 migration of hydrogen in radicals in both gaseous and liquid phases, were obtained in a tracer atom study employing hydrogen and carbon isotopes. Brown and Russell[37] chlorinated photochemically 2-methyl-[2-D]propane at −15°C. The products were t-butyl chloride, isobutyl chloride, hydrogen chloride, and deuterium hydride. This indicates the occurrence of two reactions:

$$(CH_3)_2CDCH_3 + Cl_2 \rightarrow (CH_3)_2CD\dot{C}H_2 + HCl, \quad (A)$$

$$(CH_3)_3CDCH_3 + Cl_2 \rightarrow (CH_3)_2\dot{C}CH_3 + DCl. \quad (B)$$

The occurrence of the rearrangement of radicals (A) and (B) was inferred from the DCl/HCl and t-butyl chloride/isobutyl chloride ratios respectively. The excellent agreement between these ratios clearly indicates the absence of any considerable degree of isomerisation with transfer of hydrogen according to the mechanisms

$$(CH_3)_2CD\dot{C}H_2 \rightarrow (CH_3)_2\dot{C}CH_2D \text{ and } (CH_3)_2\dot{C}CH_3 \rightarrow (CH_3)_2CH\dot{C}H_2,$$

$$(CH_3)_2CDCH_2 + (CH_3)_2CDCH_3 \rightarrow (CH_3)_2CDCH_2D + (CH_3)_2\dot{C}CH_3,$$

which constitutes essentially intermolecular isomerisation.

On the other hand, Bhardwaj and Lee[38] studied the isomerisation of [1-^{14}C]ethyl iodide and [2-^{14}C]ethyl iodide under the influence of γ-radiation and observed that at room temperature in a 2% aqueous solution of [1-^{14}C]ethyl iodide 0.28 of a molecule of [2-^{14}C]ethyl iodide is formed for each 100 eV of absorbed energy regardless of radiation dose†. However, the addition of 1% of iodine before irradiation lowers the degree of rearrangement to zero. The authors believe that the most probable process mechanism involves 1 — 2 migration of hydrogen:

$$CH_3-{}^{14}\dot{C}H_2 \rightarrow \dot{C}H_2{}^{14}CH_3. \quad (15)$$

The effect of iodine can be explained by a higher rate of its addition to the ethyl radical compared with reaction (15). The formation of [2-^{14}C]ethyl iodide via a different pathway, namely by the reaction between the main products (ethylene and hydrogen iodide),

$$CH_2={}^{14}CH_2 + HI \rightarrow CH_2I-{}^{14}CH_3,$$

is possible in principle but the marked inhibiting effect of iodine would then be unexplained. Similarly, when a 2% aqueous solution of [1-^{14}C]ethanol is irradiated with γ-rays, [2-^{14}C]ethanol with $G \simeq 0.04$ is formed[39], which is also evidence of a hydrogen shift. The higher value of G found by Bhardwaj and Lee[38] can be accounted for by the greater ease of formation of the ethyl radical from ethyl iodide than from ethanol.

There are also many experimental data of a different type, indicating the possibility of the migration of a hydrogen atom to an adjoining carbon atom with a free valence. Thus Callear and Cvetanović[40], who studied the mercury-photosensitised decomposition of C_2H_4, C_2D_4, and *cis*-$C_2D_2H_2$ at room temperature and 16 — 750 mmHg, found that the main products in this process (hydrogen and acetylene) are not obtained by a radical mechanism but in consequence of homogeneous intermolecular processes. In the photolysis of *cis*-$C_2D_2H_2$, the isotopic composition of the hydrogen formed corresponds to the ratios $H_2 : HD : D_2 = 2 : 5.7 : 1$. One explanation of this finding involves the recognition that hydrogen may migrate in excited species. The available data do not allow a rigorous proof of the process mechanism but the migration of hydrogen between carbon atoms is supported by the isomerisation of *cis*-$C_2H_2D_2$ to the *anti*-form, which can occur even on impact deactivation of the excited species (in the presence of a large amount of added carbon dioxide). On the other hand, if in the excited state of ethylene the hydrogen atoms exchange with one another, the hydrogen isotope composition should be identical regardless of whether *cis*- or *anti*-$C_2H_2D_2$ undergoes the mercury-sensitised decomposition. In the decomposition of *anti*-$C_2H_2D_2$, the hydrogen isotope composition corresponds to the ratios $H_2 : HD : D_2 = 1.8 : 4.6 : 1$.[41] This shows that intramolecular hydrogen exchange occurs in ethylene excited with $Hg(^3P_1)$. However, Okabe and McNesby[42] believe that this process is unlikely in direct photolysis *in vacuo* by ultraviolet radiation (1849 — 1236 Å).

Scala and Ausloos[43], who investigated the photolysis of $(CH_3)_2CDCH_2CH_3$ and $(CH_3)_2CHCH_2CH_3$ with light at a wavelength of 1048 — 1470 Å at a pressure of several mmHg, concluded that the rearrangements $CH_3\ddot{C}CH_3 \rightarrow CH_3CH = CH_2$ and $\ddot{C}HCD_3 \rightarrow CHD = CD_3$ take place in the propylidene and ethylidene biradicals respectively. Similarly studies of the photolysis of ethane (1048 — 1067 Å) showed[44-52] that for the above energies the most important process is splitting off of molecular hydrogen, which involves almost exclusively only one carbon atom. The vibrationally excited ethylidene formed on deactivation rearranges to ethylene: $\ddot{C}HCH_3^* \xrightarrow{M} CH_2 = CH_2$. Similar rearrangements with 1,2-shifts of hydrogen or deuterium were observed in the photolysis of other compounds. The 3*sp* migration of hydrogen in the trimethylene biradical occurs in the isomerisation of cyclopropane to propene (see the review by Lazár and Kysel[9]). It was found that[53] the activation energy for the transition

$$\dot{C}H_2CH_2\dot{C}H_2 \rightarrow CH_2{=}CHCH_3$$

is only 9.5 kcal mole^{-1}.

There are many experimental data indicating the occurrence of rearrangements of hydrocarbon radicals also in the solid phase. Ayscough et al.[54] observed a change in the hyperfine structure of the ESR spectrum of the n-propyl radical, reflecting the transformation of the latter into an isopropyl radical, and a spontaneous transformation of the spectrum of the isobutyl radical into that of the t-butyl radical. These transitions occur at the temperature of liquid nitrogen. A similar situation was observed by Iwasaki and Toryama[55] in an ESR study of the photoinduced radical transformation of isobutyl bromide at 77°K. γ-Irradiation of this compound leads to the formation of primary isobutyl radicals which during the period of storage (about 40 days) in the dark at 77°K are spontaneously converted into t-butyl radicals. Illumination of the latter with ultraviolet light at the same temperature for 90 min yields isobutyl radicals, i.e.

$$CH_3-\underset{|}{\overset{CH_2Br}{CH}}-CH_3 \xrightarrow[77°K]{\gamma} CH_3-\underset{|}{\overset{\dot{C}H_2}{CH}}-CH_3 \underset{h\nu}{\rightleftarrows} CH_3-\underset{\cdot}{\overset{CH_3}{C}}-CH_3.$$

Similar transitions occur on γ-irradiation of many polymers at 77°K. The process involving polypropylene[56] takes place as follows:

$$\text{polypropylene} \xrightarrow[77°K]{\gamma} \ldots CH_2-\underset{|}{\overset{\dot{C}H_2}{CH}}-CH_2 \ldots \underset{h\nu}{\rightleftarrows} \ldots CH_2-\underset{\cdot}{\overset{CH_3}{C}}-CH_2.$$

In general one may say that, under the influence of ultraviolet light, 3*pt* migration of hydrogen takes place at the temperature of liquid nitrogen with formation of an

† The number of molecules undergoing rearrangement following the absorption of 100 eV of energy is designated by the symbol *G*.

energetically more favourable radical. As was to be expected, the reverse process occurs spontaneously.

The isomerisation of radicals in the gas phase with 1 — 2 migration of hydrogen has not yet been investigated even qualitatively. The data examined suggest that the process can occur in principle. It is undoubtedly difficult under the usual conditions in the cracking of hydrocarbons (up to 600°C) but probably occurs in reactions of "hot" species and also in free-radical processes where subsequent reactions of the radical are "slow". Possibly intramolecular rearrangements of the simplest alkyl radicals might be observed in the study of processes at higher temperatures (about 1000 — 1500°C) and lower pressures.

III. 1 — 3 MIGRATION OF A HYDROGEN ATOM

Even fewer data have been obtained for the 4*ab* migration of hydrogen atoms in alkyl radicals in the gas phase. Apart from the studies by Trotman-Dickenson already mentioned[21,24], one may point to the work of Rabinovitch and coworkers[14], who studied the intramolecular isomerisation of many vibrationally excited alkyl radicals and concluded that rearrangements with $N < 5$ are insignificant and cannot occur as simple hydrogen transfers.

The possibility of 1 — 3 migration of hydrogen is indicated by a study of Reutov and Shatkina[57]. Using the carbon-14 isotope, they found that the free propyl radical formed on thermal decomposition in boiling carbon tetrachloride of n-butyryl peroxide labelled in the α-position,

$$(CH_3CH_2{}^{14}CH_2COO)_2 \rightarrow 2CH_3CH_2{}^{14}\dot{C}H_2 + 2\,CO_2,$$

isomerises with migration of a hydrogen atom from the β-position:

$$CH_2CH_2{}^{14}\dot{C}H_2 \rightleftarrows \dot{C}H_2CH_2{}^{14}CH_3. \qquad (16)$$

Analysis of the decomposition products showed that under these conditions such isomerisation occurs to the extent of 4.0 ± 0.5%. In their attempt to confirm reaction (16) by an independent method, Reutov et al.[58] studied the pyrolysis of [α-D_2]butyryl peroxide in boiling carbon tetrachloride. Together with the normal product, the formation (in an amount of 1.3 ± 0.1%) of the anomalous product $CD_2HCH_2CH_2Cl$ was observed, which also indicates the occurrence of the isomerisation reaction (16). The replacement of carbon tetrachloride by bromoform as a solvent leads to a decreased yield of the rearranged product (0.68 ± 0.1% at 140°C),[59] which can be explained by a decrease of the lifetime of the free radical. It was also shown that the structure of the rearrangement product cannot be accounted for by exchange reactions during analysis. One piece of evidence for the possibility of 1 — 3 migration of hydrogen, which is interesting rather than convincing, is provided by the experiments of Voevodskii and coworkers[60-63]. The authors showed by kinetic calculations[60] that the higher rate of exchange of hydrogen for deuterium in alkyl radicals observed in various studies at room temperature can be explained by the reactions $RH + D_2 \rightarrow RD + HD$, $RHD + D_2 \rightarrow RD_2 + HD$, etc., with only the hydrogen atoms linked to the carbon atom with a free valence being capable of undergoing exchange. However, further studies[61-63] showed that this limitation extends only to adjacent carbon atoms. If a free valence can migrate spontaneously to another carbon atom, further hydrogen exchange is probable. As a result, a radical with a higher deuterium content should be formed than in the absence of isomerisation. It has been shown for isobutyl radicals formed by the reaction $(CH_3)_2C = CH_2 + D \rightarrow (CH_3)_2CD\dot{C}H_2$ that the fraction of C_8 hydrocarbons, which are formed by the recombination of these radicals, is characterised by a degree of exchange of 40 — 50%, while without allowance for isomerisation the maximum degree of exchange should be 30%.[61] Consequently the following isomerisations are possible at room temperature:

$$CH_3(CH_3)\,CD\dot{C}H_2 \rightleftarrows CH_3(\dot{C}H_2)\,CDCH_3 \rightleftarrows \dot{C}H_2(CH_3)\,CDCH_3$$

in which 1 — 3 migration of hydrogen takes place. On the other hand, it has been shown for the isopropyl radical and radicals of the type $(CH_3)_2CD\dot{C}(CH_3)_2$ that the migration of the free valence to an adjacent carbon atom is impossible[63].

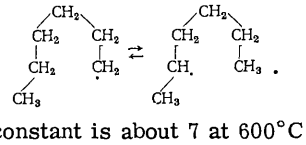
A weak feature of these experiments is the experimental technique. Atomic hydrogen was withdrawn from the discharge tube and was directed to the reactor mixed with the hydrocarbon and deuterium under a pressure of 0.2 — 0.4 mmHg at a rate up to 3 m s^{-1}. Although separate experiments showed that under these conditions the hydrocarbon hardly reached the discharge zone (the concentration of RH in the discharge zone was ≤0.25%[63]), the rate of diffusion of deuterium may be higher and the investigators might have dealt with atomic and not molecular deuterium. In this case the high degree of deuteriation cannot be accounted for by radical rearrangements.

Chesick[64], who investigated the photolysis of *cis*-but-2-ene by light at a wavelength of 2026 — 2062 Å at room temperature and 540 mmHg, concluded that 1 — 3 migration of hydrogen in the unsaturated radical $CH_3CH = \dot{C}H$ does occur:

$$CH_3CH{=}\dot{C}H \rightarrow \dot{C}H_2CH{=}CH_2.$$

IV. MIGRATION OF A HYDROGEN ATOM TO A MORE REMOTE CARBON ATOM WITH A FREE VALENCE

Rearrangements of this kind were first suggested in 1943 by Kossiakoff and Rice[65]. They believe that alkyl radicals containing five or more carbon atoms can isomerise under the usual cracking conditions. The activation energy for such isomerisation may be much lower than the decomposition energy of the radical. As a result, equilibrium should be established between two isomeric forms, for example in the isomerisation of primary n-hexyl radicals:



The equilibrium constant is about 7 at 600°C. The authors employed this hypothesis to calculate the thermal decomposition products of n-hexane and certain octanes. It was found that the calculation which includes the possibility of an intramolecular hydrogen transfer agrees better with experiment than calculation which neglects isomerisation. For radicals with longer chains, for example as obtained in the cracking of n-hexadecane[66], there is an even greater number of possibilities of isomerisation and the improvement of the agreement between the yield of reaction products and the calculation becomes even more marked when these possibilities are taken into account. Somewhat later Sefton and LeRoy[67] studied at 250 — 300°C the polymerisation of ethylene initiated by ethyl radicals labelled with carbon-14 in the methyl group.

2-Methylbut-1-ene was detected in the reaction products. If this product were formed by the addition of a labelled ethyl radical to propene with subsequent disproportionation of the 2-methylbutyl radical, its molar radioactivity should have been unity. Experiment however, yielded a value equal to only half that quantity. The authors explain the discrepancy by intramolecular radical isomerisation involving 1 — 4 and 1 — 5 migration of hydrogen.

No less convincing are the quantitative results of the experiments by Gordon and McNesby[68], who also investigated the reaction of methyl radicals with ethylene in the temperature range 300 — 500°C and at pressures in the range 109 — 360 mmHg. Under these conditions, the main product is propene. The authors suggest the following process mechanism:

$$\dot{C}H_3 + CH_2{=}CH_2 \rightarrow CH_3CH_2\dot{C}H_2 \xrightarrow{+CH_2=CH_2} CH_3CH_2CH_2CH_2\dot{C}H_2,$$

$$CH_3CH_2CH_2CH_2\dot{C}H_2 \rightarrow CH_3\dot{C}HCH_2CH_2CH_3 \rightarrow CH_3CH{=}CH_2 + \dot{C}_2H_5.$$

The reaction mixture contains also but-1-ene obtained as a result of a 1,5-rearrangement of heptyl radicals:

$$CH_3(CH_2)_3\dot{C}H_2 + CH_2{=}CH_2 \rightarrow CH_3(CH_2)_5\dot{C}H_2 \rightarrow CH_3CH_2\dot{C}H(CH_2)_3CH_3 \rightarrow$$
$$\rightarrow CH_3CH_2CH{=}CH_2 + \dot{C}H_2CH_2CH_3.$$

The validity of the above mechanism was demonstrated by the introduction of CD_3 radicals. At 300°C the propene fraction had the following isotope composition: 30% C_3H_6, 20% C_3H_5D, 30% $C_3H_4D_2$, and 20% $C_3H_3D_3$. This indicated the occurrence of exchange processes. One of the possible mechanisms, involving a number of rapid hydrogen exchanges between carbon atoms in the 1- and 4-positions and in the 1- and 5-positions, can be represented as follows:

$$CD_3(CH_2)_3\dot{C}H_2 \xrightarrow{1,5} \dot{C}D_2(CH_2)_3CH_2D \xrightarrow{1,5} CD_2H(CH_2)_3\dot{C}HD \rightarrow \text{etc.},$$
$$\downarrow 1,4 \qquad\qquad \downarrow 1,4 \qquad\qquad \downarrow 1,4$$
$$CD_3\dot{C}H(CH_2)_2CH_3 \rightarrow CD_3CH{=}CH_2 + \dot{C}_2H_5 \mid CD_2H\dot{C}H(CH_2)_2CH_2D \rightarrow CD_2HCH{=}CH_2 + \dot{C}_2H_4D,$$
$$\downarrow$$
$$CD_2H(CH_2)_2\dot{C}HCH_2D \rightarrow \dot{C}_2H_3D_2 = CH_2{=}CHCDH_2.$$

Wijnen[69], who photolysed heptan-2-one at 60 — 200°C, detected 2-methylpentane among the reaction products. This compound is produced by combinations of methyl and s-pentyl radicals. Consequently the reaction $\dot{C}H_2(CH_2)_3CH_3 \rightarrow CH_3(CH_2)_2\dot{C}HCH_3$ with 1 — 4 hydrogen migration plays a significant role not only at 250°C as, in the work of Gordon and McNesby[68], but also at a temperature as low as 150°C.

There are reliable data indicating the migration of hydrogen atoms in radicals in the liquid phase. For example, in a study of the telomerisation of ethylene by acetic acid at 140°C, Freidlina et al.[70] detected isoacids (α-ethylcaproic and α-n-butylcaproic acids) in the products. The formation of these acids can be readily explained by a rearrangement of $\dot{C}H_2CH_2CH_2CH_2CH_2COOH$ to $CH_3CH_2CH_2CH_2\dot{C}HCOOH$. On the other hand, the absence of isohexanoic acid from the reaction mixture indicates the impossibility of 1 — 3 migration of hydrogen in the $\dot{C}H_2CH_2CH_2COOH$ radical under these conditions. It has also been shown[71] that, as was to be expected, an increase of temperature favours the formation of a rearranged product, while a change in the concentration of the reactants does not have a significant influence on the yield.

Rearrangements similar to that indicated above occur also in the telomerisation of ethylene by methyl chloroacetate[72], methyl alcohol[72], propionic acid[73], methyl propionate[73], acetoacetic ester[73], etc. Probably, if the temperatures are sufficiently high and the telogens are comparatively ineffective, the rearrangement of radicals with 1 — 5 migration of hydrogen is a general phenomenon[72].

However, whereas radical isomerisation plays an appreciable role in solutions of relatively inactive telogens, in the telomerisation of ethylene in carbon tetrachloride solutions (at 140°C)[74-76] its importance is low. On passing to the gas phase (at a pressure of about 0.3 atm), 70 — 80% of the products are isomers of the normal telomers. Under these conditions, unimolecular rearrangements compete successfully with bimolecular reactions, for example:

$$Cl_3C(CH_2)_5CH_2- \begin{cases} \xrightarrow{+CCl_4} Cl_3C(CH_2)_5CH_2Cl & (38\%), \\ \xrightarrow{+C_2H_4} Cl_3C(CH_2)_7\dot{C}H_2 & (\sim 4\%), \\ \xrightarrow[\text{rearrangement}]{} Cl_3CCH_2\dot{C}H(CH_2)_3CH_3 & (\sim 58\%) \text{ etc.} \end{cases}$$

The contribution of such rearrangements diminishes very markedly with increase of pressure and ethylene and carbon tetrachloride concentrations.

Intramolecular rearrangements of radicals in the solid phase have also been mentioned[77,78]. A study of the hyperfine structure of the ESR spectra of alkyl radicals formed from n-hexadec-1-ene, n-dec-1-ene, n-oct-2-ene, n-hept-2-ene, etc. on irradiation with γ-rays (at 77°K) showed that they are spontaneously converted into energetically more favourable allylic radicals:

$$CH_2-\dot{C}H-(CH_2)_n-CH{=}CH-CH_2 \underset{h\nu}{\rightleftarrows} CH_2-(CH_2)_n-\dot{C}H-CH{=}CH-CH_2.$$

Under these conditions, the overall spin concentration remains constant. The reverse transition at liquid nitrogen temperature can be achieved on irradiation with ultraviolet light ($\lambda \leqslant 3400$ Å).

During recent years, the first quantitative data have been obtained for type 5*sp* and 6*sp* isomerisation rate constants. In a study of the photolysis of a mixture of acetone and ethylene (165 — 230°C, $P \simeq 104$ mmHg), Endrenyi and LeRoy[79] succeeded in estimating quantitatively the relative contributions of the reactions of n-propyl radicals. The radicals were obtained by the addition of $CH_3^{\cdot}$ to ethylene. The presence of isohexane among the reaction products was regarded by the authors as evidence that some of the n-pentyl radicals isomerise to s-pentyl radicals. The rate constant for the rearrangement

$$\text{n-}\dot{C}_5H_{11} \rightarrow \text{s-}\dot{C}_5H_{11} \qquad (17)$$

was found to be

$$k_{17} = 10^{7.148} \exp(-10800/RT)\ s^{-1}.$$

Watkins and Ostreko[80] studied the photolysis of a mixture of azobutane and ethylene at temperatures in the range 79 — 132°C and a pressure of about 55 mmHg. The presence of s-hexyl radicals in the system is indicated by the presence of 3-methylheptane in the products. Using the method of a previous investigation[79], the rate constant for the isomerisation

$$\text{n-}\dot{C}_6H_{13} \rightarrow \text{s-}\dot{C}_6H_{13}, \qquad (18)$$

was determined:

$$k_{18} = 10^{7.3 \pm 1.0} \exp[(-8300 \pm 1700/RT)]\ s^{-1}.$$

Rabinovitch and coworkers[14] studied the isomerisation of vibrationally excited alkyl radicals: heptyl-3· (Hp3·), octyl-4· (Oc4·), octyl-2· (Oc2·), 3-methylpentyl-2· (3MP2·), nonyl-2· (N2·), 3-methylhexyl-2· (3MH2·), and 3,3-dimethylhexyl-2· (33DMH2·). In all cases the radicals formed were chemically activated by the addition of a hydrogen atom to the corresponding alkene at room temperature. The results are compiled in Table 2, which also includes the rate constants for the competing isomerisation reactions expressed relative to the 5*ss* process, the rate of which was assumed to be unity.

Table 2 shows that the radicals the isomerisation of which is energetically feasible (i.e. for $N \geqslant 5$) rearrange almost completely and in most cases the isomerisation is the fastest process among those occurring in the given systems.

Table 2. Relative rates of isomerisation of radicals.

Radical	5sp	5 ss	5 pp	6 sp	6 ps	6 ss	7 ss	Products and absolute rates of dissociation of C-C bonds, 10^5 s^{-1}	
Hp3·	—	1(7.5)[a]	—	—	<1(<7.5)	—	—	B1+*n*-Pr·	1.2
Oc4·	—	1(2.1)	—	—	—	—	—	H1+Et	0.14
Oc2·	—	1(8)	—	—	—	75(600)	—	Pr1+P1·	1.0
N2[b]	—	1(20)	—	—	—	100(2000)	5(100)	Pr1+H1·	0.09
Oct·[b]	—	—	(<0.05)	(>300)	—	—	—	C_2H_4+H1·	1.0
3HP1[b]	(<0.5)	—	—	—	—	—	—	C_2H_4+SBu·	20.0
3MH2·	—	(2.5)	—	—	—	—	—	t- B2+*n*- Pr·	4.0
3MH1·	—	—	—	(>100)	—	—	—	C_2H_4+P2·	10.0
33DMH2·	—	(7.0)	—	—	—	—	—	2MB$_2$+*n*-Pr	2.3
33DMH1·	—	—	—	(<200)	—	—	—	C_2H_4+2MP2·	4.0

[a] The numbers in round brackets denote the ratio of the rate of isomerisation to the rate of decomposition indicated in the last column.

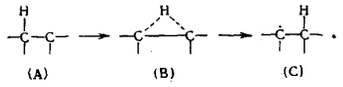
[b] The rates of decomposition have been estimated to within a factor or two.

Examination of the data leads to the conclusion that the isomerisation of alkyl radicals with hydrogen migration, proceeding via five-, six-, and seven-membered cyclic transition states, is possible. This process must undoubtedly be taken into account when specific free-radical reactions are considered.

V. THE MECHANISM OF THE MIGRATION OF HYDROGEN IN ALKYL RADICALS

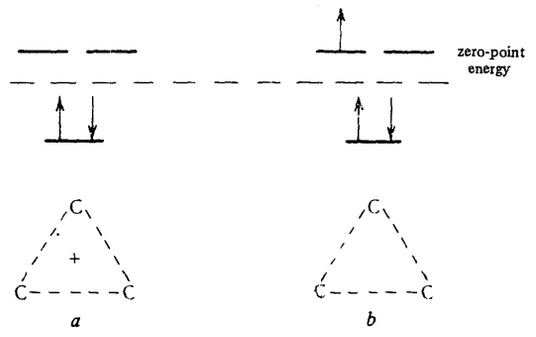
When examining the literature on the rearrangement of alkyl radicals, one cannot avoid the problem of the mechanism of hydrogen migration. Unfortunately the detailed mechanisms of the rearrangements have been little investigated and only hypothetical views have been expressed on this problem.

At the present time the hypothesis of Kossiakoff and Rice[65] that hydrogen migration in long-chain radicals proceed via a cyclic transition state is generally accepted. However, the possibility of forming a three-membered complex on transfer of hydrogen from a carbon atom to an adjacent carbon atom is nevertheless still open to some doubt[14]. Indeed approximate quantum-mechanical calculations show that a three-membered transition state should have a high activation energy, since "attack" on the bond takes place at an angle different from the most favourable angle, as a result of which the ring is strained[10,11]. In the rearrangement of a substance (A) to a substance (C), there is an intermediate with a configuration (B):



(A) (B) (C)

The activation energy for the rearrangement is determined by the energy difference between the compound (A) and the intermediate complex (B). The triatomic structure (B) has three orbitals, one of which is bonding and the other two are degenerate antibonding. In the case of the carbonium ion, the tendency of which to rearrange is well known, there are only two electrons and these can be assigned to the lowest bonding orbital (Fig. *a*).



Energy levels for a three-orbital three-carbon system[11].

The free electron of the radical must pass to one of the antibonding orbitals (Fig. *b*) which destabilises the system and increases its energy. The stabilisation and decrease of the energy of the transition state (B) are achieved by a redistribution of electron density which occurs during the shift of the migrating group, which in turn is determined by its nature (see for example data on the migration of aryl groups[81]). On the other hand, the 1 — 2 migration of halogen atoms, which take place fairly readily[13], cannot be understood on the basis of the foregoing considerations. Mayants[82] explains this contradiction by a difference between the vibration frequencies and modes of substituted and unsubstituted radicals. He believes that the rate of rearrangement is largely determined by the probability of the occurrence of the required transitional configuration as a result of intramolecular vibrations. On the other hand, the probability of the formation of such a transition state increases, other conditions being equal, with decrease of the vibration frequencies. One may expect[72] that, for radicals containing a halogen atom or an aryl group in the α-position relative to the free valence, the frequencies of the vibrations responsible for the formation of the transitional configuration will decrease in relation to unsubstituted radicals both as a result of the increase of the mass of the substituent and probably owing to a decrease of the deformation force constant. Therefore in substituted radicals one should expect an increase of the rearrangement rate constant (the 1 — 2 migration of the halogen and the aryl group) compared with the rearrangement of the unsubstituted radical (1 — 2 migration of hydrogen). If, on the other hand, the substituent is an alkyl group, then, according to Freidlina[72], isomerisation involving the migration of hydrogen atoms more remote from the radical centre and a more favourable angle of attack may compete with the 1 — 2 migration of the alkyl group.

On the other hand, if 1 — 2 and 1 — 3 migration of hydrogen is difficult on energetic grounds, the steric factors governing the rate constants for such processes should be fairly high. Indeed, within the framework of

absolute reaction rates, the pre-exponential factor for gas-phase reactions

$$A = \varkappa e \frac{kT}{h} e^{\frac{\Delta S^+}{R}}$$

is determined by the activation entropy ΔS^*, which is equal to the difference between the entropies of the activated and initial states of the system. For reactions proceeding via a three-membered cyclic activated complex, the entropies of the complex and the reactant differ mainly in terms corresponding to the loss of one hindered internal rotation and the change of the frequencies in the activated complex. This difference is of the order of −4 cal mole^{-1} deg^{-1}. On the other hand, rearrangements proceeding via five- and six-membered, etc. transition states lead to a loss of 4, 5, and more internal rotations in the complex. This greatly reduces the A factors for such rearrangements. Thus we observe the following situation: processes with 1 — 2 migration of hydrogen are characterised by a high activation energy and a high pre-exponential factor, while the kinetic parameters for many-centre processes are lower. Therefore in the series of 1 — 2, 1 — 3, 1 — 6, ... migrations of hydrogen one should expect the appearance of a compensation effect.

It is noteworthy that the anomalously low pre-exponential factors for reactions (17) and (18) cannot be accounted for within the framework of the theory of absolute reaction rates. This led Endrenyi and LeRoy to the conclusion[79] that reaction (17) has a transmission coefficient $\varkappa \ll 1$. However, experiments with added inert gases[80] did not show changes in the measured rate constant, which is evidence that the process is adiabatic. In order to account for the extremely low entropy of activation for these reactions, Watkins and Ostreko[80] proposed the model of a "rigid" cyclic transition state with very strong terminal interactions due to the fact that the hydrogen atom belongs to both "ends" of the radical. In this case the force constants of the low-frequency vibrations in the complex increase rapidly, which causes a decrease in entropy activation for the reaction in addition to a decrease owing to the loss of capacity for certain types of internal rotation.

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Heterocycles Containing the Indole Residue

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The review describes the latest advances in the synthesis of heterocyclic compounds containing the indolyl residue, among which many physiologically active substances have been found. It is the first attempt at a general and systematic account of the extensive literature data on this subject.

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I. INTRODUCTION

The pronounced physiological activity of many indole derivatives such as reserpine, serotonin, tryptamine, tryptophan, lysergic acid, etc. has aroused an unflagging interest among chemists and pharmacologists in the chemistry of indole over a period which now runs into several decades. Compounds in which the indole ring is condensed with heterocyclic compounds (numerous derivatives of carbolines, eserine, etc.) are of the greatest interest. However, during recent years there has been a considerable growth of interest in heterocyclic compounds containing the indole residue. Here one should include numerous indolyl derivatives of pyridine, piperidine, pyrrolidine, piperazine, etc. Many physiologically active compounds have been found among them. Such compounds have been isolated also from natural products—for example, the antiobiotics indolemycin and pimprinine.

Extensive data have accumulated in this field, however, they are widely scattered and hitherto have not been described systematically. Therefore we attempted to fill this gap bearing in mind that a review of this kind may prove useful in the choice of a further course of study on the preparation of new pharmacologically active indole derivatives.

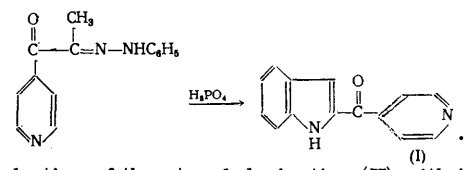
II. PYRIDINE DERIVATIVES OF INDOLE

Among indolyl derivatives of heterocycles, pyridine and piperidine derivatives probably play the most important role. The high interest in these compounds is partly due to the fact that among them many pharmacologically valuable preparations have been found and also because of their suitability as starting materials for studies on the synthesis and preparation of many indole alkaloids.

1. Indolylpyridines

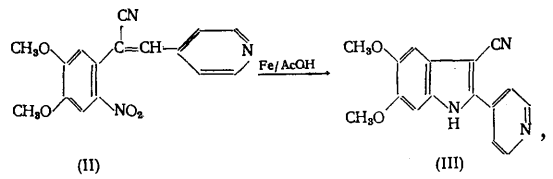
The Fischer indole synthesis is widely used for the preparation of indolylpyridines. For example, the cyclisation of the phenylhydrazones of 2-acetylpyridine in the presence of polyphosphoric acid leads to 2-(2-pyridyl)-indole [1,2]. 2-(3-Pyridyl)indole [1-4], 2-(4-pyridyl)indole [1,3], and 2-(5-ethyl-2-pyridyl)indole [1] were synthesised in the same way. Some of these compounds exhibit a diuretic activity and others may be used to reduce aldosterone concentration or in the treatment of cardiovascular diseases [5]. In addition, certain chemical reactions of the indolylpyridines synthesised have been investigated, such as, for example, their conversion into Mannich bases and cyanoethylation [1].

2-Isonicotinoylindole(I) was also synthesised by the Fischer reaction [6]:



(I)

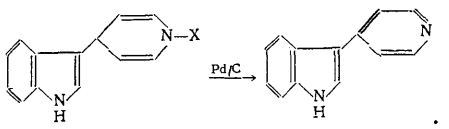
The reduction of the styryl derivative (II) with iron in acetic acid constitutes a very convenient synthesis of 5,6-dimethoxy-2-(4-pyridyl)indole-3-carbonitrile (III),



(II) (III)

and also of its thiophen and furan analogues [7].

3-(4-Pyridyl)indole (IV) is formed as a result of the debenzoylation and simultaneous dehydration of the *N*-benzoyl derivative (V) with atmospheric oxygen [8,9]. It can be obtained in large amounts by refluxing compound (V) in phenyl ether in the presence of palladised charcoal and one equivalent of dibenzylamine [10]:

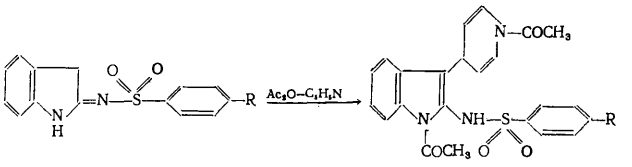


(V, X=C_6H_5CO)
(VI, X=CN)

(IV)

Compound (V) is readily formed from indole, pyridine, and benzoyl chloride [8]. Products with a similar structure are formed by quinoline, isoquinoline, phenanthroline, and scatole [9].

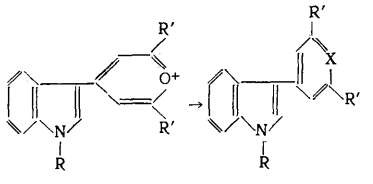
Another example of this kind of reaction is the formation of dihydropyridines of type (VII) from indole and tosyl azide or *N*-acetylsulphanilyl azide [11]:



(VII, R=CH_3, $NHCOCH_3$)

The benzoyl derivative (V) reacts with benzaldehyde to form diphenyltetrahydroindolocarbazole [12], while its analogue (VI) decomposes with formation of indole on treatment with 2% NaOH in aqueous alcohol [13].

The reaction, proposed by Dorofeenko et al. [14], of ammonia with indolylpyrylium salts (VIII), obtained by the interaction of (3-indolyl)-1,5-diketones with triphenylmethyl perchlorate, constitutes a very convenient method for the preparation of 4-(3-indolyl)pyridines (IX) containing various substituents in the pyridine ring. Treatment of compound (VIII) with tri(hydroxymethyl)phosphine in pyridine yields the phosphorus analogues (IX)—derivatives of indolylphosphabenzene (X): [15]

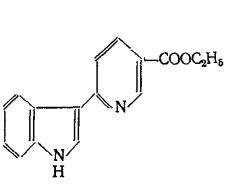


(VIII)

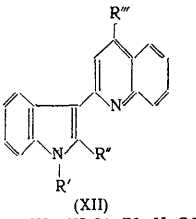
(IX, X=N)
(X, X=P)

This reaction may be of definite interest, since the salts (VIII) are readily formed in high yield also on treatment of *N*-substituted indoles with two moles of a 2,6-diarylpyrylium salt in dimethylformamide (DMF). [16]

Activated pyridine derivatives, such as the *N*-oxides, have been recommended as convenient starting materials for the synthesis of pyridine derivatives of indole. 2-(3-Indolyl)-5-ethoxycarbonylpyridine (XI) is formed from indole and the *N*-oxide of ethyl nicotinate in the presence of benzoyl chloride [17], while quinoline *N*-oxides yield a series of 2-(3-indolyl)quinoline derivatives of type (XII). [17] These reactions have been widely investigated in the interaction between indole, 2-phenylindole, and 1-methyl-2-phenylindole with *N*-acyloxyquinolinium, *N*-acyloxyisoquinolinium, and *N*-acyloxylepidinium derivatives [18]:



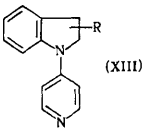
(XI)



(XII)

R'=H, CH_3, CH_3CO; R''=H, C_6H_5; R'''=H, Cl.

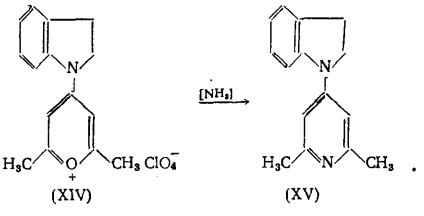
A series of pyridine derivatives of indoline have been described. For example, *N*-(4-pyridyl)indolines of type (XIII) can be readily obtained by fusing together the hydrochlorides of 2,3-dihydroindoles with *N*-(4-pyridyl)-pyridinium chloride [19,20]:



(XIII)

N-(5-Nitro-2-pyridyl)indolines, which have been recommended as polymer stabilisers, can be synthesised by the reaction of 2-chloro-5-nitropyridine with indolines at 80–110°C. [21]

1-(2,6-Dimethyl-4-pyridyl)indoline (XV) is formed in a high yield when 4-(1-indolinyl)-2,6-dimethylpyrylium perchlorate (XIV), obtained from indoline and 4-methoxy-2,6-dimethylpyrylium perchlorate, is treated with ammonium acetate or carbonate [22].



(XIV)

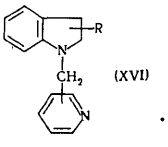
(XV)

The synthesis of indolines containing the isoquinoline residue by the interaction of benzoylisoquinolinium chloride with *N*-substituted indolines was described recently [23]. 1-Acylpyridinium salts are converted by the same reaction into 5-pyridylindolines [24] and 1-acylquinolinium salts give rise to 5-(2-quinolyl)indolines [25].

Many of the pyridine derivatives of indolines suppress the motor capacity of animals stimulated by amphetamine, suppress the orientation reflex, and sharply prolong the duration of Nembutal narcosis in mice, while exhibiting a moderate antiserotonin activity [19].

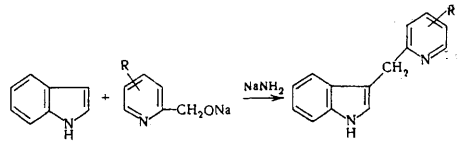
2. Indolylmethylpyridines

Pyridylmethylindolines (XVI) are obtained by the reaction of chloromethylpyridines with indoline [19]:



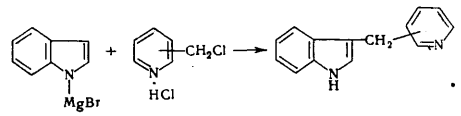
(XVI)

Other methods of synthesis are also known. One of these consists in the interaction of sodium salts of 2-hydroxymethylpyridines with indole [26]:



(R = 3-CH_3, 5-CH_3, 6-CH_3, 5-C_2H_5)

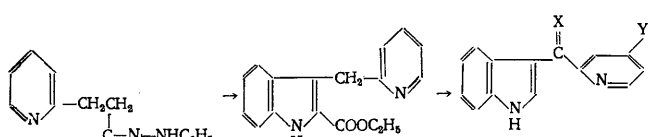
Another involves the interaction of indolylmagnesium bromide with chloromethylpyridine hydrochloride [27]:



Certain 2-scatylpyridines (and their iodides) exhibit anticholinergic and antihistamine activities [28].

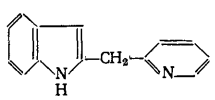
The interaction of indole-3-aldehyde with 2-pyridyllithium leads to the formation of (3-indolyl)(2-pyridyl)methanol (XVII). [29] The same compound is formed when indolylmagnesium halides react with 2-formylpyridine at −25°C, together with a small amount of di-indolylpyridylmethane [30]. The corresponding carbinols form 4-formylpyridine and 3-formylisoquinoline [30].

2-Scatylpyridine can be readily obtained by the Fischer reaction [31]:



(XVII, X=H,OH, Y= H)
(XVIII, X=H_2, Y=H)
(XX, X=O, Y=H)
(XXI, X=H_2, Y=CH_3)

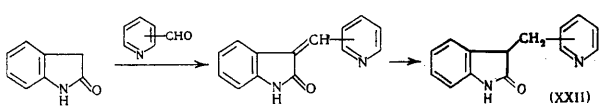
It has also been shown [31] that 2-scatylpyridine (XVIII) rearranges in the presence of $AlCl_3$ to 2-(2-indolylmethyl)pyridine (XIX) and on oxidation with selenium dioxide is converted into 3-indolyl-2-pyridyl ketone (XX).



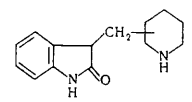
(XIX)

The hydrogenation of 4-methyl-2-scatylpyridine (XXI) methiodide and phenylethiodide, obtained by the Fischer method from the phenylhydrazone of (4-methyl-2-pyridyl)propionaldehyde, leads to tetrahydropyridine, which is cyclised under the influence of phosphoric acid to indolo-[2,3-*f*]morphan. [32] These compounds exhibit analgesic, expectorant, and anti-inflammatory activity.

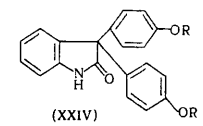
Oxindoles containing pyridylmethyl residues (XXII) are formed when oxindole is condensed with formylpyridines and the products are hydrogenated in ethyl acetate at 20°C in the presence of palladium on charcoal [33]. Further hydrogenation in ethyl acetate at 75°C or in acetic acid gives piperidine derivatives (XXIII). The latter exhibit a marked cholinergic effect [33].



(XXII)



(XXIII)



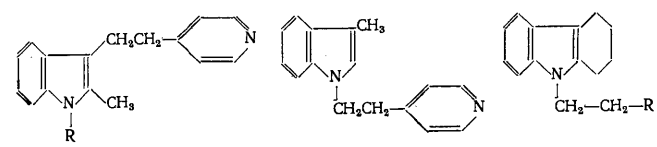
(XXIV)

[R = 3-pyridinoyl or (3-pyridyl)acryloyl]

Pyridine derivatives of oxindole of type (XXIV) were found to have a laxative effect [34].

3. Indolylethylpyridines

The pyridylethylation reaction has led to the wide employment of indole for the synthesis of pyridine derivatives [35]: in an acid medium it leads to 3-pyridylethylindole derivatives and in an alkaline medium it involves the indole nitrogen atom [36]. 4-Vinylpyridine reacts with 2-methylindole in boiling acetic acid to form 2-methyl-3-(4-pyridylethyl)indole (XXV) in 54% yield, while 1-ethylindole gives under the same conditions 1-ethyl-3-pyridylindole [37]. In the presence of sodium ethoxide, scatole reacts with 4-vinylpyridine to form 3-methyl-1-pyridylethylindole (XXVI) in 38% yield [37]. The same product is obtained albeit in an insignificant yield on prolonged refluxing of the reactants in acetic acid [37]. In the indole series, the same type of behaviour may be noted also for the Michael reaction, where, for example, acrylonitrile reacts with 2-phenylindole to form 1-cyanoethyl-2-phenylindole when catalysed by bases and 3-cyanoethyl-2-phenylindole when catalysed by acids [38]:



(XXV, R=H)
[XXIX, R = 2-(4-pyridyl)ethyl]

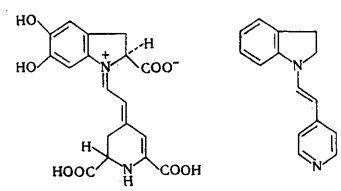
(XXVI)

(XXVII, R = 4-pyridyl)
(XXVIII, R = 2-pyridyl)

It was found that 3-(4-pyridylethyl)indole may increase the stimulation of motor activity by amphetamine [37]. 1-Pyridyl-2,3-tetramethyleneindoles (XXVII) and (XXVIII) and their salts stimulate the activity of the central nervous system [39].

Kost and coworkers [40] suggested that a higher-boiling alcohol be employed for the pyridylethylation reaction and obtained a greater number of pyridylethyl derivatives of indole when the reaction was carried out in hexyl alcohol.

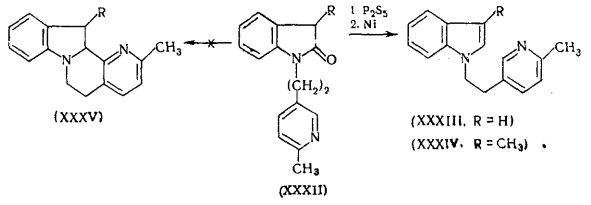
Pyridylethylation of indolines in acetic acid leads to *N*-pyridylethylindolines [19,41]. Analogues of these products have been detected in natural products, for example betanidine (XXX). [42] A simpler analogue (XXXI) was obtained by the condensation of *N*-formylindoline with γ-picoline. [43] Total synthesis of neobetanidine and neobetenamine-derivatives has been achieved [44]:



(XXX)

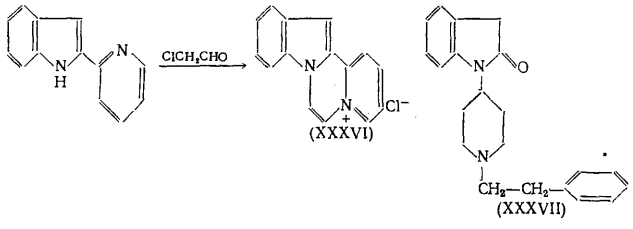
(XXXI)

The 1-(3-pyridyl)ethyl derivative (XXXIII) can be obtained via the corresponding oxindole derivative (XXXII, R = H):[45]



(XXXV) (XXXII) (XXXIII, R = H) (XXXIV, R = CH_3)

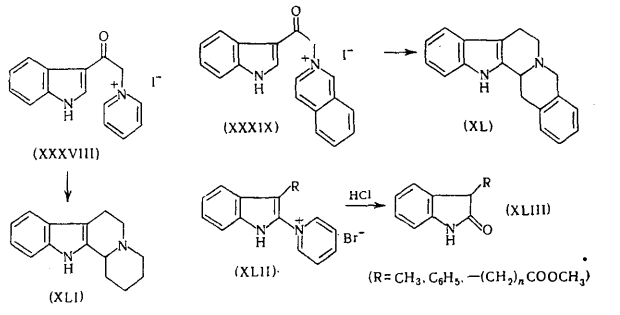
Compound (XXXIV) was synthesised according to the same scheme[46]. Certain reactions of compounds (XXXIII) and (XXXIV) have been investigated: bromination, nitration, the Mannich reaction, and formylation[41]. Compound (XXXII) could not be cyclised to the eburnamenine derivative (XXXV).[47] Its tetracyclic analogue (XXXVI) can be synthesised in a slightly different way[48]:



(XXXVI) (XXXVII)

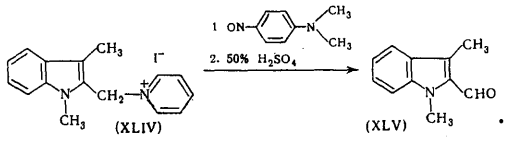
Biological tests showed that many bispyridylethyl derivatives of indole of type (XXIX) and also their piperidine analogues exhibit anticonvulsant activity[49]. The methiodide of compound (XXXII, R = CH_3) has a very pronounced curarelike activity at dilutions of the order of 1 : 10 000, the reactivity being extremely specific, since it disappears in the absence of the methyl group at the 3-carbon atom of the indole ring[45]. Oxindole derivatives of type (XXXVII) and their salts with non-toxic acids were found to have an analgesic activity and absorb ultraviolet light, which makes them valuable for protection from sunlight[50].

Certain indacylpyridium salts (XXXVIII), formed in the interaction between indolylmagnesium halides and iodoacetyl chloride followed by condensation with pyridine[51], should probably be also included in the section on pyridylethylindole compounds. They are obtained in better yields and in only one stage from 3-acetylindole, iodine, and a pyridine (or quinoline and isoquinoline) base via the King reaction[52,53]. These compounds are of interest also as starting materials for the synthesis of many indole alkaloids. In particular, the reduction of the salts (XXXIX) with lithium aluminium hydride and subsequent cyclisation constitute the simplest method for the formation of the yohimbine system (XL).[53] The reduction can also be carried out with sodium borohydride[54]. For example, compound (XLI) was synthesised in this way[55]:



(XXXVIII) (XXXIX) (XL) (XLI) (XLII) (XLIII) (R = CH_3, C_6H_5, $-(CH_2)_nCOOCH_3$)

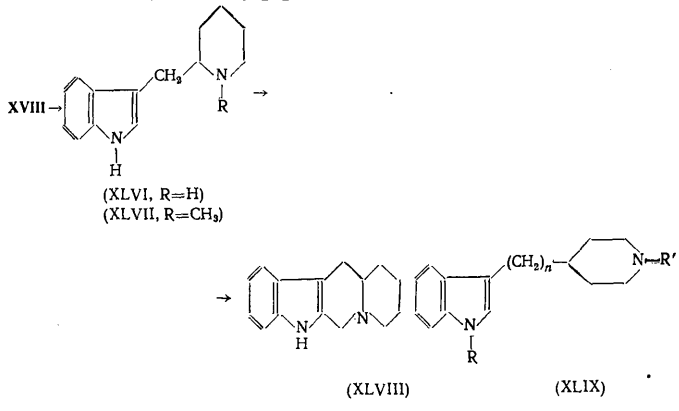
Many *N*-indolylpyridinium salts (XLII) are obtained by the bromination of indoles in the presence of pyridine bases and are then converted into oxindole derivatives (XLIII).[56-58] The salt (XLIV), formed when 1,2,3-trimethylindole is treated with iodine in pyridine, is subsequently converted into 2-formyl-1,3-dimethylindole (XLV):[59]



(XLIV) (XLV)

III. PIPERIDINE DERIVATIVES OF INDOLE

The principal method for the preparation of indolylpiperidines is reduction of the corresponding pyridines. When the pyridine derivative (XVIII) is hydrogenated in the presence of a palladium catalyst in an alcohol–acetic acid mixture, 2-scatylpiperidine (XLVI) is formed:



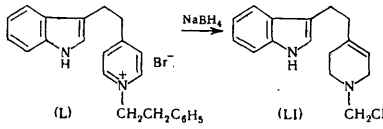
(XLVI, R=H) (XLVII, R=CH_3) (XLVIII) (XLIX)

It is methylated to compound (XLVII) and on treatment with formaldehyde and formic acid is converted into indolohexahydroquinolizine (XLVIII).[29] 1-Methyl-2-scatylpiperidine (XLVII) can also be obtained by the condensation of isatin with α-picoline and the reduction of the resulting dioxindole with sodium in butanol followed by *N*-methylation[60].

The hydrogenation of (3-indolyl)(4-pyridyl)methanol in the presence of Adams catalyst leads to 4-scatylpiperidine (XLIX, n = 1, R,R′ = H), which may be methylated with chloral[61] to the *N*-methyl derivative (XLIX, n = 1, R = H, R′ = CH_3).[30]

Catalytic hydrogenation of pyridylethylindoles in the presence of a platinum catalyst in glacial acetic acid or in aqueous alcoholic HCl leads to the formation of the corresponding piperidines (XLIX, n = 2, R = H or CH_3, R′ = H, CH_3, $C_6H_5CH_2$, etc.). In tests on mice these compounds were found to have an analgesic activity comparable with that of morphine[63]. An approximately similar activity is observed for compounds containing the phenylethyl, benzyl, and phenylacyl residues at the piperidine nitrogen atom; substitution of the indole nitrogen atom has an unfavourable effect on the activity[63].

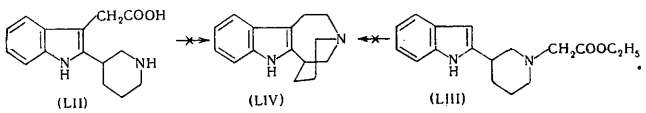
The reduction of salts of type (L) with sodium borohydride gives rise to piperidines (LI):[63]



(L) $CH_2CH_2C_6H_5$ (LI) $CH_2CH_2C_6H_5$

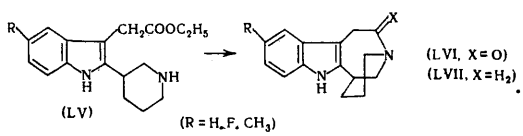
There are many other examples of the reduction of pyridinium salts with sodium borohydride. For example, this reaction has been used to prepare 2-(3-piperidinyl)-indole-3-acetic acid [62] (LII). In general, the reduction of salts of 3-substituted pyridinium with sodium borohydride to 1,3-disubstituted 1,2,5,6-tetrahydropyridines is a well known reaction [64].

Numerous attempts have been made to cyclise the aminoacid (LII) and also the piperidine derivatives (LIII) to the ibogamine structure (LIV), but were unsuccessful: [62]



(LII) (LIV) (LIII)

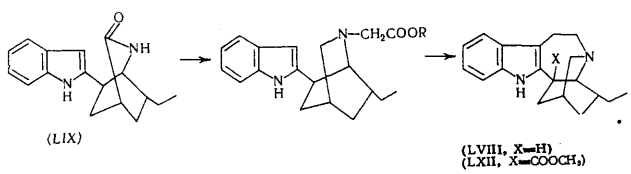
The search for methods of synthesis of systems similar to the ibogamine molecule is important for practical applications, since this alkaloid from *Tabernanthe iboga* (*Apocynaceae*) is well known to have a psychotomimetic activity. An extremely elegant solution has been recently found for the above problem [65]:



(LV) (R = H, F, CH_3) (LVI, X = O) (LVII, $X = H_2$)

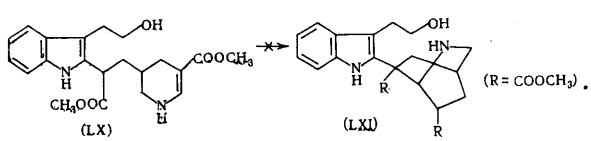
The piperidine derivatives (LV) were converted into ketones (LVI) at a reduced pressure and a temperature of 165–170°C and the ketones themselves were reduced further to compound (LVII) with lithium aluminium hydride in monoglyme.

Epi-ibogamine (LVIII) can be obtained from the piperidinone (LIX): [66]



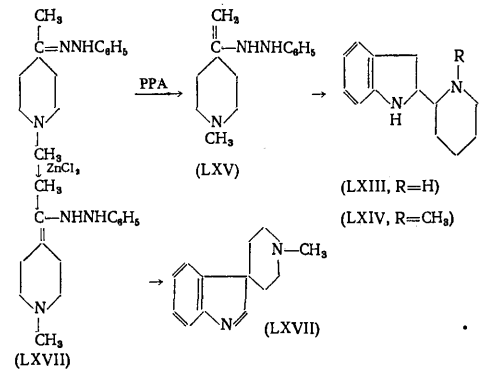
(LIX) (LVIII, X=H) (LXII, X=$COOCH_3$)

Wenkert et al. [67] were unable to cyclise the tetrahydronicotine derivative (LX) to the quinuclidine compound (LXI), which they intended to convert into coronaridine (LXII):



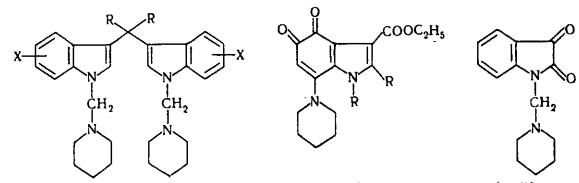
(LX) (LXI) (R = $COOCH_3$)

The piperidine derivative (LXIII) was obtained both on reduction of the corresponding pyridine derivative [62,68] and via the Schmidt reaction from 2-(2-indolyl)cyclopentanone [69]. Its *N*-methyl derivative (LXIV) is formed via the Fischer reaction on treatment of the phenylhydrazone of 4-acetyl-1-methylpiperidine with polyphosphoric acid, probably via the intermediate (LXV). It is interesting that, when zinc chloride is employed in this reaction, the cyclisation is completed by the formation of the 3*H*-indole derivative (LXVII), probably via the intermediate (LXVI): [70]



(LXV) (LXIII, R=H) (LXIV, R=CH_3) (LXVII)

The Mannich reaction has been used to synthesise piperidine derivatives of indole:



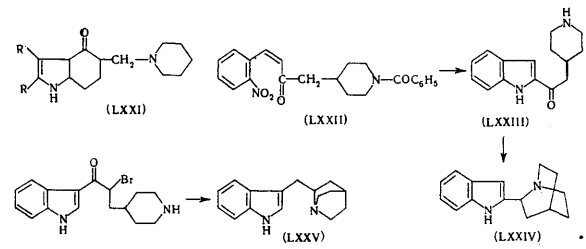
(LXVIII) (LXIX) (LXX)

(X = NO_2, halogen; R, R' = H, CH_3, C_3H_7)

Compounds of type (LXVIII) synthesised in this way and also their morpholine analogues act on the central nervous system [71].

Tests of the antimicrobial properties of indolequinones (LXIX) showed that they are not appreciably active [72]. A high antiviral activity was found in piperidine derivatives of isatin of type (LXX) [73] and the Mannich bases (LXXI) obtained from 6,7-dihydroindol-4(5*H*)-ones proved to be effective depressants of the central nervous system [74].

On heating with triethyl phosphite and subsequent debenzoylation, the *o*-nitrostyrene derivative (LXXII) gives 2-(4-piperidinyl)acetylindole (LXXIII), the reduction of which with sodium borohydride and subsequent refluxing in decalin lead to the quinuclidine derivative (LXXIV): [75]



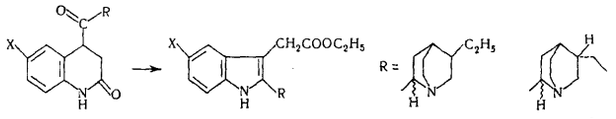
(LXXI) (LXXII) (LXXIII) (LXXV) (LXXIV)

Scatylquinuclidine (LXXV) can be obtained similarly via a stage involving the formation of the 3-indolylpiperidine derivative [76].

A mixture of epimers of quinuclidine derivatives (LXXVII) is formed when 2-oxohexahydrocinchoninones (LXXVI) are heated with hydrogen chloride in alcoholic solution [77,78].

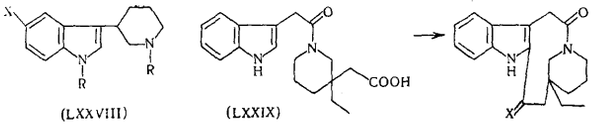
A series of 3-(3-indolyl)piperidines (LXXVIII) were obtained by heating salts of α-indolylglutaric acid with the corresponding amine without a solvent and by the reduction

of the resulting piperidinediones with lithium aluminium hydride[79]. 3-(1-Methyl-3-indolyl)piperidine (LXXVIII, R = CH_3, R′, X = H) and its *N*-methyl derivative (LXXVIII, X = H, R, R′ = CH_3) have a prolonged sedative effect, the second compound also showing some analgesic activity[79].



(LXXVI) (LXXVII) (X = H, CH_3O)

The synthesis of the alkaloid quebrachamine (LXXXI) by the cyclisation of an acylpiperidine (LXXXIX) in polyphosphoric acid and subsequent reduction of the diketone (LXXX) has been described[80]:



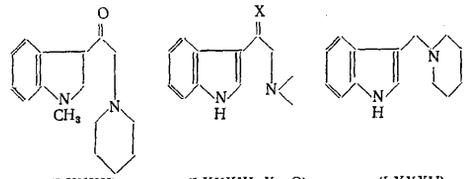
(LXXVIII) (LXXIX)

(LXXX, X = O)
(LXXXI, X = H_2)

1-[γ-(3-indolyl)propyl]piperidine can be conveniently synthesised from indole-3-propionic acid and piperidine[81].

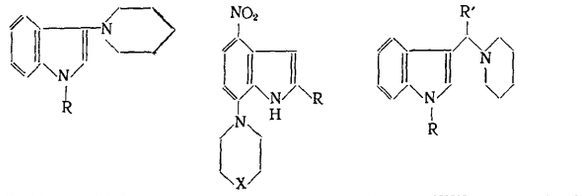
Prolonged refluxing of 3-chloroacetyl-1-methylindole with piperidine in alcohol leads to 1-methyl-3-(*N*-piperidinylacetyl)indole (LXXXII).[82]

When aminoketones of type (LXXXIII) are reduced with lithium aluminium hydride or by hydrogenation over nickel, the aminoalcohols (LXXXIV)[83]—the indole analogues of adrenaline—are formed[83]:



(LXXXII) (LXXXIII, X=O) (LXXXV)
(LXXXIV, X=H,OH)

When the molecules of these alcohols contain a secondary amino-group, they increase arterial blood pressure, but the presence of a tertiary amino-group (piperidine, morpholine, and other residues) leads to a lowering of arterial blood pressure and reduces the tone of the peripheral vessels[83]:



LXXXVI, R=H, CH_3, CH_3CO) (LXXXVII, X=CH_2; R=H,$COOC_2H_5$) (LXXXIX,R=H,R′=CN)
(LXXXVIII, X=NCH_3) (XC, R=CH_3,R′=CN)
(XCI, R=CH_3; R′=CH_2NH_2).

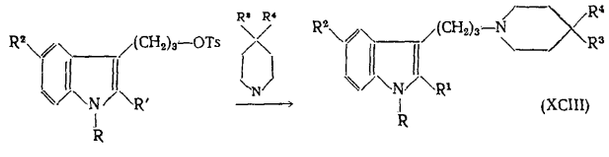
Piperidine can be *N*-alkylated with gramine[84], *N*-acetylindoxyl[85], and 7-chloro-4-nitro-derivatives of indole[86] with formation of the piperidine derivatives (LXXXV), (LXXXVI), and (LXXXVII) respectively.

When the lithio-derivative of piperidine reacts with 5-bromoindole, a mixture of 4-(1-piperidinyl)indole (60%) and 5-(1-piperidinyl)indole (40%) is formed in 59% yield.

The same substances can be isolated also as a result of the interaction of 4- and 5-aminoindoles with 1,5-dibromopentane[87].

The reduction of the nitrile (LXXXIX) and its *N*-methyl derivative (XC), obtained by the Strecker reaction, with lithium aluminium hydride has been investigated[88]. It was found that the reduction is somewhat unusual: the nitrile (LXXXIX) is converted into *N*-scatylpiperidine and compound (XC) gives rise to the tryptamine derivative (XCI).[88]

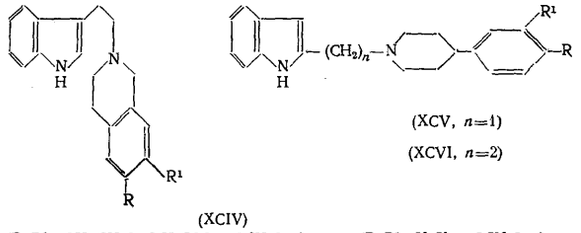
A pronounced sedative, analgesic, spasmolytic, anti-inflammatory, and hypocholesteremic activity was found in a number of piperidine derivatives of type (XCIII) formed when 1-(3-indolyl)-3-propyl *p*-toluene sulphonate (XCII) reacts with 4,4-disubstituted piperidines in alcohol in the presence of potassium carbonate[89-91]:



(XCII) (XCIII)

[R, R^1 = H, alkyl, or aryl; R^2, R^3 = H, alkyl, alkoxy, alkylthio, halogen, CN, etc.; R^4 = aryl, $N(Alk)_2$, or R^3; R^4 = alkylene or a heterocyclic residue].

In order to investigate the dependence of the physiological activity of reserpine on its structure, a series of 2-[β-(3-indolyl)ethyl]-1,2,3,4-tetrahydroquinolines (XCIV) were synthesised[92]:

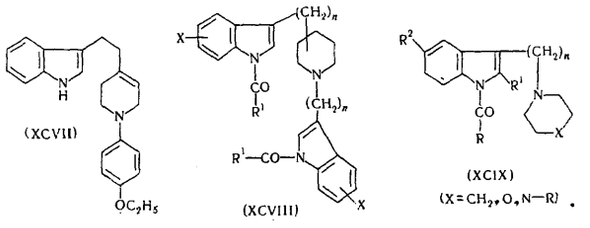


(XCV, *n*=1)
(XCVI, *n*=2)

(XCIV)
(R, R^1=OH, CH_3O, C_6H_5COO,—OCH_2O—) (R, R^1=H,Cl, —OCH_2O—).

The piperidine isomers (XCIII) containing the *N*-piperidinylalkyl group in the 2-position of the indole ring (XCI) are formed when isotryptamine is refluxed with ethyl β-aryl-δ-bromovalerate in xylene in the presence of potassium carbonate with subsequent reduction of the pyridones isolated under these conditions[93]. These compounds and also their salts were found to be effective analgesic and muscular relaxants[93]. The monomethyl derivative (XCV) can be obtained by the reaction of (2-indolyl)methylamine with the anhydrides of 3-aryl-substituted glutaric acids in benzene, the cyclisation of the products to piperidine-2,5-dione in acetic anhydride, and its reduction[93].

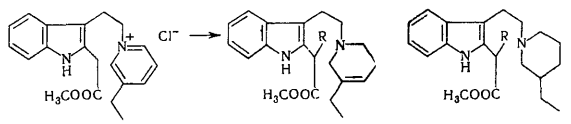
The tetrahydro-derivative (XCVII) was found to have an analgesic activity and also a vasodilating activity[94], while the piperidine derivatives (XCVIII) were found to have a sedative, hypotensive, depressant, anticonvulsive, and analgesic activity[95-97]:



(XCVII) (XCVIII) (XCIX)
(X=CH_2,O,N—R).

Anti-inflammatory, antipyretic, analgesic, antidepressant, and psychostimulating activity is shown by indolylpiperidines (XCIX) and also by their pyrrolidine, morpholine, and piperazine analogues[98]. Numerous *N*-[(1-piperidinyl)alkyl]-*N*-[(3,2,1-indolyl)alkyl)amines, which exhibit hypotensive, analgesic, psychomotor, depressant, anti-inflammatory, bacteriostatic, adrenolytic, antihelminthic, and antifungal activity, have been patented[99].

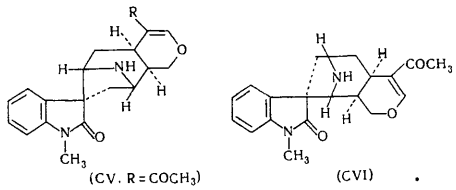
The structure of the alkaloid 16,17-dihydrosecodin-17-ol (CI), isolated from *Rhazya orientalis*, was demonstrated by synthesis from the pyridinium derivative (C):[100]



(C) (CI, R = CH_2OH) (CIII, R = CH_3) (CII, R = CH_2OH) (CIV, R = CH_3)

Tetrahydrosecodin-17-ol (CII) was isolated from the same plant and dihydrosecodine (CIII) and tetrahydrosecodine (CIV) were identified in *Rhazya stricta*[101].

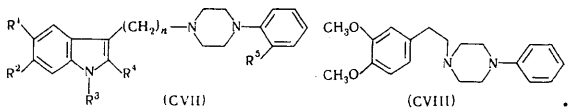
The alkaloids alstonerine (CV) and "alkaloid C" (CVI) were isolated from *Alstonia muelleriana*[102]:



(CV, R = $COCH_3$) (CVI)

IV. PYRAZINE AND PIPERAZINE DERIVATIVES OF INDOLE

A fairly considerable amount of attention is being devoted to piperazine derivatives of indole, mainly after the report in 1962 that the condensation of indolylalkanoic acids with 4-arylpiperazines followed by reduction of the resulting *N*-arylpiperazides yields 4-aryl-1-[(3-indolyl)-alkyl] piperazines (CVII) which are effective depressants of the central nervous system[103]. Among these, the highest activity was shown by compounds in which the methylene bridge consists of 2 or 3 methylene groups. Probably the activity is due to the presence of the indole moiety, because the phenyl analogue of this compound (CVIII) is inactive[103].

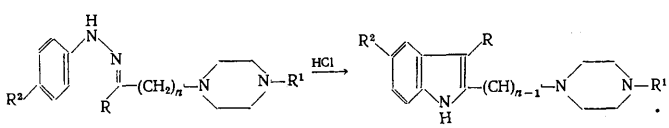


(CVII) (CVIII)

(R^1 R^2 R^3 R^4 = H, CH_3, OCH_3; R^5 = H, CH_3)

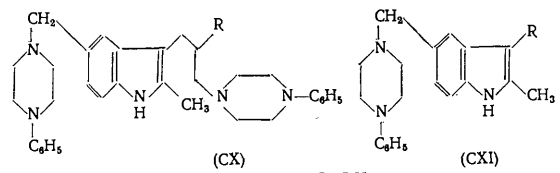
Sedatives, antipyretic agents, and muscle relaxants[104,105] and also compounds with adrenolytic, hypotensive, antipyretic, and sedative activity[106,108] were found among indolylalkylpiperazines.

A series of (2-indolyl)alkylpierazines (CIX) were synthesised by the Fischer reaction[106,107]:



(CIX)

Many compounds of type (CX) and(CXI) containing piperazine residues in the 5-position of the indole molecule were obtained[109,110]:

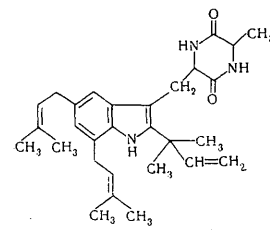


(CX) (CXI)

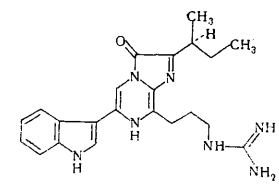
(R=H, CH_3, C_3H_7, C_4H_9, C_6H_5)

N-Scatylpiperazine is formed from (3-indolyl)methanol and piperazine[111]. Alkylation of piperazine with gramine in an aqueous medium leads to *NN*-discatylpiperazine[84]. The interaction of 6-chloro-4-nitroindole and its 2-ethoxycarbonyl derivative with 4-methylpiperazine is completed by formation of the corresponding 6-(4-methyl-1-piperazinyl)indole (LXXXVIII).[88]

Piperazine derivatives of indole have been found in natural products. Echinuline (CXII)[112,113] can be regarded as a piperazinedione in which the tryptophan residue has the configuration of a D-aminoacid and alanine has the L-configuration[114]:



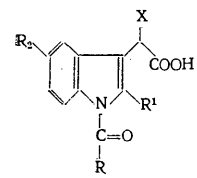
(CXII)



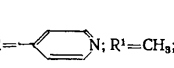
(CXIII)

Another natural pyrazine derivative of indole is luciferin (CXIII),[115-118] a negligible amount of which (5 mg) can produce sufficient light to read a newspaper for 30 min. It was synthesised recently[117].

Many α-halogenomethylindolylacetic acids (CXIV) containing a pyrazinecarboxylic acid residue at the nitrogen atom have been patented[119]. These acids and also their esters, amides, and salts exhibit antipyretic and anti-inflammatory activity and can be used to prevent and suppress the formation of tissue granuloma or to treat arthritis and dermatological affections[119]:



(R^1, R^2=H, Alk, Ar etc, X=CH_2Y, CHY_2, CY_3; Y=F, Cl, Br)

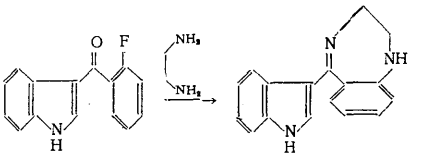
(CXIV, R=); (CXV, R=  ; R^1=CH_3; R^2=CH_3O; X=H)

Many analogues of compound (CXIV) containing aromatic and heterocyclic residues and exhibiting a considerable anti-inflammatory activity are known[120-127]. Among numerous compounds of this type, indomethacin, containing the *p*-chlorobenzoyl residue in the 1-position, may be recommended in practice. The *N*-isonicotinoyl derivative (CXV) is known to show a high anti-inflammatory activity and to be less toxic than indomethacin[129,130].

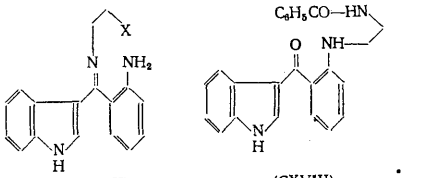
A number of analogues obtained on the basis of indole-3-carboxylic acids also show anti-inflammatory activity[128].

V. INDOLYLAZEPINES AND DIAZEPINES

5-(3-Indolyl)-2,3-dihydro-1*H*-1,4-benzodiazepines of type (CXVI), formed when 3-(*o*-halogenobenzoyl)indoles are treated with ethylenediamine in pyridine or on cyclisation of the imines (CXVII) or imides (CXVIII),[131] show antidepressant activity[132,133]:



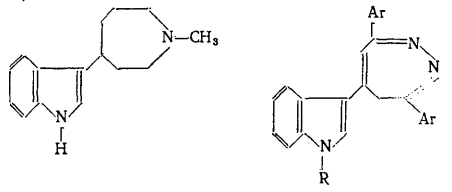
(CXVI)



(CXVII) (CXVIII)

A number of 4-indolylhexahydroazepines of type (CXIX) were found to possess an antiviral and antibacterial activity[134].

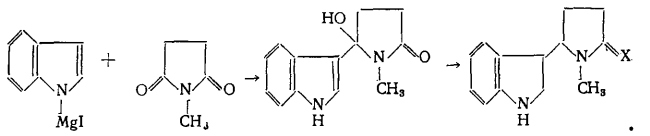
1,2-Diazepine derivatives of indole (CXX) can be simply and conveniently synthesised by the interaction of indolylpyrylium salts (VIII) with hydrazine hydrate[135]:



(CXIX) (CXX, R=CH$_3$, C$_6$H$_5$CH$_2$)

VI. INDOLYLPYRROLIDINES

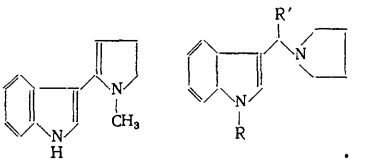
2-(3-Indolyl)-1-methylpyrrolidine-5-one (CXXI), formed by the reaction of indolylmagnesium iodide with *N*-methylpyrrolidine-2,5-dione, proved to be an effective tranquiliser[136]. It has also been reported that compound (CXXII), obtained by its reduction, inhibits the activity of pseudocholinesterase[137]:



(CXXI, X=O)
(CXXII, X=H$_2$)

N-Scatylpyrrolidine can be obtained both by the Mannich reaction[138] and by the alkylation of pyrrolidine with gramine[84].

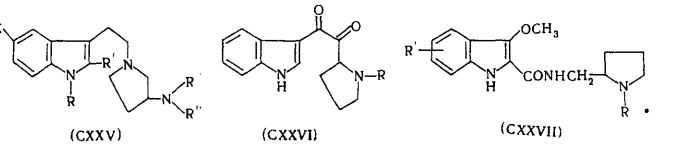
It is interesting to note that 3-(1-alkyl-2-pyrrolinyl)-indoles of type (CXXIII), which have been recommended as intermediates for the synthesis of pyrrolidinylindoles, exhibit anti-inflammatory activity and a capacity to reduce the appetite[139]:



(CXXIII) (CXXIV)

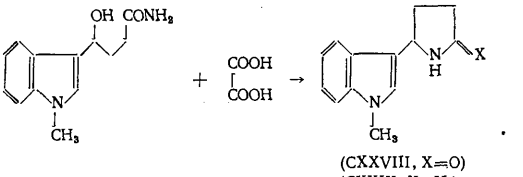
When the nitriles (CXXIV, R = H, R′ = CN) and (CXXIV, R = CH$_3$, R′ = CN) are reduced with lithium aluminium hydride, the latter compound gives rise to α-pyrrolidinyltryptamine (CXXIV, R = CH$_3$, R′ = CH$_2$, NH$_2$), while the former is converted into *N*-scatylpyrrolidine with elimination of the nitrile group[88].

3-Amino-substituted *N*-(β-indolylethyl)pyrrolidines (CXXV) were found to be capable of decreasing appreciably the tremor and muscular rigidity in Parkinson's disease[140] and the pyrrole derivative (CXXVI) was found to exhibit a depressive and an anticonvulsant activity[141]. The pyrrolidine derivatives (CXXVII) have an antipyretic effect, are capable of enhancing the effect of barbiturates, and are morphine antagonists[142]:



(CXXV) (CXXVI) (CXXVII)

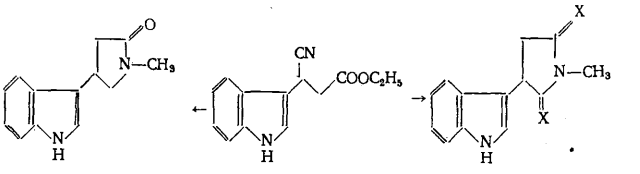
A patent was published recently for the preparation of 5-(3-indolyl)pyrrolidin-2-ones of type (CXXVIII) which exhibit antiviral and sedative activity in tests on birds and animals. Their reduction yielded the corresponding indolylpyrrolidines (CXXIX), which are used in the treatment of neuroses[143]:



(CXXVIII, X=O)
(CXXIX, X=H$_2$)

It has also been suggested that 3-(4-nitrobutyryl)indoles be used for the synthesis of derivatives of 3-(2-pyrrolidinyl)indoles, which show anti-inflammatory and anaphylactic activity and are capable of suppressing the appetite[144]. 2-(3-Indolylpyrrolidine) is obtained by the hydrogenation of 3-(β-cyanopropionyl)indole[145].

3-(3-Indolyl)-1-methylpyrrolidine (CXXX) has been synthesised by the reaction of indolylsuccinic acid[146] with 1,3-dimethylurea at 185–190°C and subsequent reduction of the resulting indolylsuccinimide (CXXXI):[146]

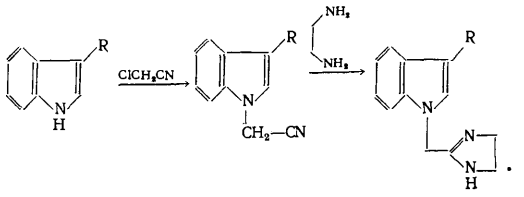


(CXXXIII) (CXXXII) (CXXX, X=H$_2$)
(CXXXI, X=O)

Hydrogenation of the nitrile (CXXXII) in the presence of a nickel catalyst at 80°C (100 atm) leads to 4-(3-indolyl)-pyrrolidin-2-one (CXXXIII) in 50% yield[147].

VII. INDOLYLIMIDAZOLES

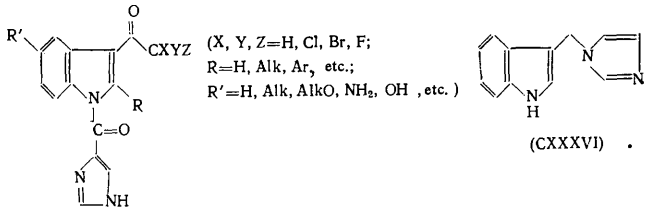
Certain 3-alkyl-1-(2-imidazolinylmethyl)indoles (CXXXIV) show vasoconstrictor activity [148]:



(CXXXIV)

A number of indole derivatives (CXXXV) containing the imidazolecarboxylic acid residue (and also carboxylic acid derivatives of pyrimidine, oxazole, thiazole, isoxazole, isothiazole, pyrazole, etc.), which may be used as intermediates in the synthesis of various derivatives of indolylacetic acids, have been patented [149,150].

1-Scatylimidazole (CXXVI) and its 2-methyl derivative are formed in the alkylation of imidazole with gramine [152]. 1-Scatylindazole, 1-scatylbenzimidazole, and 1-scatylpyrazole were obtained in the same way [153]:

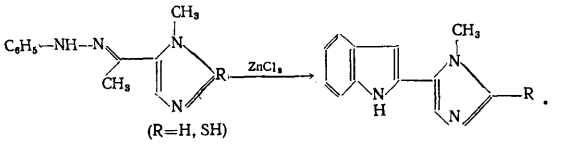


(X, Y, Z=H, Cl, Br, F; R=H, Alk, Ar, etc.; R′=H, Alk, AlkO, NH_2, OH, etc.)

(CXXXV)

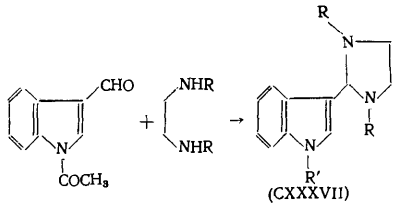
(CXXXVI)

Indole derivatives containing the imidazole residue in the 2-position in indole can be obtained by the Fischer reaction from 5-acetylimidazoles [151]:



(R=H, SH)

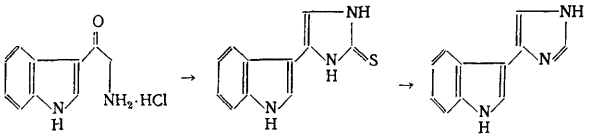
Suvorov and coworkers obtained 1,3-disubstituted 2-(3-indolyl)imidazolines (CXXXVII) from 1-acetylindole-3-aldehyde and *N*-substituted ethylenediamines [154]:



(CXXXVII)

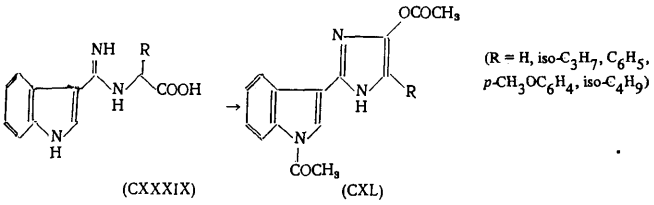
(R=C_6H_5, p-$CH_3OC_6H_4$, $C_6H_5CH_2$, p-BrC_6H_4; R′=H, $COCH_3$)

They also synthesised 4-(3-indolylimidazole (CXXXVIII) by the reaction of 3-chloroacetylindole with formamide or by treating 3-aminoacetylindole with potassium thiocyanate in the melt with subsequent elimination of sulphur from 2-mercapto-4-indolylimidazole formed [155]. The imidazole derivative (CXXXVIII) has a weak bacteriostatic effect in relation to *Mycobacterium tuberculosis* [155]:



(CXXXVIII)

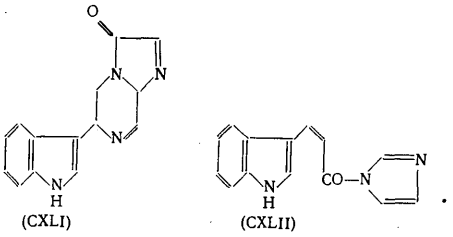
N-Acetyl derivatives of a number of 2-(3-indolylimidazoles (CXL) are formed when indole-3-carbamidicic acids (CXXXIX) are refluxed with acetic anhydride [156]:



(R = H, iso-C_3H_7, C_6H_5, p-$CH_3OC_6H_4$, iso-C_4H_9)

(CXXXIX) (CXL)

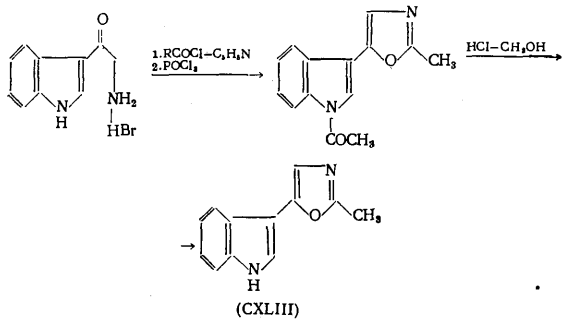
Imidazo[1,2-*a*]pyrazinone (CXLI) was obtained from 2-amino-5-(3-indolyl)pyrazine and methylglyoxal [158]. The synthesis of 1-[β-(3-indolyl)acryloyl]imidazole (CXLII) has also been described [157]:



(CXLI) (CXLII)

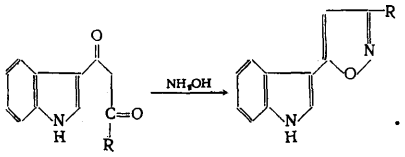
VIII. INDOLYLOXAZOLES AND INDOLYLISOXAZOLES

Compounds of this type have been isolated from natural sources. The antibiotic pimprinin, identified as 5-(3-indolyl)-2-methyloxazole (CXLIII), was obtained from *Streptomyces pimprina* [159]. The structure of pimprinin was subsequently confirmed by synthesis [160]:

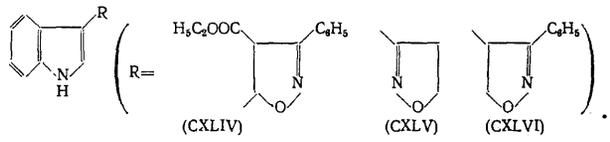


(CXLIII)

Sanna reported previously the synthesis of indolylisoxazoles from β-diketones of the indole series [161]:

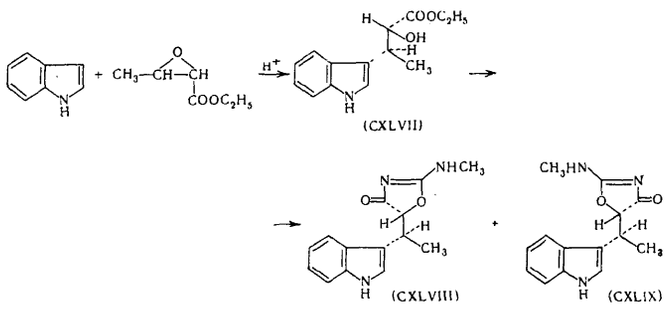


It is also known that the interaction of ethyl indolylacrylate in benzonitrile oxide leads to the formation of the isoxazoline (CXLIV) and that the isoxazoline (CXLV) and compound (CXLVI) may be obtained from 3-indolyl vinyl ketone and hydroxylamine by reaction with benzonitrile oxide [162]. Isoxazole derivatives could not be obtained by the reaction of benzylidene-3-acetylindole with hydroxylamine and benzonitrile oxide [162]:



(CXLIV) (CXLV) (CXLVI)

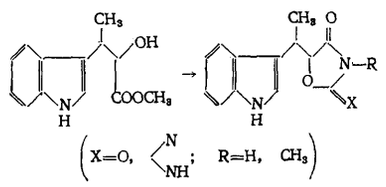
Strain BA-3972 of *Streptomyces albus* is known to suppress certain strains of staphylococci which are resistant to the usual commercially available antibiotics [163]. The active principle (an antibiotic), which was called indolmycin, was soon isolated [164], its structure (CXLVIII) was established, and it was synthesised according to the following scheme [165]:



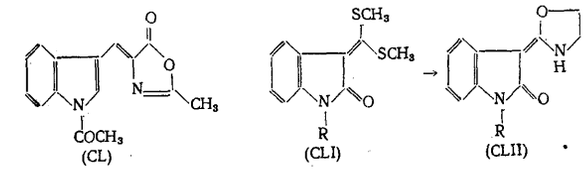
(CXLVII) (CXLVIII) (CXLIX).

The ethyl ester of α-indolmycenic acid (CXLVII), which can also be synthesised by the reaction of indolylmagnesium halides with ethyl *trans*-2,3-epoxybutyrate, is condensed with *NN*-dimethylguanidine. Apart from indolmycin itself, this results in the formation also of a certain amount of isoindolmycin (CXLIX) owing to the ready epimerisation of indolmycin under alkaline conditions [165].

In a stereospecific synthesis of indolmycin, Suvorov, Preobrazhenskaya, and coworkers also began with the ethyl esters of indolmycenic acids [166,167], the isomers of which they were able to resolve by crystallisation. In the last stage a mixture of approximately equal amounts of indolmycin and isoindolmycin was obtained with an overall yield of 40%. When *N*-methylthiourea, urea, and methyl isocyanate were introduced into this reaction, structural analogues of indolmycin were obtained [168]:

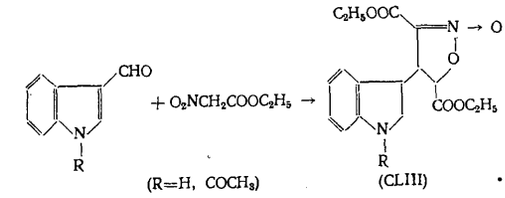


The interaction of indole-3-aldehyde with acetylglycine resulting in the formation of the azlactone (CL) has been described [169]. 3-(2-Oxazolidinylidene)oxindoles (CLII) are readily obtained when 3-bismethylthiomethyleneoxindoles (CLI) are refluxed with ethanolamine in alcohol [170]:



(CL) (CLI) (CLII)

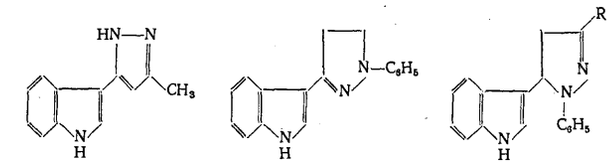
Isoxazoline *N*-oxides (CLIII) were obtained recently by treating indole-3-aldehyde and its *N*-acetyl derivative with nitroacetic ester [171]:



(R=H, $COCH_3$) (CLIII)

IX. INDOLYLPYRAZOLES, INDOLYLPYRAZOLINES, AND INDOLYLQUINOXALINES

The indolylpyrazole derivatives known at present are comparatively few although it would appear that these compounds might include preparations of pharmacological interest, since pyrazoles are in general interesting as biologically active substances [172]. Certain compounds of this type were obtained by the interaction of β-diketones of the indole series with hydrazine derivatives [161]. Thus the reaction of 3-acetoacetylindole with hydrazine hydrate led to the isolation of the pyrazole (CLIV). [173] The pyrazoline (CLV) is formed from 3-indolyl vinyl ketone and phenylhydrazine [162] and a series of Δ^2-pyrazolines (CLVI) were obtained from scatylideneketones and phenylhydrazine [174]:

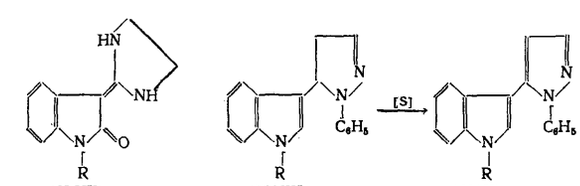


(CLIV) (CLV) (CLVI)

(R=C_6H_5, *p*-CH_3—, *p*-Cl—, *p*-Br—, *p*-$CH_3OC_6H_4$, etc.)

When 3-bismethylthiomethyleneoxindoles (CLI) are refluxed with ethylenediamine, 3-pyrazolidinylideneoxindoles (CLVII) are formed [170].

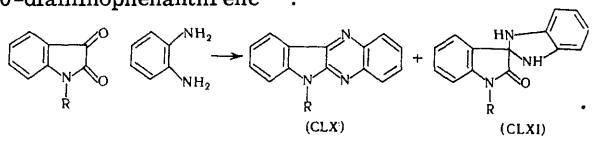
Suvorov and coworkers [175] showed recently that β-indolylacrylic aldehyde and its *N*-acetyl derivative are converted, on prolonged refluxing with phenylhydrazine (or with hydrazine) in acetic acid, into 5-indolylpyrazolines (CLVIII), which can be further dehydrogenated to the corresponding 5-(3-indolyl)pyrazoles (CLIX):



(CLVII) (CLVIII) (CLIX)

(R=H, $COCH_3$)

On reaction with *o*-phenylaminediamine in acetic acid, isatin is converted into 6*H*-indolo[2,3-*b*]quinoxaline (CLX, R = H).[176] When this reaction is carried out in alcohol, the spiro-derivative (CLXI, R = H) is also formed[177,178]. Its analogues have been synthesised also by the interaction of isatin with 4,5-diamino-1,3-dimethyluracil[174], 4,5-diaminopyrimidine[178], 1,2-diaminonaphthalene[177], and 9,10-diaminophenanthrene[178]:

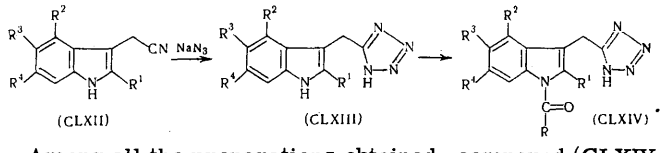


(CLX) (CLXI)

It is interesting that 2,3-diaminonaphthalene forms with isatin only quinoxaline[177], while its reaction with methylisatin gives a spiro-derivative[178] which on recrystallisation from acetic acid isomerises to the corresponding quinoxaline[178].

X. INDOLYLTETRAZOLES

1-(*p*-Chlorobenzoyl)-5-methoxy-2-methylindole-3-acetic acid ("indomethacin") is a powerful anti-inflammatory preparation[179]. In order to seek more effective preparations with similar activity, a number of compounds containing the tetrazole residue instead of the carboxy-group were synthesised from the nitriles (CLXII)[180] or from the tetrazoles (CLXIII) by acetylating the latter in DMF in the presence of sodium hydride[180-183]:



(CLXII) (CLXIII) (CLXIV)

Among all the preparations obtained, compound (CLXIV, R = *p*-ClC$_6$H$_4$, R^1, R^2, R^3, R^4 = H) proved to be the most active[180]. However its effectiveness is appreciably lower than that of "indomethacin". In addition, it is noteworthy that this compound has been found to have an antiserotonin and antihistamine activity[184].

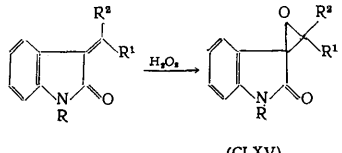
The tetrazole analogue of indole-3-acetic acid stimulates weakly the elongation of *Avena* cells[185].

XI. OTHER INDOLYL DERIVATIVES OF HETEROCYCLES

1. Derivatives of Oxygen-containing Heterocycles

A number of oxirans obtained from oxindole are of definite interest. When products of the condensation of oxindole with ketones are treated with 30% hydrogen peroxide in the presence of alkali in methanol, high yields of 3,1′-epoxides of 2-oxoindoline (CLXV) are obtained[186,187]. Among these compounds, preparations with sedative, diuretic, and anticonvulsant activity were discovered.

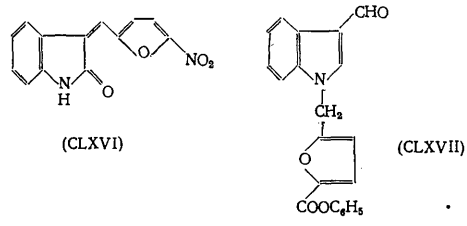
The 3,1′-epoxide of 3-cyclopentyl-2-oxoindoline exhibits a contraceptive effect[186]:



(CLXV)

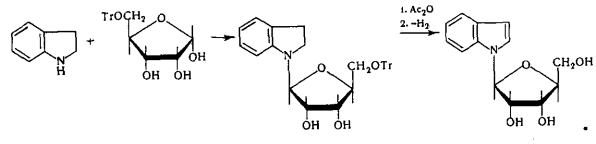
[R = H or CH$_3$; R^1, R^2 = (CH$_2$)$_n$, lower alkyls, aryls, arylalkyls, or pyridyl]

Among other oxygen-containing heterocycles with an indolyl residue, mention should be made of 3-(5-nitrofurfurylidene)oxindole (CLXVI), which shows antibacterial activity[188]. A compound containing a furan ring at the nitrogen atom of the indole molecule (CLXVII) has also been described[189]:



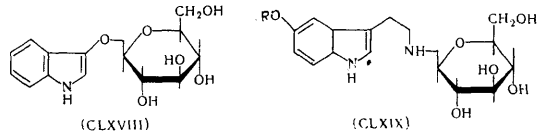
(CLXVI) (CLXVII)

N-Glycosylindoles may be obtained from indoline according to the following scheme[190]:

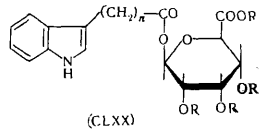


A number of indolyl-β-D-glycopyranosides (CLXVIII) have found application as agents for the histochemical location of individual β-glycosidases in mammalian tissues[191,192].

The synthesis of the *N*-glucosides of serotonin, 5-methoxytryptamine, and melatonin (CLIX) by brief refluxing of the corresponding indole derivatives with D-glucose in methanol has been described[193]:



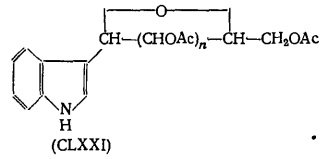
(CLXVIII) (R = H, CH$_3$, C$_6$H$_5$CH$_2$) (CLXIX)



(CLXX)

The glucuronides of 3-indolyl derivatives of aliphatic acids (CLXX) exhibit high anti-inflammatory activity and low toxicity[194].

The interaction of indolylmagnesium bromide with certain acetohalogenoses yielded tetra-acetyl-β-indolylglucose, tetra-acetyl-β-indolylgalactose, and tri-acetyl-β-indolylxylose—the indole series of *C*-glycosides of type (CLXXI), which had not been described hitherto[195]:

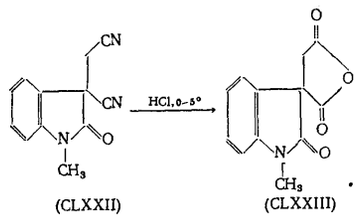


(CLXXI)

The application of mass spectrometry in the investigation of acetylated derivatives of glucopyranosylamine containing the indole residue was described in a review published recently[196].

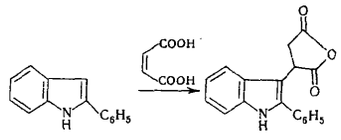
Certain additional information concerning the preparation of a series of carbohydrate derivatives of indoles may be found in a recent review[197].

Spiro[oxindole-3,3′-succinic]anhydride (CLXXIII) is formed in 79.5% yield on acid hydrolysis of the oxindole derivative (CLXXII) in a dioxan–methanol mixture [198]:



(CLXXII) (CLXXIII)

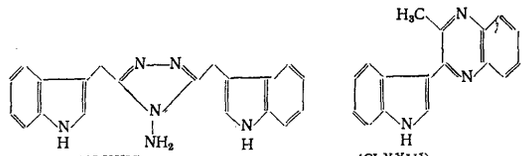
The interaction between 2-phenylindole and maleic acid with brief heating to 140°C leads to the formation of 3-(2-phenyl-3-indolyl)succinic anhydride (CLXXIV): [199]



(CLXXIV)

2. Derivatives of Nitrogen- and Sulphur-containing Heterocycles

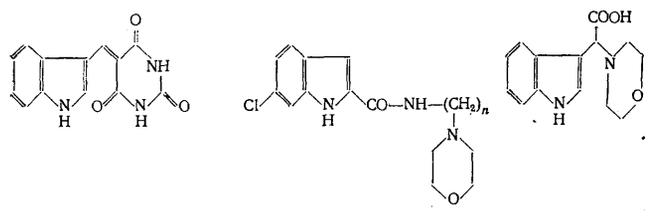
Prolonged refluxing (18 h) of indole-3-acetonitrile with anhydrous hydrazine leads to the formation of 4-amino-3,5-discatyl-*sym*-triazole (CLXXV). [200] As was to be expected, the product of the reaction of 1-(3-indolyl)propane-1,2-dione and *o*-phenylenediamine in alcohol is 2-(3-indolyl)-3-methylquinoxaline (CLXXVI): [201]



(CLXXV) (CLXXVI)

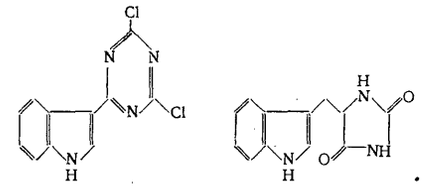
5-Scatylidenebarbituric acid (CLXXVII) is obtained in 84% yield by the condensation of indole-3-aldehyde with barbituric acid [202]. The attempts to reduce the product of this reaction to the 5-scatyl derivatives with triethylammonium formate were unsuccessful [203].

Morpholinylamides of type (CLXXVIII) were found to have antidepressant activity [204]. The morpholine derivative (CLXXIX) is formed by the Mannich reaction from indole, glyoxylic acid, and morpholine [205]:



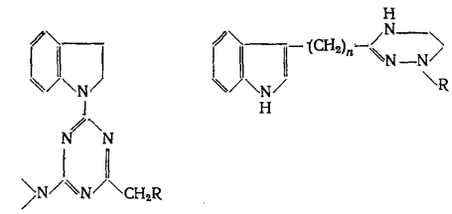
(CLXXVII) (CLXXVIII) (CLXXIX)

When indole reacts with cyanuryl chloride, the product is the derivative (CLXXX) [206] and cyclisation of the phenylhydrazone of β-(5-hydantoyl)propionaldehyde by an alcoholic solution of hydrogen chloride leads to 5-scatylhydantoin (CLXXXI): [207]



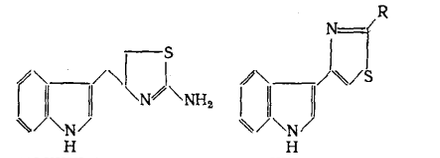
(CLXXX) (CLXXXI)

A number of 2-amino-4-(1-indolinyl)-*S*-triazines (CLXXXII) were found to have anti-inflammatory and analgesic activity [208], while indolylalkyltriazine derivatives (CLXXXIII) and their salts exhibit an antidepressant effect [209]:



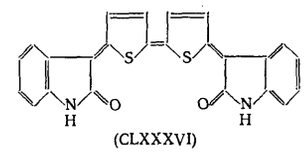
(CLXXXII, R=H, CH_3) (CLXXXIII, n=1, 2, 3; R=H, alkyl.)

In connection with their search for agents affording protection against radiation, Japanese chemists recently described the synthesis of 2-amino-4-scatylthiazoline (CLXXXIV) from α-chloromethyltryptamine and thiourea [210]. It is also known that the interaction of 3-chloroacetylindole with thioformamide, thiourea, and ammonium dithiocarbamate leads to the corresponding derivatives of 4-(3-indolyl)thiazole (CLXXXV): [211]



(CLXXXIV) (CLXXXV, R=H, NH_2, SH)

The indophenine pigment formed on interaction between isatin and thiophen may be included among compounds of this type; the structure (CLXXXVI) was recently finally demonstrated for this derivative [212]:



(CLXXXVI)

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Polymerisation of Isocyanates

R.P.Tiger, L.I.Sarynina, and S.G.Entelis

The review deals with the present state of the problem of the ionisation of isocyanates: cyclic di- and trimerisation, homopolymerisation, and copolymerisation of isocyanates with other monomers. The mechanisms of the processes involving various catalytic systems are considered and the results of investigations of the polymerisation of isocyanates and their theoretical and practical importance are discussed.
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I. INTRODUCTION

The chemical reactions of isocyanates are extremely varied, but so far only some of them have been used industrially, in particular in polymer chemistry. They include mainly the reactions of isocyanates with nucleophilic agents containing a so called active (mobile) hydrogen atom (alcohols, diols, water, amines, etc.). The formation of urethanes has been most thoroughly investigated. They were studied and are still being studied systematically both on model and polymeric systems and the advances achieved in the understanding of the mechanism of these reactions have been described in a number of reviews [1-3]. Other reactions of isocyanates have been less thoroughly investigated, which to some extent restricts the scope of their useful applications.

Of the numerous reactions in which isocyanates are involved, cyclic dimerisation and trimerisation and also homopolymerisation of isocyanates and their copolymerisation with other monomers with formation of high-molecular-weight products are of significant interest for polymer chemistry. Several tens of publications dealing with the polymerisation of isocyanates have now appeared. They have not been discussed so far from a single standpoint and the brief reviews of the literature in certain papers [4,5] and monographs [1,6] on the dimerisation and trimerisation reactions of isocyanates, discovered as early as the past century by Hoffmann, cannot claim to give a complete coverage of the data. The possibility of the homopolymerisation of isocyanates with formation of high-molecular-weight products was first established by Shashoua in 1959 [17] and since then many papers dealing with a quantitative treatment of the polymerisation of isocyanates in the presence of various catalytic systems and with the search for new polymerisation initiators have been published.

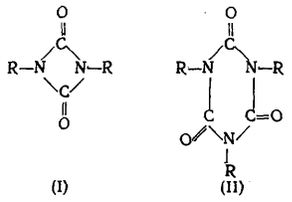
The fact that isocyanates are capable of entering into autocyclisation or polymerisation reactions with formation of linear high-molecular-weight products is not surprising if one bears in mind the electronic structure of the NCO group, which consists of a cumulative system of N=C and C=O double bonds. In this respect isocyanates are extremely similar to ketens $R_2C=C=O$, the capacity of which for cyclisation and homopolymerisation is well known [8].

The present review deals with almost all studies concerned in one way or another with the polymerisation reactions of isocyanates. We believe it reasonable to combine the discussion of the results of the study of the dimerisation and trimerisation of isocyanates, since in many cases they occur in the presence of the same or chemically similar catalysts, although there are a number of fundamental differences between these processes.

The problem of the homopolymerisation and of the copolymerisation of isocyanates with other monomers requires separate consideration. Together with its importance for polymer chemistry, the question of the possibility of the dissociation of the C=O bond in the NCO group in reactions involving the addition of nucleophilic agents to isocyanates, which has been frequently discussed (also by the authors of this review [2,3,9-11]) in connection with the mechanism of urethane formation, has a direct bearing on this problem.

2. CYCLIC DIMERISATION AND TRIMERISATION

The cyclic dimers (I) and trimers (II) of isocyanates are products of autocyclisation which takes place with dissociation of the N=C bonds:

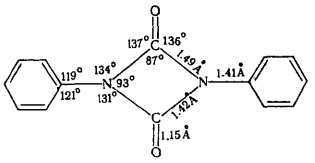


(I) (II)

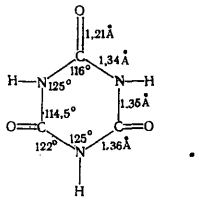
The dimers are a kind of symmetrical diketones (1,3-disubstituted uretidinediones); the trimers are derivatives of cyanuric acid (1,3,5-trisubstituted isocyanurates). The structures of isocyanate dimers and trimers have been demonstrated spectroscopically, by chemical analysis [4,12], and also by comparing the dimerisation and trimerisation products of isocyanates with products obtained by independent synthesis. For example, triphenyl isocyanurate was obtained from phenylcyanamide [13] and trimethyl isocyanurate was synthesised from cyanuric acid and diazomethane [14]. Compounds of type (II) were also

obtained by the condensation of cyanuric acid with oxiran, allyl chloride, ethyl chloroacetate, and acrylonitrile [15].

The structure of the phenyl isocyanate dimer was established by X-ray diffraction [16]:



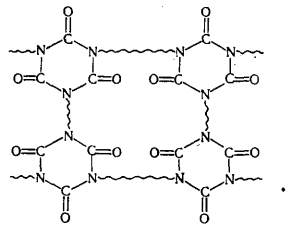
The central four-membered ring is planar. The length of the C–N bond corresponds approximately to its length in amides, for example in acetamide (1.426 Å), [17] and the length of the C–C bond in the aromatic ring differs only slightly from the usual length of this bond in benzene. There are no literature data on the structure of the trimers but some idea about it may be gained from an X-ray diffraction study of cyanuric acid [18]:



The six-membered ring of cyanuric acid is planar. One can hardly expect a significant change in the structure of the central six-membered ring on passing from cyanuric acid to isocyanurate. Before considering the dimerisation and trimerisation of isocyanates in the presence of various catalytic systems, we shall note why these reactions, which so far have been of purely academic interest (for the chemical properties of the NCO group), may be employed successfully in polymer chemistry for the synthesis of new materials.

The main procedure usually employed in the synthesis of structured (cross-linked) polyurethanes involves the introduction of various branching additives into the polymerising system. In the reactions of oligomeric polyesterdiols with di-isocyanates, triols are used for this purpose; polyesterpolyols or polyisocyanates containing more than two NCO groups per molecule can also serve as branching centres. The principal difficulty arising in the practical realisation of these processes reduces to the maintainance of an exact ratio of the concentrations of the NCO and OH groups and also involves the necessity to regulate with the aid of special catalytic additives or temperature conditions the ratio of the rates of all the reactions occurring in the system between NCO and OH groups, the reactivities of which are different depending on whether they are primary, secondary, or tertiary [1].

In the synthesis of structured polyurethanes by the trimerisation of isocyanates [19,20], a prepolymer containing terminal NCO groups, which are usually introduced by the reaction of a hydroxyl-containing polyol with di-isocyanates the NCO groups of which have fairly different reactivities (for example, 2,4-tolylene di-isocyanate), has been suggested as the starting material. In the presence of trimerisation catalysts, prepolymers with terminal NCO groups form a three-dimensional network:



In a system without hydroxy-groups, there is only one reaction—trimerisation of the isocyanate, the rate of which can be readily regulated by selecting an appropriate trimerisation catalyst.

Foams, varnishes, and polyaliphatic resins, which are hardened by the trimerisation of terminal NCO groups, are promising as regards technical applications. Polyisocyanurate resins formed, for example, by the cyclic polymerisation of aliphatic di-isocyanates, are distinguished by a high strength, thermal stability, and good optical properties and may be used to prepare plastics with improved optical transparency, which are used in aviation [20].

At the present time, the cyclic di- and trimerisation reactions of NCO groups in polymeric systems have been investigated inadequately, although some data concerning these reactions with participation of monomeric isocyanates are available. The catalytic systems used for this purpose and certain kinetic relations observed in the reactions are of main interest.

From the standpoint of the employment of the trimerisation reactions in polymer chemistry, it is significant that isocyanurates are much more thermostable than the usual polyurethanes. Thus the urethane chain breaks at a temperature as low as 150–200°C, while the thermal degradation of isocyanurates does not begin until 300°C. [21] Structured polymers, formed as a result of the trimerisation of NCO groups, are extremely rigid. In order to obtain fairly elastic materials, it is necessary to employ as the initial prepolymers oligomers the molecular weight of which is 3000–5000; plasticisers can also be employed.

The dimerisation of isocyanates is a reversible reaction, while the equilibrium in the trimerisation is almost completely displaced to the right. The equilibrium concentrations of the 2,4-tolylene di-isocyanate dimer are 8.5 and 7.1% respectively at 78° and 100°C. [22] When the temperature is reduced, there is a significant increase of the equilibrium concentration of the dimer and at 25° and 10° it amounts to as much as 71–74% and 90% respectively [4]. At 150–175°C the 2,4-tolylene di-isocyanate dimer is almost completely converted into the monomer.

Numerous catalytic systems for the dimerisation of isocyanates have been described [4–6]. The possibility of spontaneous non-catalytic dimerisation, which is extremely slow, has also been noted. Thus the equilibrium concentration of the 2,4-tolylene di-isocyanate dimer is reached at 78°C only after 1500 h. The activation energy for the spontaneous dimerisation of this isocyanate is 21 kcal mole^{-1}. [22] The best dimerisation catalysts are trialkylphosphines [23,24]; aryl- and alkylaryl-phosphines are less active.

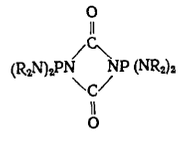
Isocyanates dimerise also in the presence of tertiary amines such as trialkylamines, pyridine, and its derivatives [4,5,25]. In recent years it was established that the

dimerisation of isocyanates also occurs in the presence of sodium benzoate [26], various organometallic compounds [6], and metal chelate complexes [6,27]. In most cases dimerisation is accompanied by trimerisation, but the above catalytic systems, particularly phosphines and tertiary amines, mainly promote the dimerisation reactions.

In the presence of iron acetylacetonate, the dimerisation of isocyanates is greatly accelerated compared with the non-catalytic process [27]. The reaction is then found to be of first order with respect to the catalyst and the activation energy is somewhat reduced, amounting to 19.5 kcal mole^{-1} for the dimerisation of 2,4-tolylene di-isocyanate.

The reasons for the catalytic activity of nucleophilic agents such as phosphines and amines should not be sought solely in their high basicity. For example, the basicities of dimethylphenylphosphine and dimethylaniline are similar, but the former is much more active as a dimerisation catalyst. Certain phosphines and their oxides catalyse the formation of carbodiimides R–N=C=N–R from isocyanates [28,29]. This reaction is a kind of dimerisation of RNCO with liberation of CO_2; $2RNCO \rightarrow R-N=C=N-R + CO_2$. The kinetics of the formation of carbodiimides in the presence of a number of catalytic systems have been investigated in fair detail [30,31].

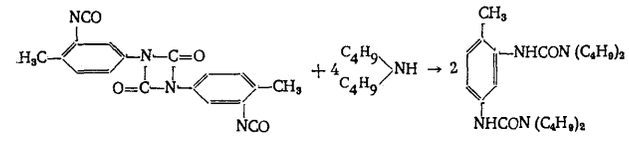
The capacity for dimerisation greatly depends on the structure of isocyanates. Aromatic isocyanates dimerise much more satisfactorily, owing to their lower electrophilicity. Teh dimerisation and trimerisation of acyl isocyanates RCONCO, in particular of benzoyl isocyanate and its methoxy-, chloro-, and nitro-derivatives in the presence of triethylamine, has also been described [32]. The formation of acyl isocyanate dimers and trimers is accompanied by side reactions involving the formation of cyclic products with breakdown of the C=O carbonyl bonds. Dimers of isocyanates derived from tervalent phosphorus acids with the general formula



were described recently [33]. Uretidinediones consisting of two different types of cyanates can be obtained [12].

The kinetics of the dimerisation reactions have been very little studied. One can only point to Davis's infrared spectroscopic investigations [22,27] of the solid-phase dimerisation of 2,4-tolylene di-isocyanate. The presence of an extremely intense band due to the stretching vibrations of the C=O group of the uretidinedione ring in the region of 1790 cm^{-1} makes it possible to identify the dimers readily and to investigate the kinetics of their formation from isocyanates. Downs and Haas [34,35] quote the infrared spectra of a number of dimers derived from phenyl isocyanate and the ^{19}F NMR spectra of isocyanate dimers with a fluorine substituent. Aryl isocyanate dimers melt in the range 160–200°C, depending on their structure [4].

The reactivity of the dimers is due to their capacity for dissociation with formation of the initial isocyanates and therefore their reactions with alcohols, water, and amines result in the formation of urethanes, ureas, and biurets respectively. Since the dimers may be formed spontaneously when isocyanates are stored, the problem of the correct chemical determination of the isocyanate number of monomers is important [36]. For example, it has been shown [37] that the reaction of the 2,4-tolylene di-isocyanate dimer with dibutylamine takes place according to the equation



and at a temperature as low as 50°C the conversion of NCO groups is in excess of 70%. The high reactivity of the dimer in the determination of the content of NCO groups in the monomer can lead to high isocyanate numbers. This factor has a direct bearing on the problem of finding the optimum NCO/OH ratio for the synthesis of polyurethanes from di-isocyanates and hydroxyl-containing polyester-polyols. The reactivity of the dimers in relation to the hydroxy-groups of alcohols and polyols is extremely low and a very long time is required for the urethane-formation reactions to occur even in pure alcohol. The reaction with acidic alcohols (for example with phenols) takes place to an appreciable degree only at 100–150°C.

There are no quantitative literature data on the reactivity of the dimers.

The trimerisation of isocyanates takes place in the presence of catalytic amounts of triethylphosphine [38], alkaline earth metal acetates, formates, and carbonates [13,39], metal naphthenates [40], aluminium chloride [41], oxalic acid [42], triethylamine [43], and iron, sodium, magnesium, mercury, nickel, copper, zinc, aluminium, tin, chromium, etc. salts soluble in organic solvents [44]. The brief review by Arnold et al. [4] of the early studies on the trimerisation contains a list of the catalytic systems for the trimerisation of isocyanates discovered up to 1957. In recent years there has been a considerable growth of interest in this reaction. New trimerisation catalysts have been discovered: sodium benzoate in dimethylformamide (DMF), [26,45] pyridine oxide [32], quaternary ammonium and phosphonium bases [46], metal alkoxides [47], tertiary amines [21], organic derivatives of quadrivalent tin [48], trialkylarsenic and arsenic oxides [49], metal acetylacetonates, and other complexes [27,50,51]. Trimers are also formed in the synthesis of urethanes in the presence of tertiary amines. Kogon showed [52] showed that, in the reaction of phenyl isocyanate with ethanol at 125°C in the presence of *N*-methylmorpholine, the phenyl isocyanate trimer is formed together with the urethane. It is interesting that the trimer appears only in systems containing an amine and an alcohol. In the presence of an amine and a urethane (ethyl carbamate) the trimerisation does not occur. In their attempt to prepare *N*-substituted oxazolidinones by the condensation of epoxides with isocyanates in the presence of pyridine, Jones and Savill [53] showed that the trimerisation reaction takes place vigorously under these conditions. Triphenyl isocyanurate was obtained in oxiran, propene, styrene, and epichlorohydrin solutions in the presence of traces of pyridine in a yield close to 100%. In the presence of oxides, quaternary ammonium bases also catalyse the trimerisation reaction, but much less effectively [53,54]. Subsequently these results served as a starting point in the search for new cocatalysts of the trimerisation in the presence of tertiary amines.

Isocyanate trimers are also formed in the high-temperature (230–250°C) condensation of bisurethanes of the type $RO-\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{N}}-(CH_2)_n-\overset{H}{\overset{|}{N}}-\overset{O}{\overset{\|}{C}}-OR$ in the presence of titanium butoxide [55]. Isocyanate dimers and higher-molecular-weight products of different compositions are also formed

under these conditions. In those cases where the trimerisation and dimerisation of isocyanates take place simultaneously, the yield and rate of accumulation of each product vary significantly as a function of the conditions and the structure of the monomer. For example, in a study of the cyclic polymerisation of phenyl isocyanate in DMF at temperatures in the range 0–70°C under the influence of sodium benzoate, it was shown [26] that at 70°C the yield of the trimer was 50% of theoretical after 3 h and that of the dimer was less than 5%. At 0°C the content of the trimer fell to 30% and that of the dimer rose to 10%. At 30°C the ratio of the rates of dimerisation and trimerisation was 0.05%. [26] In the cyclic polymerisation of benzoyl isocyanate and its derivatives in the presence of tertiary amines and pyridine oxide, a significant change in the mode of reaction as a function of the structure of the isocyanate was established: at 50–80°C benzoyl isocyanate forms mainly the dimer under these conditions, while the less reactive *p*-methoxybenzoyl isocyanate yields the trimer—tribenzoyl isocyanurate [32].

Herbstman [49] made a detailed study of the trimerisation of isocyanates of different structures in the presence of a number of organic derivatives of antimony and arsenic. In the presence of 2 mole % of tri-n-butylarsenic and triisobutylarsenic oxides, phenyl isocyanate, and *m*-chlorophenyl isocyanate trimerise with a yield of 94–100% at room temperature over a period less than 1 h. The less reactive isocyanates *p*-$CH_3OC_6H_4NCO$ and C_2H_5NCO form trimers only on heating to 80°C with a yield of 95–97%. Isocyanates are very readily trimerised at low temperatures in the presence of catalytic amounts of tri-n-butylantimony diethoxide and diacetate. In the presence of triphenylarsenic oxide, even an inert monomer such as CH_3NCO trimerises in 15 min and *m*-chlorophenyl isocyanate forms under these conditions 30% of the trimer and 70% of carbodiimide. Antimony derivatives of the type $(t\text{-}C_4H_9)_5Sb$ and $(t\text{-}C_4H_9)_3SbCl_2$ do not catalyse the trimerisation process. It was established that tributylantimony oxide forms a stable complex with phenyl isocyanate, which is probably responsible for the catalysis [49]. The infrared spectrum of the complex has an intense C=O absorption band (1725 cm^{-1}); the N–H, N=C=O, and C=O bands of triphenyl isocyanurate (1705 cm^{-1}) are absent. A complex of the catalyst and triphenyl isocyanurate is not formed.

Organotin compounds are much less active as trimerisation catalysts. Bloodworth and Davies [48] showed that tributylmethoxytin $[(C_4H_9)_3SnOCH_3]$ and bistributyltin oxide $[(C_4H_9)_3Sn-O-Sn(C_4H_9)_3]$ react with isocyanates in equimolecular proportions to form 1:1 adducts. Under these conditions, the conversion of RNCO into the trimer is extremely slow.

There are no accurate quantitative literature data on the rates of trimerisation under the influence of organometallic compounds, with the exception of the results of a study of the trimerisation of 2,4-tolylene di-isocyanate in the presence of iron acetylacetonate [27]. The trimerisation reaction is of first order with respect to the catalyst, the catalytic effect of iron acetylacetonate in the trimerisation being more pronounced than in the dimerisation. Thus, 0.51 wt.% of the catalyst accelerates the solid-phase dimerisation reaction at 78°C by a factor of 60 and the trimerisation process by a factor of 200. The activation energy for spontaneous trimerisation in the absence of a catalyst is 16 kcal $mole^{-1}$ [22] and in the presence of iron acetylacetonate, 10.5 kcal $mole^{-1}$. [27] It is noteworthy that the cyclopolymerisation of isocyanates in the presence of iron acetylacetonate leads to an additional consumption of NCO groups in urethane formation, where iron acetylacetonate is frequently employed as a catalyst [56,57]. In the general case this is important, but comparison of the rate of urethane formation in the reaction between 2,4-tolylene di-isocyanate and the hydroxy-groups of a polyesterpolyol and the rate of the di- and trimerisation of this isocyanate in the presence of 0.5 wt.% of iron acetylacetonate shows that, while the first reaction is accelerated by a factor of approximately 50, [57] the consumption of NCO groups in the di- and trimerisation side reaction is only 0.1%, [27] i.e. it may be disregarded.

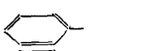
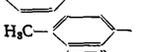
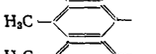
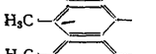
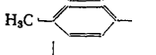
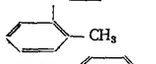
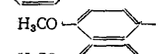
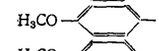
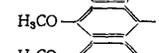
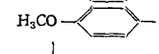
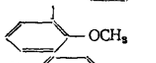
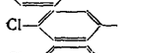
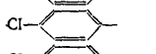
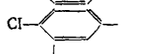
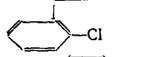
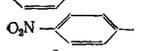
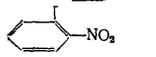
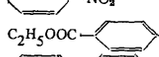
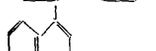
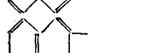
In the presence of organometallic compounds, isocyanate trimers do not form complexes with the catalyst [48,49], although isocyanurates are known to form readily molecular complexes even with the usual organic solvents, which can be identified spectroscopically [58]. The 1:1 complexes of a number of aryl isocyanurates with benzene, acetone, and DMF can be readily isolated in the form of colourless crystals. The infrared spectra of the complexes contains virtually the same bands as the spectrum of the free isocyanurate, but the relative intensity and position of the C=O band are altered. Table 1 lists the vibration frequencies of the C=O group in a number of isocyanurates and their complexes with solvents. Methanol, ether, and benzophenone do not form complexes with isocyanurates, but ethylene carbonate forms at 130°C a stable 1:1 complex with triphenyl isocyanurate having a molecular weight of 230, which corresponds to the formula $(C_6H_5NCO)_3.C_3H_4O_3$. [59] It is noteworthy that in the presence of traces of *N*-methylmorpholine the trimerisation of isocyanates is much faster when ethylene carbonate is introduced into the system as a cocatalyst, the reactivity of the resulting trimer bound in a complex with ethylene carbonate being higher in the reaction with primary amines than that of the free trimer [59].

The complexes of aryl isocyanurates with organic solvents are fairly stable at room temperature. *In vacuo* at 100–200°C the complexes decompose into the initial components. Aliphatic isocyanurates form complexes much less readily.

The mechanism and kinetics of the trimerisation of NCO groups can be inferred at the present time only from studies on trimerisation in the presence of tertiary amines and tertiary amine–cocatalyst catalytic systems [21,60,61]. As already stated, alkylene oxides are usually employed as cocatalysts; aldehydes, lactones, alkylene carbonates, and imines also exhibit a high cocatalytic activity. The trimerisation of NCO groups probably involves an anionic mechanism. In particular, this is indicated by data on the reactivity of aryl isocyanates in trimerisation: electron-accepting substituents accelerate trimerisation, while electron-donating substituents retard it (Table 2). [21] Interpretation of data for the relative reactivities of *meta*- and *para*-substituted phenyl isocyanates on the basis of the Hammett equation yields $\rho = 3.5$, which confirms the nucleophilic nature of the trimerisation of isocyanates. Steric factors play a significant role. This is reflected in a markedly lower reactivity of *ortho*-substituted aryl isocyanates (Table 2).

The trimerisation reaction in the presence of amines is significantly faster in polar media than in solvents with a low dielectric constant. Thus the relative reactivities of phenyl isocyanate in benzene ($D = 2.3$), chlorobenzene ($D = 5.7$), acetonitrile ($D = 37.5$), and dimethyl sulphoxide (DMSO) ($D = 45.0$) are 1.5, 2.4, 8.4, and 12.3 respectively [21]. The acceleration of the reaction in media with a high dielectric constant indicates a significant polarity of the transition complex in the trimerisation process.

Table 1. The position of the C=O bond in the spectra of isocyanurates and their complexes with organic solvents[58].

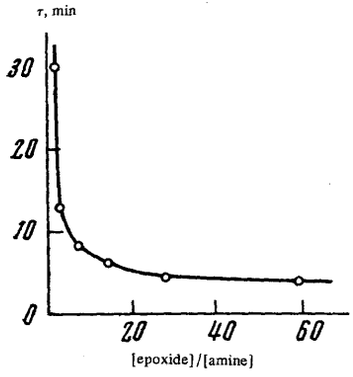
Group	M.p. of trimer, °C	Solvent	ν, cm^{-1}
	280	—	1695[52], 1710
	—	DMF	1700, 1670
	264	—	1765, 1715, 1690
	—	DMF	1700, 1675
	—	Benzene	1700
	—	Acetone	1700
	180	—	1695[52]
	260	—	1765, 1715, 1690
	—	DMF	1700, 1680
	—	Benzene	1700
	—	Acetone	1700
	261	—	1703[52]
	318	—	1770, 1715, 1690
	—	DMF	1700, 1670
	—	Acetone	1700
	201	—	1700[52]
	350	—	1765, 1715, 1685
	260	—	1703
	246	—	—
	374	—	1709[53]
	335	—	1713[53]
	344	—	1700[53]
	162 (decomp.)[32]	—	—
$-CH_2CH=CH_2$	19—22 [15]	—	—
$-CH_2COOC_2H_5$	71—78 [15]	—	—
$-CH_2CH_2CN$	228—230 [15]	—	—

The principal data on the catalytic activities of tertiary amines combined with cocatalysts of different types are quoted by Beitchman[60], who investigated the catalytic activities of a large number of tertiary amine–catalyst compositions by calorimetric methods from the rate of attainment of the maximum temperature rise in the system. It is striking that in the presence of triethylenediamine–alkylene oxide systems the kinetic curve is S-shaped. At the end of the induction period, the duration of which depends significantly on the concentration of both components of the catalytic system and the isocyanate, the reaction is of first order with respect to the monomer and 100% conversion is reached. The S-shape of the kinetic trimerisation curve is not a result of the autocatalytic effect of the reaction product: the shape of the kinetic curves remains unaltered when the dimer or trimer is introduced into the system before the start of the reaction.

The rate of the reaction catalysed by tertiary amine–alkylene oxide systems increases sharply with the [oxide]/[amine] ratio (see Figure) and reaches an approximately constant value from a ratio of about 30 : 1. It was shown subsequently[61] that the rate of trimerisation is proportional to the product of the concentrations of the components of the catalytic system; the presence of the induction period observed in the catalysis by the triethylenediamine–propylene oxide system[60] is not a general characteristic of reactions catalysed by tertiary amine–alkylene oxide systems

Table 2. Effect of the ring substituent in phenyl isocyanate on the reactivity of the monomers in the trimerisation reaction.

Substituent	σ	Relative reactivity
o-OC_2H_5		Very low
o-CH_3		0.06
m-CH_3	—0.07	1.92
p-CH_3	—0.17	3.95
o-Cl		0.09
H	0.00	10.0
m-Cl	0.37	70.0
p-Cl	0.23	128.0
p-Br	0.23	144.0
o-NO_2		20.5
m-NO_2	0.71	Very high
p-NO_2	0.78	Very high



Variation of the time of attainment of the maximum temperature rise in the system in the solid-phase trimerisation of tolylene di-isocyanate in the presence of the triethylenediamine–methyloxiran catalytic system with the [epoxide]/[amine] ratio (plotted on the basis of Beitchman's data[60]).

The catalytic activity of amines under the conditions of joint catalysis in the presence of oxides and other cocatalysts depends significantly on their structure but there is no direct relation with the basicity of the amines. Tertiary amines can be arranged in the following sequence in terms of their catalytic activity: triethylenediamine > triethylamine > *NNN'N'*-tetramethyl-1,3-butylenediamine > *N*-methylmorpholine > 2-methylimidazole[60].

It is also noteworthy that tertiary amines incorporating heterocycles with structures resembling that of the isocyanurate ring, for example the symmetrical *NN'N''*-tri-(dimethylaminopropyl)hexahydrotriazine or 2,4,6-tri-(dimethylaminomethyl)phenol, exhibit a high catalytic activity in the reaction [21]. One cannot rule out the possibility that, together with the basicity factor, the possibility of the coordination of the monomer to the catalyst plays a significant role in the mechanism of the catalysis by such amines. In order to elucidate this factor, detailed studies on the kinetics of the reaction and of the formation of a complex between the catalyst and the monomer are required.

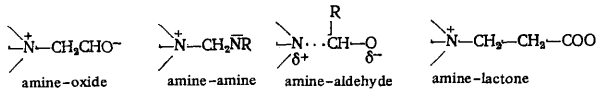
Table 3. Reactivities of olefin oxides, aldehydes, and imines as cocatalysts of the trimerisation of isocyanates (trimerisation of 2,4-tolylene di-isocyanate) in the solid phase (26–27°C; catalyst—0.0022 M triethylenediamine).

Cocatalyst*	τ, min**	t_{max}, °C***
Oxiran (0.020)	3.0	207
Methyloxiran (0.030)	6.0	202
Ethyloxiran (0.030)	7.7	—
Phenyloxiran (0.030)	49.0	164
Acetaldehyde (0.055)	16.0	73
Butyraldehyde (0.063)	45.0	110
Heptanal (0.056)	93.0	53
Trihydroxymethylenealdehyde (0.056)	67.0	128
Anisaldehyde (0.063)	242.0	70
Isodecanaldehyde (0.066)	128.0	87
Benzaldehyde (0.055)	69.0	82
1-Naphthaldehyde (0.056)	>76.0	—
Aziridine (0.0023)	3.0	164
N-Methylaziridine (0.0018)	<2.0	141
2-Methylaziridine (0.0018)	59.0	129

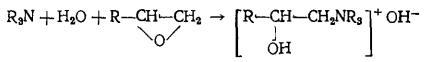
*The molar concentration is indicated in brackets.
**The time of attainment of the maximum temperature rise in the reaction characterising the relative reactivity of the cocatalyst.
***The maximum temperature rise in the reaction mass.

Table 3 shows that in the series of cocatalysts of different chemical types, alkylene oxides are the most effective. Although the times required for the attainment of the maximum temperature rise in the system cannot be strictly speaking regarded as criteria of catalytic activity, they can nevertheless be used for qualitative estimates.

The question of the nature of the active centre in the catalysis of the trimerisation by tertiary amine–cocatalyst systems is controversial. Despite the fact that there exists a possibility, in principle, of the opening of the epoxide, lactone, or imine rings in the presence of tertiary amines [62,63] and despite the significant polarisation of the carbonyl group when amines interact with aldehydes, the experimental proof of the involvement of zwitterions such as



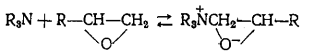
as active catalyst species in the reaction has not so far been found. One should also bear in mind the possibility of the formation in the amine–alkylene oxide systems of quaternary ammonium bases [64–66] as a result of the interaction with traces of water frequently present in solution in fairly large amounts (compared with the catalyst):



Definite information about the nature of the active centre in the reaction could be obtained from NMR data, but such experiments have not been performed. For catalytic systems of a similar chemical type (triethylphosphine–aldehyde and triethylphosphine–acrylonitrile) in the polymerisation of formaldehyde and acrylonitrile, it has been established by NMR [67,68] that the active species are zwitterions of the type $(C_2H_5)_3\overset{+}{P}-CH_2-\overline{O}$ and $(C_2H_5)_3\overset{+}{P}-CH_2-\overset{-}{C}H$, which interact with water or alcohol to form
|
CN

quaternary phosphonium compounds analogous to quaternary ammonium bases.

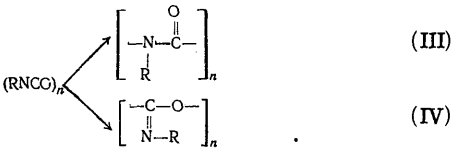
Petrov et al. [61] showed that, when dimethylbenzylamine and glycidyl phenyl ether are mixed together, the electrical conductivity of the mixture increases very rapidly, approximately by a factor of 200, and then remains unchanged for several hours. The opening of the epoxy-ring of glycidyl phenyl ether is much slower. The fact that in the trimerisation of NCO groups in the presence of this catalytic system an induction period is not observed, the electrical conductivity does not change after a sharp rise at the beginning of the reaction, and there is a linear relation between the rate of the process and the product of the concentrations of the components of the catalytic system enabled the authors to suggest the possibility of the formation of ion pairs at catalytically active species without the opening of the epoxy-ring:



The final determination of the nature of the active centre in the trimerisation reaction, the causes of ring closure in the trimer or dimer stage, and the relation between the yield of the trimer or dimer and the type of catalyst will be possible only as a result of a detailed investigation of the reaction kinetics under different conditions and a study of the processes occurring in the catalyst–cocatalyst interaction. These studies are directly related to the investigation of the polymerisation of isocyanates and the formation of high-molecular-weight products, since in both cases the process has an anionic mechanism consisting of a nucleophilic attack on the electrophilic carbon atom of the NCO group.

3. LINEAR HOMOPOLYMERISATION

In view of the structure of the isocyanate group, one must consider the possibility of the existence in a linear polyisocyanate or at least two types of homopolymers formed as a result of the dissociation of the N=C (III) or C=O bonds (IV) respectively:



In the first case the macromolecular chain has the structure of an *N*-substituted polyamide and in the second it has

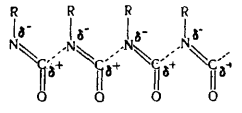
a polyacetal structure. A similar phenomenon is known in polymer chemistry. Thus, when ketens ($\begin{matrix}R\\R\end{matrix}\!\!>\!C=C=O$), which have a structure similar to that of isocyanates, are polymerised, both polyketones (polymerisation via the C=C bond) and polyacetals (polymerisation via the C=O bond) can be formed, depending on the conditions and the chemical nature of the catalyst. In a more general case, there is a possibility of the formation of polymers with alternating blocks or polymers having the ester structure [69,71]. In the homopolymerisation of isocyanates, it is very difficult to incorporate in the polymer chain structures (III) and (IV) simultaneously and can be achieved only in certain specific cases. Moreover, the isocyanate homopolymer with a purely polyacetal chain structure has not so far been obtained, although, as will be shown below, in certain copolymerisation reactions chain propagation takes place mainly as a result of the dissociation of the C=O bond.

Shashoua [7,72] and Natta [73] showed that in the presence of anionic catalysts the homopolymerisation of monoisocyanates involves the formation of high-molecular-weight ($M = 10^4-10^5$) polymers with a structure of type (III) in the main chain, i.e. substituted 1-nylons. The anionic polymerisation of about 30 different isocyanates has been studied [72]. The polymerisation takes place with a high yield in the presence of NaCN, sodionaphthalene, and sodiobenzophenone in DMF between $-20°$ and $-100°C$. The polymerisation of aliphatic and aromatic isocyanates has been investigated in the presence of ethyl-lithium, diethylberyllium, n-octylsodium, and lithium ethoxide in various solvents between $-60°$ and $-78°C$. [73]. It has been shown by X-ray diffraction that highly crystalline polymers are formed in all cases. Their infrared spectra have characteristic absorption bands in the region of 1700 cm^{-1} due to the presence of the C=O group. In the presence of cationic catalysts [$AlBr_3$ and $BF_3(C_2H_5)_2O$], amorphous polymers are formed in much lower yields [73]. In this case a mixed structure (III and IV) is probably formed in the main chain.

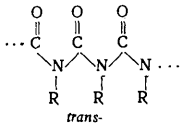
The yield and the molecular weight of the polymer obtained under the conditions of anionic polymerisation pass through a maximum as a function of catalyst and monomer concentrations in the mixture. When the temperature is reduced, the yield and molecular weight increase significantly [72].

The polymerisation of monoisocyanates under the influence of water-soluble initiators—alkalis and inorganic and organic acid salts in DMF at $-50°C$—has been described [50,74]. In the presence of alkalis the polymerisation is initiated by OH^- ions and in the presence of inorganic salts, by the acid anions. When alkali metal salts of carboxylic and dicarboxylic acids are used as the initiating system, the polymer yield is found to depend very markedly on the pK_a of the acid. In the presence of sodium salts of carboxylic acids with pK_a (in water) of the order of 1–3, there is hardly any polymerisation, while in the presence of salts formed by weaker acids (pK_a = 3–6) the yield of the polymer is 50–80%. With increase of the [H_2O]/[monomer] ratio, the yield and the molecular weight of the polymer fall.

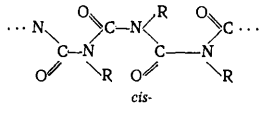
It has been established that the homopolymerisation of isocyanates occurs spontaneously on prolonged heating of the monomer [75] and also on radiation-chemical [76] and electrochemical initiation [77]. The pyrolysis of 2,4-tolylene di-isocyanate yielded linear dimers, trimers, heptamers, with the 1-nylon structure in the main chain [75]. It is interesting that radiation-induced polymerisation by γ-irradiation from cobalt-60 at temperatures between 20° and $-196°C$ can give high yields of isocyanate homopolymers, which, as in the presence of typical anionic catalysts, are formed by polyaddition with dissociation of the N=C double bond. Characteristic features of the radiation-induced polymerisation are the absence of an induction period, direct proportionality between the rate of polymerisation and the dose rate, and the acceleration of polymerisation at low temperatures when the polymer is in the solid state. It is also significant that in the presence of diphenylpicrylhydrazyl the yield of the polymer does not change, which shows that the radiation-induced polymerisation has a non-radical mechanism. The infrared spectra of polymers obtained in the liquid and solid phases are different and the stereoregularity of the "solid-phase" polymer is much higher. The structure of this polymer is identical with that of the polyisocyanates obtained by anionic polymerisation [72,73] and electrochemically [78]. It is suggested [77] that in the crystalline state the radiation-induced polymerisation takes place as a result of a cooperative interaction of the excited monomer molecule via the N=C bond:



Thus the available data show that in the anionic polymerisation of monoisocyanates the fundamental unit of the polymer chain is the amide group. Dielectric measurements [79] and also studies on the viscosity and sedimentation of poly(n-butyl isocyanate) [80] showed that the polyisocyanates obtained by polymerisation via the N=C bond are extremely rigid and probably have a helical conformation. X-ray diffraction data for poly(n-butyl isocyanate) obtained by the anionic polymerisation of n-butyl isocyanate confirmed the hypothesis of a helical configuration of the polymer chain [81]. The helix has a translation of 1.94 Å; the hexagonal unit cell parameters are a = 13.3 Å and c = 15.4 Å. It is suggested that the conformation of the elementary polyisocyanate unit is more consistent with the *cis*-structure than the *trans*-structure [81]:



trans-



cis-

The viscosity and light scattering data for solutions of poly(n-hexyl isocyanate) in tetrahydrofuran (THF) lead to an analogous conclusion [82].

Burchard [80] measured by sedimentation and diffusion methods the molecular weights of poly(n-butyl isocyanate) obtained by anionic polymerisation and established a relation between the viscosity of the polymer in benzene and tetrahydrofuran and the molecular weight:

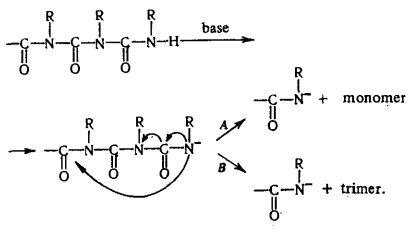
$$[\eta]_{THF} = 0{,}457 \cdot 10^{-3} \cdot M^{1{,}18}; \quad [\eta]_{benzene} = 1{,}10 \cdot 10^{-3} \cdot M^{1{,}11}.$$

A study of the dielectric properties of poly(n-butyl isocyanate) in benzene established a strong dependence of the relaxation time on the molecular weight [79]. Thus, when the molecular weight changes from 1.4×10^5 to 2.3×10^6, the change in τ_{obs} is from 1.6×10^{-6} to 5×10^{-3} s. Hence follows the conclusion of a broad

molecular weight distribution in the polymer. For example, it has been shown [79] by an independent determination of M_w and M_n for different polymer specimens obtained in toluene at −78°C in the presence of n-butyllithium that $M_w/M_n = 3.2-4.3$.

The amide structure of the polyisocyanates obtained on anionic polymerisation of monoisocyanates has been demonstrated by Iwakura et al. [83] by investigating the products and characteristics of the chemical degradation of the polymers in the presence of di-n-butylamine. The products of the reactions occurring at temperatures in the range 30−100°C over a period of several tens of hours are mainly cyclic trimers and the corresponding *NN*-di-n-butyl-*N'*-substituted ureas. The reaction is accelerated in the presence of bases and electron-donating solvents. In certain cases the formation of small amounts of free isocyanate (degradation of polymers formed from aryl isocyanates with electron-donating substituents in the ring) was observed.

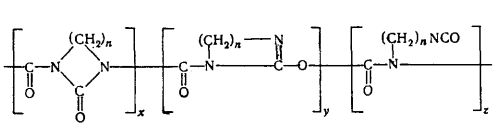
The mechanism of degradation in the presence of a base, the role of which reduces to the abstraction of a proton from the end of the polymer chain with formation of a macroanion, can be represented as follows:



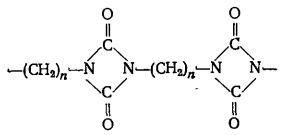
Depending on the chemical nature and conformation of the polymer chain, the reaction can proceed mainly via pathway *A* or *B* or via both simultaneously.

Interesting relations have been observed in the homopolymerisation of aliphatic isocyanates with different lengths of the methylene bridge between two NCO groups. Sections with a polyacetal chain structure were observed for the first time in the homopolymers formed from such monomers, which demonstrates the possibility of the homopolymerisation of isocyanates with dissocation of the C=O double bond. The polymerisation of aliphatic $\alpha\omega$-polymethylene di-isocyanates $OCN(CH_2)_nNCO$ with $n = 1-4$ in the presence of sodium cyanide in DMF at low temperatures was studied simultaneously by King [84] and Iwakura et al. [85] The polymers formed have an extremely high thermal stability and decompose as a rule above 350°C with the exception of the polymers formed from ethylene di-isocyanate. The polymers are soluble in hot sulphuric acid, *m*-cresol, DMSO, and ethylene carbonate.

It was shown that the infrared spectra of the polymers contain two types of absorption band due to the C=O group: at 1710−1770 and 1690 cm^{-1}. This demonstrates the simultaneous presence in the polymer of carbonyl groups in the ring (high frequencies) and in the main chain (low frequencies). On the basis of these data [84,85] and data obtained for the chemical degradation of the polymers [85], it was established that in the general case the polymer contains three types of structure:



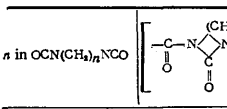
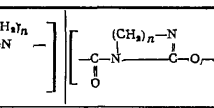
The quantitative proportions of various structures in the chain depend on the nature of the monomer, in particular on the length of the polymethylene chain (Table 4). Studies of the infrared spectra of the polymers led to the rejection of the "polydimeric" chain structure:



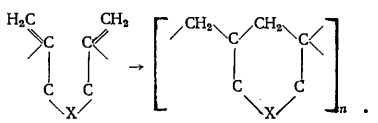
although the polymerisation of certain di-isocyanates did in fact occur in the presence of typical cyclic dimerisation catalysts, for example pyridine [85].

Linear cyclopolymerisation was also observed when cyclohexylene di-isocyanate, hydroxymethylene di-isocyanate, and 1,2,3-propylene tri-isocyanate were employed as monomers [84].

Table 4. The content of various structures in the chain of $\alpha\omega$-polymethylene di-isocyanate polymers (in %).

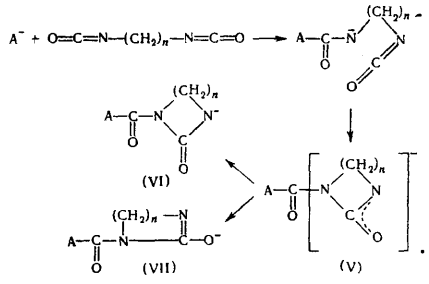
n in $OCN(CH_2)_nNCO$			
1	66	34	
2	0	100	0
3	76	24	0
4	40	60	0

Thus one may conclude that in the anionic polymerisation of $\alpha\omega$-polymethylene di-isocyanates the formation of linear polymers containing repeating cyclic units in the main chain takes place in accordance with alternating intermolecular and intramolecular chain propagation mechanisms. Ring formation of this kind in the growing main macromolecular chain is well known from studies on the polymerisation of dienes [86] and other bifunctional compounds containing ring double bonds [87]. The fundamental unit of such linear cyclopolymers can be readily represented if it is assumed that polymerisation requires the operation of alternating intramolecular and intermolecular chain propagation mechanisms:



In the linear cyclopolymerisation of di-isocyanates, initiation takes place as a result of the attack by the catalyst anion on the carbon atom in the isocyanate group located at one of the ends of the monomer. This results in the dissociation of the C=N bond, as in the anionic polymerisation of mono-isocyanates, with formation of 1-nylons. The second, intramolecular propagation stage may consist of the coordination of the nitrogen atom in the

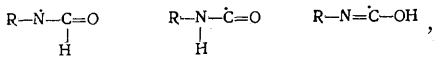
anion to the carbon atom of the second isocyanate group in the monomer with formation of a ring:



In the cyclic intermediate (V), the negative charge is in general delocalised between the nitrogen and oxygen atoms. Depending on the structure of the monomer, structure (VI) or (VII) is formed. Intermolecular chain propagation takes place via the attack by the macroanion on another monomer molecule at the N=C bond.

The question of the dissociation of the N=C or C=O bond in various reactions involving isocyanates is crucial to the chemistry of these compounds. Calculations on the distribution of electron density in the NCO group by the MO-LCAO method have shown that, depending on the structure of the isocyanate, electron density may be enhanced both at the nitrogen and at the oxygen atom [88]. The possibility of urethane formation and the hydrolysis of isocyanates via a stage involving the dissociation of the C=O bonds was recently demonstrated by oxygen isotope exchange [11]. There are no literature data permitting a comparison of the N=C and C=O bond energies in the N=C=O cumulative systems, but indirect information concerning a greater or lesser ease of dissociation of a particular bond may be obtained from the ESR spectra of the radicals formed on γ-irradiation of isocyanates and isothiocyanates and in their reactions with thermal hydrogen atoms [89].

Of the possible radicals formed in such reactions with various alkyl and aryl isocyanates involving the NCO group,

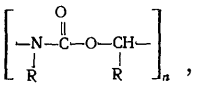


only the first two were detected in the system employed [89] and, depending on the structure of the isocyanate, a radical with an unpaired electron at the nitrogen or at the carbon atom was produced. However, these extremely useful data cannot be treated as proof of the impossibility of the dissociation of the C=O bond in nucleophilic reactions of isocyanates.

The relations in the polymerisation of isocyanates considered here and the data for this copolymerisation which are described below merely emphasise the earlier conclusion [10,11] that the reactions of isocyanates can involve the dissociation of both N=C and C=O bonds, which depends both on the structure of the monomer and hence on the distribution of electron density in the NCO group and on the mechanism of the process and reaction conditions.

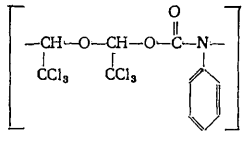
4. COPOLYMERISATION OF ISOCYANATES WITH OTHER MONOMERS

The majority of known copolymers of isocyanates have been obtained by their copolymerisation with aldehydes. Copolymers of formaldehyde with phenyl and alkyl isocyanates [90,91], of acetaldehyde with phenyl and ethyl isocyanates with tolylene di-isocyanate [92], and of butyraldehyde with phenyl isocyanate [92] have been described. Copolymers of phenyl isocyanate and *N*-sulphinyl isocyanate with chloral have also been obtained [93,94]. In most cases copolymerisation occurs in the presence of anionic initiators—sodium cyanide, sodionaphthalene, and fluorenylsodium, but in the copolymerisation of chloral the reaction occurs in the presence of tertiary amines [93] and organometallic complexes such as metal acetylacetonates [95,96]. It has been shown that the chemical nature of the monomers plays such a significant role in their capacity for copolymerisation that in some cases the reaction does not take place at all. Thus acetaldehyde, benzaldehyde, acrolein, and metacrolein do not copolymerise with phenyl isocyanate [92]; on the other hand, butyl isocyanate does not copolymerise with chloral [93]. The copolymers with aldehydes have a fundamental unit with a urethane structure:



(VIII)

i.e. in the copolymerisation the N=C bond of the isocyanate and the C=O bond of the aldehyde dissociate. The presence of the carbonyl group is evident from the infrared spectra (ν = 1725 cm^{-1}) of the copolymers. The molecular weight of the copolymers with chloral, obtained in the presence of triethylamine and triethylenediamine, is $(1-2) \times 10^4$. [93] The polymers have a high melting point (240–250°C) and are white powders readily soluble in benzene, chloroform, carbon tetrachloride, and other solvents. It has been shown by infrared spectroscopy and elemental analysis that the copolymers with chloral formed by anionic copolymerisation do not contain dimeric and n-meric isocyanate blocks, while two monomeric chloral units enter into the fundamental unit of the copolymer with phenyl isocyanate [92]:

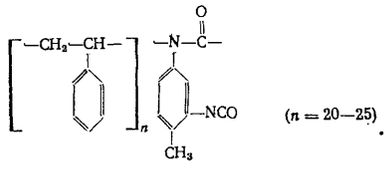


(IX)

In this copolymer the content of chloral corresponding to different monomer ratios (ranging from 3 : 1 to 1 : 3) varies from 62 to 75%. In the copolymer obtained in the presence of a tertiary amine, the content of chloral is 52–66%. The copolymerisation constants for the phenyl isocyanate–chloral system are respectively 0 and 0.4, [92] i.e. the phenyl isocyanate adds at a higher rate to the chloral than to the phenyl isocyanate molecule and conversely phenyl isocyanate is more reactive than chloral in relation to the anion of the latter. 1 : 1 copolymers of phenyl isocyanate and butyl isocyanate with chloral are formed in the presence of metal acetylacetonates, the catalytic activity of the latter depending on the nature of the metal and increasing in the sequence [96] Fe < Cu < Co < Ni. It has been shown by ultraviolet spectroscopy [96] that the formation of a complex by metal acetylacetonate with chloral is responsible for the initiation of polymerisation. The carbonyl group of chloral, inserted between the metal ion and the oxygen atom of acetylacetone, is polarised, which leads to an increase of the negative charge on the oxygen atom of chloral. Thus the copolymerisation has an anionic mechanism.

Isocyanates readily copolymerise with ketens; the mechanism of chain formation in this reaction does not show significant differences from the copolymerisation with aldehydes. At 0°C and room temperature in the presence of n-C_4H_9Li, LiOR, NaOR, and NaCN, diphenylketen and phenyl isocyanate form an alternating copolymer as a result of the dissociation of the C=O bonds of the keten and the C=N bonds of the isocyanate [97]. Block-copolymers containing several phenyl isocyanate units in succession are formed at lower temperature (−45°C).

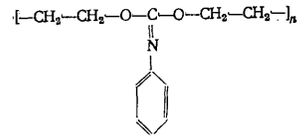
Copolymers of isocyanates with acrylonitrile and vinyl acetate [97], styrene, isoprene, methyl methacrylate, etc. [98-100] have been described. In the copolymerisation of tolylene di-isocyanate with styrene at 20−100°C in the presence of benzoyl peroxide and isopropylphenyl hydroperoxide initiators, the block copolymers (X) are formed:



(X)

The block-copolymerisation of vinyl monomers with butyl isocyanate and 2,4-tolylene di-isocyanate, which proceeds via a "live" polymerisation mechanism at low temperatures in the presence of n-C_4H_9Li in toluene–tetrahydrofuran mixtures has been studied in very great detail. The molecular weight distribution in the copolymers was investigated by gel chromatography: M_w/M_n is 1.14−1.17 in block-copolymers of styrene with butyl isocyanate and 1.5−1.6 in the copolymers of styrene, methyl methacrylate, and isoprene with tolylene di-isocyanate [99]. The di-isocyanate copolymers containing free NCO groups [copolymer (X)] are readily cross-linked by diols, water, and diamines and therefore are of significant practical interest. The trimerisation of the NCO groups can be used for the cross-linking of these copolymers.

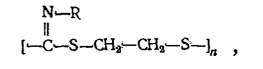
Studies on the copolymerisation of isocyanates with olefin oxides have a direct bearing on the possibility of the dissociation of the C=O bond in reactions involving isocyanates which we are considering. Furukawa and coworkers [101,102] were the first to establish that in the presence of triethylaluminium the monomers are copolymerised in the phenyl isocyanate–oxiran system together with the formation of polyoxiran. The copolymers contain acetal units in the main chain:



(XI)

The structure of the fundamental unit was demonstrated spectroscopically and by studying the hydrolysis products of the copolymers: one of the hydrolysis products of the copolymer (XI) is aniline. *N*-phenylmonoethanolamine should be formed in the hydrolysis of the copolymers formed by the addition of oxiran with dissociation of the N=C bond of the isocyanate.

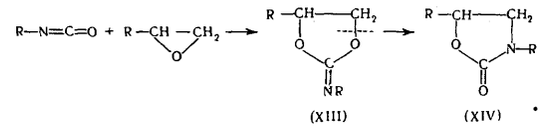
Subsequently a number of isothiocyanates were copolymerised with thi-iran in the presence of triethylamine [103], n-C_4H_9Li, and sodionaphthalene [104,105]. It was shown that the copolymerisation involves the formation of a polymer having the following structure:



(XII)

i.e. the addition of thi-iran to the isothiocyanate proceeds with dissociation of the C=S bond. The copolymerisation of thi-irans with isothiocyanates in the presence of typical anionic initiators involves the "live" polymerisation mechanism, which makes it possible to obtain block-copolymers of the required composition [105].

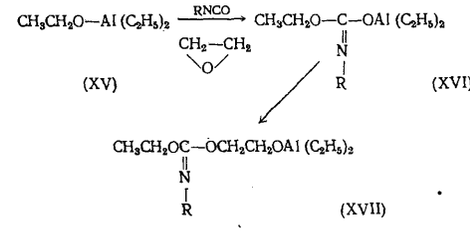
The very fact of polymerisation via the C=O and C=S bonds is not unexpected. Gulbins and Hamann [107] showed that the formation of the addition product (XIII) with dissociation of the C=O bond is an intermediate stage preceding the formation of 2-oxazolidinones (XIV) from epoxides and isocyanates:



(XIII) (XIV)

The conversion of compound (XIII) into 2-oxazolidinone (XIV) as a result of a rearrangement with opening of the dioxolan ring takes place at temperatures in the range 150−200°C and is catalysed by Lewis acids [108].

However, it has been shown [109,110] that compounds of type (XIII) and (XIV) are not intermediates in the copolymerisation of isocyanates with epoxy-compounds in the presence of triethylaluminium. The copolymerisation has a coordination-anionic mechanism with alternating insertion of the monomers in the Al−O bond of the diethylaluminium monoalkoxide (XV) and compound (XVI) being formed:



(XV) (XVI)

(XVII)

The structure of the intermediate (XVI) was established by infrared and NMR spectroscopy.

The data discussed above show that, despite the considerable number of studies concerned in some way with the problem of the polymerisation of isocyanates, the question of the mechanism of the processes involving various catalytic systems is still far from being finally elucidated. The limited number and in some cases the total absence of quantitative kinetic studies hinders greatly both the interpretation of the results and the possibility of a deliberate regulation of the rates of the processes and of the composition of the polymers formed. Much still remains to be done in the field of isocyanate polymerisation and one of the aims of the present review was to draw the attention of investigators to this interesting problem, which is important from the practical point of view.

After the manuscript had been sent to the editors, a number of studies with data on new catalytic systems and on the trimerisation [111-113], polymerisation [112,113], and copolymerisation of isocyanates with various monomers [114-121], as well as data on the thermal degradation of polymers with isocyanurate rings in the chain [122] and detailed studies on the properties and structures of polyisocyanates in solution [123-125] were published.

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Chemical Dosimetry of Pulsed Electronic Radiation

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Existing methods for chemical dosimetry of pulsed electronic radiation are reviewed. Sources of this type of radiation are described, and the special problems arising in the dosimetry of high dose rates (up to 10^{14} rad s^{-1}) are discussed. The effect of dose rate on the yield of radiolysis products is discussed in detail for a number of systems used in dosimetry (aqueous solutions, organic liquids, polymers, gases, etc.). Dosimetric systems particularly suitable for different ranges of dose rate are listed. 112 references.

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1. INTRODUCTION

Pulsed electronic radiation, generated by electron accelerators, has become widely used in radiation chemistry during the last few decades. This development arose, in the first instance, as a result of the penetration of pulse radiolysis into radiation-chemical practice. A powerful, short pulse of high-energy electrons can generate short-lived particles (free radicals, ions, excited molecules) in quantities sufficient to allow their detection by existing physicochemical methods. This enables the particles to be identified and their reaction kinetics to be measured directly. The method has been discussed in monographs [1,2] and in review articles [3,4], and it has given results of fundamental significance in radiation chemistry and in many other fields of science (chemical kinetics, photochemistry, radio-biology, etc.).

A system subjected to a pulse of this type receives a fairly high dose (up to 10^6–10^7 rad). The pulse is of very short duration (usually 10^{-6}–10^{-9} s). Hence, radiolysis by pulsed radiation usually involves very high dose rates (up to 10^{13}–10^{14} rad s^{-1}), which give rise to a number of special features in the radiolytic reactions induced in the system. For example, competitive reactions of the radical–solute and radical–radical type become important in aqueous systems (see Ref. 1). This is an additional reason for the growing popularity of pulsed electron radiation among research workers.

Lastly, electron accelerators are already fairly widely used in radiation chemistry (see, for example, Ref. 5). Hence, accelerators capable of generating pulsed radiation are also likely to find applications.

Obviously, correct dosimetry of pulsed radiation is one of the main prerequisites to the successful application of this type of radiation in radiation-chemical experiments. The recent literature contains a large number of papers on the chemical dosimetry of pulsed radiation. The earlier work is discussed in recent books [1,2] and in a recent review [6]. The present review deals with results published up to the middle of 1971.

2. SOURCES OF PULSED ELECTRONIC RADIATION

Pulsed electronic radiation is usually generated with linear accelerators. These machines can produce either trains of pulses with a prescribed periodicity or single pulses. Pulses of electrons can be obtained also in accelerators of other types with special attachments. In recent years, pulse accelerators of the "Febetron" type, operating on the capacitor discharge principle, have become popular in radiation chemistry laboratories outside the Soviet Union. They are the most powerful accelerators yet developed, giving electron pulses corresponding to currents of thousands of amperes. Other accelerators capable of producing pulsed electron radiation include the dynamitrons and resonance transformers. The operating characteristics of typical sources of pulsed electron radiation are listed in Table 1.

The length of the pulses produced by linear electron accelerators is usually of the order of 10^{-6}–10^{-9} s. However, these pulses usually have a fine structure. For example, a single pulse from the Vickers accelerator at Toronto University, 3.5×10^{-8} s long, actually consists of approximately 100 pulses 2×10^{-11} s long separated by 3×10^{-10} s intervals [13]. The linear accelerator installed at the Argonne National Laboratory (USA) has very similar characteristics: the fine structure of the pulses generated by this accelerator [14] is shown in Fig. 1. Thus, modern electron accelerators offer pulses as short as $\sim 10^{-11}$ s to the research worker.

Pulsed electron accelerators can be used also to generate pulses of X-rays by focussing the electron beam from the accelerator on a heavy-metal target (tungsten, lead, gold, etc.). The method has been used to measure the radiation-induced electrical conductivity of various liquids [21-23].

Table 1. Characteristics of pulsed electron accelerators.

Type of accelerator	Electron energy, MeV	Pulse length, μs	Maximum pulse current, A	References
"Metropolitan Vickers" linear accelerator	1.8	2	0.5	7
"Associated Electrical Industries" linear accelerator	4	0.2 or 2	0.1	8
"Applied Radiation Corporation" linear accelerator	13	0.4—5	0.15	9
"Varian Associates" linear accelerator	7	1.5—5	0.18	10
Ditto	4	0.006—0.05	0.5	11
	4	1.6	0.32	
"U-12" linear accelerator	4—5	2—3	0.1—0.2	12
"Vickers Engineering" linear accelerator	48	0.035	1.0	13
	48	$2 \cdot 10^{-5}$	~15	
	11	0.5—10	2.5	14
"Applied Radiation Corporation" linear accelerator	19—21	0.01	20	
"Febetron 705" (Field Emission Corporation) accelerator	2	0.05	$5 \cdot 10^3$	15
"Febetron 706" (Field Emission Corporation) accelerator	0.5—0.6	0.003	up to ~10^4	16
Cockroft-Walton accelerator	0.8—1.2	0.6 and 5	0.8	17, 18
	3	0.001—0.1	5	19
"High Voltage Engineering" Van de Graaf accelerator	3	5	1	
"Mitsubishi" Van de Graaf accelerator	3	0.3—3.5	0.2	20

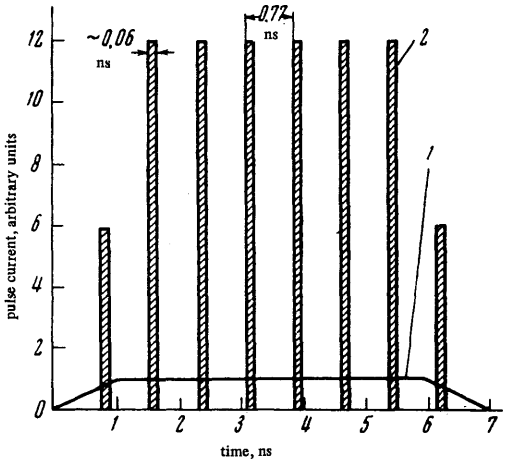

Figure 1. Fine structure of the electron pulses generated by the "Applied Radiation Corporation" (USA) linear accelerator: *1*) macro-pulse, *2*) individual micro-pulse.

3. GENERAL COMMENTS

A knowledge of the following basic parameters is needed in radiation-chemical experiments with pulsed radiation: the dose per pulse absorbed by the system, the pulse length, and the pulse waveform. As an example, oscillograms of the electron pulses generated by various accelerators are shown in Fig. 2.

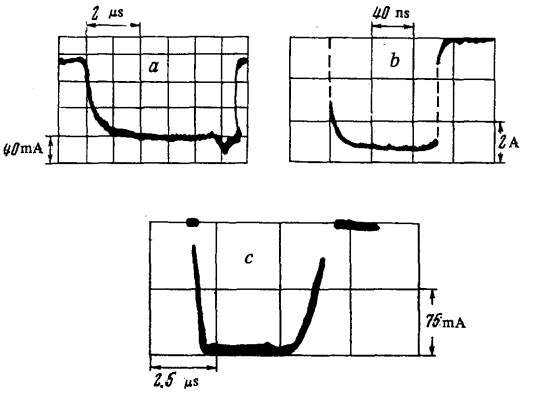

Figure 2. Oscillographic traces of electron pulses generated by (*a*) a linear accelerator [9], (*b*) a Van de Graaf accelerator [19], (*c*) a Cockroft–Walton accelerator [17].

If the duration of the pulse is $\leqslant 10^{-6}$ s the resulting, short-lived radiolysis products have half-lives greatly in excess of the pulse length. The reactions involving these products take place, effectively, after the pulse has subsided. Hence, in these reactions the dose per pulse (which determines the concentration of short-lived products) is more important than the dose rate (which determines the rate of formation of these products). The dose per pulse is measured by physical or by chemical methods. Among the former, calorimetric methods are the most important [19,24-26]. Willis and coworkers [19,26] used an aluminium disk as the calorimeter. With liquid samples, the calorimetric disk was identical in shape and size to the volume of the experimental liquid [26]. However, the method does not lend itself to studies of radiolysis in gaseous systems. In this case, thin disks covering a range of thickness are used, and the dose in an infinitely thin calorimeter is found by extrapolation to zero thickness [19]. Ionisation methods are not suitable for dose measurements in pulsed radiation experiments because the intensities are too high [27,28]. If the average energy of the electrons in the irradiated system is known, the dose can be found by measuring the charge in the system (if sufficiently conducting) [1,17]. The charge can be conveniently measured with an integrator based on capacitor discharge.

In the vast majority of radiation-chemical experiments, doses have been measured by chemical methods. The dose is calculated from the amount of chemical reaction induced by the radiation in some suitably chosen system. Chemical dosimetry has been discussed in recent monographs [29,30] and reviews [6].

Two types of dosimetric measurement are used in pulse radiolysis, depending on the aim of the experiment. If the experiment is designed to measure the radiation-chemical yield of a specific product, we need to know the mean dose over the whole sample volume. If, on the other

hand, we are monitoring short-lived particles by some optical method we need to know the optical density of the system as well as the dose. In this case, since the dose field is never uniform within the cell, one measures the dose absorbed along the path of the monitoring light beam rather than over the whole of the sample.

At the very high dose rates produced by pulsed electron radiation the radiation-chemical yields of many dosimetric systems differ from the values measured at less extreme dose rates. In aqueous dosimetric systems the effect is due to recombination of the primary radiolysis products of water (hydrated electrons $e^-_{aq.}$, hydrogen atoms, OH radicals). Evidently, we must allow for this effect when using aqueous systems for the dosimetry of pulsed radiation.

Many authors have reported a characteristic change in the yield of the radiation-chemical changes of practically all dosimeters based on aqueous solutions. The recombination of the primary radiolysis products of water can be inhibited by using relatively high concentrations of solutes.

The yields under pulsed radiation conditions can also be different (as compared, for example, with γ-radiolysis) in gaseous dosimeters. The effect has been reported, in particular, in mixtures of oxygen and nitrous oxide (see Section 9).

Electron accelerators are complex machines whose operation presents a number of special problems. Although the current does not usually vary by more than 10% from pulse to pulse, much larger variations are occassionally produced. A significant shift in the position of the beam is also possible. These effects can lead to large experimental errors: in order to ensure against these errors it is desirable to monitor the dose rate continuously throughout the experiment. Various methods have been used for this purpose. Keene [8,31] has monitored the electron beam with a secondary emission ionisation chamber, in which the electrons pass through a thin metal foil in a vacuum before reaching the sample cell. Slow secondary electrons appear at the surface of the foil, giving a charge which is proportional to the number of incident fast electrons [8,31-33]. The chamber can be calibrated, for example, against the ferrous sulphate dosimetric system. Schmidt and Buck [34] monitored the dose by bringing the beam to rest in a copper target situated behind the sample cell and measuring the charge acquired by the target. Other methods of monitoring the dose rate have also been described [1,35-37]. In linear accelerators a change in beam current usually gives rise to a significant change in electron energy. Gass and coworkers [38] have described a novel magnetic analyser for measuring electron energies, which can be located within the accelerator in front of the exit window.

4. THE FERROUS SULPHATE DOSIMETRIC SYSTEM

The ferrous sulphate system, usually called the Fricke dosimeter, is most commonly used in radiation chemistry to measure dose. The dosimeter consists of a 10^{-3} M solution of Fe^{2+} in 0.4 M H_2SO_4, saturated with air and containing 10^{-3} mole litre^{-1} of NaCl. Irradiation causes oxidation of bivalent to tervalent iron, with a $G(Fe^{3+})$ value of 15.6 ions/100 eV for solutions of this composition at low dose rates.

Many workers [17,18,24,39-50] find that $G(Fe^{3+})$ for the Fricke dosimeter begins to decrease at dose rates of $\sim 10^8$ rad s^{-1}. The decrease is found [40,44,47] to be even greater when the solution contains NaCl. However $G(Fe^{3+})$ can be made practically independent of dose rate up to $\sim 6 \times 10^9$ rad s^{-1} by increasing the concentration of Fe^{2+} ions to 10^{-2} M and saturating the solution with oxygen [42,44,47-49]. $G(Fe^{3+})$ is 16.07 ions/100 eV for the γ-radiolysis of a solution of this composition [48]. Table 2 lists the results of some recent measurements by Fricke and coworkers [48] of $G(Fe^{3+})$ for solutions of the above compositions. According to Thomas and Hart [44], $G(Fe^{3+})$ in an oxygen-saturated 10^{-2} M solution of Fe^{2+} in 0.4 M H_2SO_4 is 11.2 ions/100 eV at dose rates of $\sim 10^{11}$ rad s^{-1}.

Table 2. Values of $G(Fe^{3+})$ for the ferrous sulphate dosimetric system at high dose rates.

Dose rate, rad s^{-1}	$G(Fe^{3+})$, ions/100 eV	
	10^{-3} M soln. of Fe^{2+} in 0.4 M H_2SO_4 (saturated with air)	10^{-2} M soln. of Fe^{2+} in 0.4 M H_2SO_4 (saturated with O_2)
$\leqslant 10^8$	15.60	16.07
$7.14 \cdot 10^8$	15.33	16.07
$1.43 \cdot 10^9$	15.04	16.07
$2.86 \cdot 10^9$	14.55	16.02
$5.72 \cdot 10^9$	13.76	15.88
$1.14 \cdot 10^{10}$	12.68	15.65
$2.29 \cdot 10^{10}$	11.33	15.20
$5.58 \cdot 10^{10}$	9.64	14.61

Thus, an oxygen-saturated 10^{-2} M solution of Fe^{2+} in 0.4 M H_2SO_4 (often called the modified Fricke dosimeter) can be used to measure the dose of pulsed radiation at dose rates up to $\sim 6 \times 10^9$ rad s^{-1}.

The concentration of Fe^{3+} ions formed by irradiation is usually determined spectrophotometrically by measuring light absorption at 304 nm. The molar extinction coefficient of Fe^{3+} in 0.4 M H_2SO_4 is 2197 litre mole^{-1} cm^{-1} at 25°. Its temperature dependence [6] is 0.69% per degree.

5. OTHER AQUEOUS DOSIMETRIC SYSTEMS

The yield $G(Ce^{3+})$ in the cerium dosimetric system (10^{-4}–10^{-3} M solution of Ce^{4+} in 0.4 M H_2SO_4) has been found [41,42,44,46,51] to increase at dose rates above $\sim 10^8$ rad s^{-1}. For example, in a 2×10^{-4} M solution of Ce^{4+} in 0.4 M H_2SO_4 the yield $G(Ce^{3+})$ is ~ 3.3 ions/100 eV at a dose rate of $\sim 8 \times 10^9$ rad s^{-1}, [51] as compared with 2.3–2.5 ions/100 eV for the same solution exposed to γ-radiation from ^{60}Co. Hence, the cerium system is not very useful for the dosimetry of pulsed radiation at dose rates in excess of $\sim 10^8$ rad s^{-1}.

According to Hutchinson [52], the yield of the bleaching reaction of Methylene Blue in aqueous solutions is drastically lowered under pulsed electron radiation conditions. Thus, the dose required to lower the optical density of a 5×10^{-6} M solution of this dye by 37% at a dose rate of $\sim 10^{10}$ rad s^{-1} is greater by a factor of 2–4 than at lower dose rates.

Bjergbakke and Sehested [53] studied the effect of dose rate under pulsed electron radiation conditions on $G(Fe^{3+})$ in a 5×10^{-3} M solution of H_2SO_4 containing 10^{-3} mole litre^{-1} of Fe^{2+} and 10^{-2} mole litre^{-1} of Cu^{2+}. They found that $G(Fe^{3+})$ in a deaerated solution is practically independent of dose rate up to 5×10^8 rad s^{-1}, whereas in an oxygen-saturated

solution the yield ceases to be constant at 10^8 rad s^{-1}. In the former solution $G(Fe^{3+})$ is 0.65, in the latter 0.75 ion/100 eV. The yield is independent of dose between 5×10^4 and 8×10^6 rad. At higher doses $G(Fe^{3+})$ begins to increase. At normal dose rates the value of $G(Fe^{3+})$ in this system is ~0.7 ion/100 eV.[53-56]

Feng and coworkers[54] published a more detailed study of the radiolysis of aqueous $FeSO_4$–$CuSO_4$–H_2SO_4 solutions at high dose rates. They found that $G(Fe^{3+})$ increases with dose rate, acidity, and oxygen concentration to ~4 ions/100 eV. However, the dependence of $G(Fe^{3+})$ on dose rate is much less marked when the solution contains large concentrations of Cu^{2+} ions. In a solution containing Fe^{2+}, H^+, O_2, and Cu^{2+} at the concentrations 10^{-3}, 10^{-2}, 2.4×10^{-4}, and 5×10^{-2} mole $litre^{-1}$ respectively, $G(Fe^{3+})$ is independent of dose rate up to ~$(1.0-1.4) \times 10^{10}$ rad s^{-1}. (The yield of Fe^{3+} under these conditions is 0.58 ion/100 eV) At slightly higher (0.1 M) concentrations of Cu^{2+} the yield remains constant up to a dose rate of ~3×10^{10} rad s^{-1}.

The yield of Fe^{2+} in a 5×10^{-3} M solution of H_2SO_4 saturated with air and containing Fe^{3+}, Cu^{2+}, and formic acid decreases at high dose rates[45]. Even at dose rates of ~10^8 rad s^{-1} the value of $G(Fe^{2+})$ in solutions containing large amounts of Cu^{2+} or HCOOH is lower than the yield for γ-radiolysis.

Sehested and coworkers[57,58] have studied the behaviour of an aqueous oxalic acid dosimeter at high dose rates. They found that the yield for the decomposition of oxalic acid (at a dose corresponding to 25% decomposition) is independent of dose rate up to 2×10^8 rad s^{-1} when the concentration of oxalic acid is up to 2×10^8, 2×10^9, and 2×10^{10} rad s^{-1} when the concentration of oxalic acid is 0.05, 0.1, and 0.2 M respectively. The yield for the decomposition of $H_2C_2O_4$ was 4.9 molecules/100 eV.

Anderson and Hart[59] measured the yield of radiolysis products in an oxygen-saturated solution containing 10^{-2} mole $litre^{-1}$ of HCOOH and 5×10^{-4} or 5×10^{-3} mole $litre^{-1}$ of H_2SO_4 at dose rates of ~3×10^9 rad s^{-1}. The results (in molecules/100 eV) are: $G(H_2O_2) = 3.25$, $G(CO_2) = 2.75$, $G(-O_2) = 2.82$, and $G(H_2) = 0.43$. These values are practically identical to the yields observed with γ-radiation from ^{60}Co.

Pikaev and Glazunov[45] found that $G(Fe^{3+})$ in deaerated sulphuric acid solutions of Fe^{2+} under pulsed electron irradiation is considerably lower than under γ-radiolysis conditions. Thus, $G(Fe^{3+})$ for a 3×10^{-3} M solution of Fe^{2+} in 0.4 M H_2SO_4 is ~6.7 ions/100 eV even at a dose rate of 5×10^7 rad s^{-1}.

The yield of phenol in solutions of benzene saturated with air or oxygen is strongly dependent on the dose rate of the pulsed radiolysis[9,60,61]. For example, $G(C_6H_5OH)$ is found[60,61] to be 0.8 molecule/100 eV at a dose rate of 3.6×10^9 rad s^{-1}, as compared with 1.9–2.1 molecules/100 eV during γ-radiolysis.

Pikaev and coworkers[61-63] found that in sulphuric acid solutions of Fe^{2+} containing oxygen and benzene or ethanol the $G(Fe^{3+})$ value decreases very substantially at high dose rates. For example, in a 2.5×10^{-4} M solution of Fe^{2+} in 0.4 M H_2SO_4 saturated with benzene and air the $G(Fe^{3+})$ value is ~15 ions/100 eV at a dose rate of ~5×10^8 rad s^{-1}, as compared with 64 ions/100 eV for γ-radiation from ^{60}Co in the same solution.[61,62]

Many workers[44,59,64-66] have studied the pulse radiolysis of water at different pH values. Fricke and Hart[6] recommend the use of a deaerated solution of H_2SO_4 at pH 3–4 for the dosimetry of pulsed radiation. In this solution, $G(H_2O_2) = G(H_2) = 1.16$ molecule/100 eV at dose rates up to ~2×10^9 rad s^{-1}.[65] According to Willis and coworkers[66], $G(H_2)$ in deaerated, neutral water decreases from ~1 to ~0.8 molecule/100 eV as the dose rate is increased from ~1.6×10^{12} to ~1.6×10^{14} rad s^{-1}. At a dose rate of ~1.6×10^{14} rad s^{-1}, $G(H_2)$ increases from 0.8 to 1.1 molecule/100 eV as the pH decreases from 7 to 1.

6. USE OF HYDRATED ELECTRON FORMATION IN DOSIMETRY

Hart and coworkers[6,67-71] suggested the use of the hydrated electron formation reaction in 10^{-2} M NaOH solutions saturated with hydrogen (7×10^{-4} mole $litre^{-1}$ H_2) in pulsed radiation dosimetry†. In these solutions the $e^-_{aq.}$ species produced by doses between 1 and 100–150 rad per pulse decay mainly by recombination.

The hydrated electron is characterised by a strong optical absorption in the visible region of the spectrum, with a band maximum at 720 nm. According to some recent measurements[73], the molar extinction coefficient of $e^-_{aq.}$ is 1.85×10^4 litre $mole^{-1}$ cm^{-1} at 715 nm. Evidently, the concentration of hydrated electrons can easily be measured spectrophotometrically. However, $e^-_{aq.}$ is a short-lived particle, with a half-life of ~25 ms in a solution of the above composition[69]. Hence, fast spectrophotometric methods must be used to measure the concentration of $e^-_{aq.}$: these methods are discussed in Refs. 1 and 2.

The dosimetric method consists in measuring the kinetics of the decay of optical absorption associated with the $e^-_{aq.}$ species. To calculate the dose from these measurements we need to know the initial optical density E_0 of the hydrated electron and the product $G\cdot\epsilon$ (where ϵ is the extinction coefficient of $e^-_{aq.}$) at the chosen wavelength. The quantity E_0 is found by extrapolating the kinetic curve to $t = 0$ (where t is time). The value of $G\cdot\epsilon$ at 700 nm for a hydrogen-saturated solution (pH 12) is 1.21×10^5 (litre $mole^{-1}$ cm^{-1})·molecules/100 eV. The formula for the dose D in this case is

$$D = \frac{0.994 \cdot 10^9 E_0}{1.21 \cdot 10^5 l} = 7.8 \cdot 10^3 \frac{E_0}{l} \text{ rad/pulse} \qquad (1)$$

where l is the optical path length of the measuring beam in the cell (in cm).

This dosimetric method enables[69] doses between 1 and 100–150 rad/pulse to be measured. With doses below 1 rad/pulse accurate measurements are difficult. With doses in excess of 100–150 rad per pulse the product $G\cdot\epsilon$ begins to decrease because the transformation of OH into $e^-_{aq.}$ is incomplete. The upper limit of measurable dose can be raised by lowering the pH of the medium to 9 and by replacing H_2 by, for example, methanol (at a concentration to 10^{-3} M). In this solution H and OH are not converted into $e^-_{aq.}$, and therefore $G\cdot\epsilon$ at 700 nm remains equal to 5.0×10^4 (litre $mole^{-1}$ s^{-1})·molecules/100 eV. Using this solution, doses per pulse up to 10^4 rad can be measured[6].

This dosimetric method cannot be used with pulses longer than a few microseconds[69], because the duration of the pulse must be kept shorter than the half-life of the $e^-_{aq.}$ species so that the recombination of $e^-_{aq.}$ during the pulse can be ignored. However, at low doses per pulse (~1 rad) the half-life of $e^-_{aq.}$ is long enough for pulses of 10^{-3} s duration to be acceptable. Fielden and Hart[69] showed that the limitations can be defined as

†The formation of $e^-_{aq.}$ by the radiolysis of aqueous systems and the properties of these particles are discussed in recent monographs[67,72].

follows: for doses of ~100 rad per pulse the minimum dose rate must be 10^7 rad s^{-1}, while for doses of ~1 rad the dose rate must be at least 10^3 rad s^{-1}. The dosimeter gives the same results for electron pulses and for pulses of X-rays.

The dosimetric solution can be used repeatedly. Fielden and Hart [69] obtained reproducible results over a period of 2 years, during which the total dose was greater than 1 Mrad, with a solution sealed in a quartz cell. Traces of oxygen present in the original solution are removed by a preliminary irradiation. If the solution is accidentally exposed to an excessive dose rate, the resulting hydrogen peroxide can be destroyed by irradiating the cell at a low dose rate.

Hart and Anbar [67] recommend, for measurements at high dose rates (up to 10^{10} rad s^{-1} with microsecond pulses and up to 10^{12} rad s^{-1} with nanosecond pulses), a method based on the steady-state concentration of hydrated electrons. In a solution free from acceptors for the $e^-_{aq.}$ particle the maximum concentration of these particles is reached at the end of the pulse. However, if the solution contains a relatively high concentration of electron acceptors, a steady-state concentration of $e^-_{aq.}$ is set up during the application of the pulse. The dose rate can be found by measuring this concentration, using the formula

$$I = \frac{k[S][e^-_{aq}]_{st} \cdot 6{,}02 \cdot 10^{25}}{G(e^-_{aq})} \qquad (2)$$

where I is the dose rate (eV litre^{-1} s^{-1}), k is the rate constant of the reaction between the acceptor S and $e^-_{aq.}$ (litre mole^{-1} s^{-1}), [S] and $[e^-_{aq.}]$ are the molar concentration of S and the steady-state concentration of $e^-_{aq.}$ during the pulse, and $G(e^-_{aq.})$ is the yield of $e^-_{aq.}$ (2.7 electron/100 eV).

Perchloric acid at 10^{-3}–10^{-2} M concentration can be used as the acceptor for $e^-_{aq.}$. The value of k for H^+ ions is 2.2×10^{10} litre mole^{-1} s^{-1}. [74] The main weakness of this method is that $G(e^-_{aq.})$ may be a function of the acceptor concentration [75].

Evidently, the most serious drawback of these methods of dosimetry is the complicated equipment needed to measure the optical absorption of $e^-_{aq.}$. Hence, these methods are used only in laboratories already committed to pulse radiolysis studies with optical monitoring of short-lived particles.

7. DOSIMETERS BASED ON POLYMER SYSTEMS

Various polymers have bean suggested for the dosimetry of pulsed radiation. Boag [76] recommends the use of plates of poly(methyl methacrylate) between 1 and several millimeters thick. Irradiation of this polymer produces optical absorption with a maximum at 292 nm. The optical density at this wavelength is linearly related to the dose in the range from 5×10^4 to ~10^6 rad.

Harrah [77,78] used polystyrene and polyhalogenostyrene plates containing various additives. He showed [77] that polystyrene plates containing *trans*-stilbene are suitable for dose measurements in the range 2×10^5–10^8 rad at dose rates between 300 and 7.5×10^{13} rad s^{-1}. Under these conditions the effect is independent of the energy of the radiation over the range 1.25×10^{-3}–4.7 MeV. The plates were prepared from benzene solutions of polystyrene (10 wt.%) and *trans*-stilbene (0.025 wt.%). Irradiation induces the isomerisation of *trans*-stilbene into the *cis*-isomer. This transformation is conveniently monitored spectrophotometrically from the absorption of light at 324 nm: at this wave length the extinction coefficient of *trans*-stilbene is more than an order of magnitude greater than the extinction coefficient of *cis*-stilbene. The measurement consists in finding the ratio $R = (D_0 - Dt)/D_0$, where D_0 is the initial optical density of the plate at 324 nm and Dt is the optical density after absorption of the dose. The radiation-chemical yield of the disappearance of *trans*-stilbene is 0.73 molecule/100 eV. The precision of this method is ±5% at doses greater than 1.5×10^6 rad, and ±10% at lower doses.

In his next paper [78], Harrah showed that polyhalogenostyrene plates containing the methoxide of Malachite Green can be used to measure doses between 5×10^4 and 1.5×10^7 rad at dose rates up to 10^{14} rad s^{-1}. The plates were prepared from benzene or chloroform solutions containing 10 wt.% of the polymer and 0.1 wt.% of the dye. The dye was used in its leuco-form, obtained by slowly adding a methanol solution of Malachite Green to a 1 M solution of sodium methoxide with vigorous stirring, followed by recrystallisation from benzene after treatment with activated charcoal. Irradiation induces a colour in the plate. The intensity of the colour is measured spectrophotometrically from the light absorption at 630 nm (for doses up to ~3×10^6 rad) or at 430 nm (for doses of 10^6–1.5×10^7 rad). The extinction coefficient of the dye at 430 nm is ~20% of the extinction coefficient at 630 nm. The effect of dose rate was tested with poly(4-chlorostyrene) plates. The measured optical densities at dose rates up to ~10^{14} rad s^{-1}, produced by electron pulses 2×10^{-8} s long (electron energy 2 MeV), differed by no more than 2% from those obtained with dose rates of 300 rad s^{-1} of γ-radiation from ^{60}Co. For a dose rate of 10^{15} rad s^{-1} the difference increases to 8%. All measurements were done in vacuum. In the presence of air the sensitivity of the films to γ-radiation is 25% higher than for vacuum irradiation. With poly(4-bromostyrene) plates the effect of oxygen is less marked (only ~4%). The existence of an oxygen effect is one of the drawbacks of this method of dosimetry. Another drawback is the marked dependence of the results on the presence of impurities in the plates.

Willis and coworkers [26] examined the possibility of using blue Cellophane films marketed by the firm of Dupont (USA) for the dosimetry of pulsed radiation from an accelerator of the "Febetron" type. These films contain the dye dimethoxyphenyl-*bis*-azo-*bis*-8-amino-1-naphthol-5,7-disulphonic acid [79], which is bleached by irradiation. The extent of bleaching is measured in a spectrophotometer at 655 nm. Willis and coworkers found that these films can be used to measure doses between 5×10^5 and 1.4×10^7 rad.

The energy of the radiation is not fully absorbed in the films, which must therefore be calibrated and can be used only as relative dosimeters.

8. ORGANIC LIQUIDS AS DOSIMETRIC SYSTEMS

Willis and coworkers [26] found that $G(H_2)$ for the radiolysis of liquid benzene by pulsed electrons generated by a "Febetron 705" accelerator (dose rate 10^{14} rad s^{-1}) is 0.04 molecule/100 eV. Thus, the yield of hydrogen is almost the same as reported [80–82] for lower dose rates (0.036–0.040).

The same workers pointed out a special feature of dosimetric measurements at very high dose rates using benzene (and possibly also other liquids of low electrical conductivity). Each pulse injects a charge of a few hundredths of a microcoulomb into the liquid. The relaxation time of the conductivity in these liquids is of

the same order as (or greater than) the duration of the pulse ($\sim 3 \times 10^{-8}$ s). Hence, the strong electric charge induced in the liquid by the leading edge of the pulse will tend to repel the electrons arriving during the main period of the pulse, and the measured dose will be seriously in error. Obviously, the magnitude of this effect increases with the thickness of the sample. It is found[26] to be negligible with sample thicknesses of 0.2–1.0 cm (for which $G(H_2) = 0.04$ molecule/100 eV), but it becomes significant with benzene samples 1.5 cm thick, for which $G(H_2) = 0.02$–0.03 molecule/100 eV.

Boyd and coworkers[83] studied the radiolysis of cyclohexane by electron pulses at dose rates up to $\sim 10^{14}$ rad s^{-1}. Under these conditions $G(H_2)$, though smaller than in γ-radiolysis, remains constant (14 molecules/100 eV) for dose rates between 6×10^{12} and 1.3×10^{14} rad s^{-1}. $G(H_2)$ is also independent of dose over the range which was explored (4×10^5–2.4×10^7 rad).

Dvornik and coworkers[84] recommend the use of ethanolic solutions of chlorobenzene containing 4 vol.% of water for the dosimetry of pulsed electronic radiation. With this system, the dose is measured by the formation of H^+ or Cl^- ions. They found that if the solution contains more than 10 vol.% of C_6H_5Cl the value of $G(HCl)$ is practically the same for γ-rays from ^{60}Co and for pulsed electron radiation at a dose rate of 10^9 rad s^{-1} (pulse length 7×10^{-6} s, electron energy 10 MeV). The following values of $G(HCl)$ were obtained for different concentrations of C_6H_5Cl (shown in brackets as vol.%): 4.53(10), 4.95(15), 5.19(20), 5.34(30), and 5.47(40).

9. GASEOUS DOSIMETRIC SYSTEMS

The possibility of using ethylene, oxygen, and nitrous oxide as dosimetric systems for pulsed electronic radiation has been investigated[15,85–89]. $G(H_2)$ for the radiolysis of ethylene at dose rates of $\sim 10^{14}$ rad s^{-1} is found[15] to vary with pressure. The yield of hydrogen decreases from 1.9 to 1.04 molecule/100 eV as the pressure is increased from 0.5 to 10 atm. In the γ-radiolysis of ethylene (at 1 atm pressure) $G(H_2) = 1.31$ molecule/100 eV.[90]

The yield of ozone in the radiolysis of gaseous oxygen by electron pulses (dose rate 10^{12}–3×10^{13} rad s^{-1}) is much higher than in γ-radiolysis[87–89,91]. According to Willis and coworkers[88], $G(O_3) = 12.8 \pm 0.6$ molecules/100 eV at the above dose rates, whereas only 6.2 ± 0.6 molecules of O_3 are produced by 100 eV in γ-radiolysis. The dose rate at which $G(O_3)$ begins to vary has not been identified precisely. Hence, oxygen can be used as a dosimetric system only at dose rates in the range 10^{12} to 3×10^{13} rad s^{-1}, for which $G(O_3)$ is known[88] to have a constant value of 12.8 molecules/100 eV. Under these conditions $G(O_3)$ remains constant over the pressure range 0.04–1 atm and for total doses in the range 0.05 to 0.35 Mrad. The ozone produced by the electron pulses is conveniently detected spectrophotometrically by light absorption at 254 nm. Its extinction coefficient at this wavelength[92] is 132 cm^{-1}, or[93] 135 cm^{-1} (both values being reported for normal pressure and temperature). Alternatively, the ozone can be determined iodometrically when higher precision is required. Boyd and coworkers[94] have recently made a detailed study of the reaction between I^- and O_3: they find that at pH 7 one molecule of O_3 generates 1.53 molecules of I_2.

In the radiolysis of gaseous nitrous oxide, $G(N_2)$ increases by approximately 20% as the dose rate is raised from the $\sim 10^2$–10^3 rad s^{-1} level to $\sim 10^{12}$ rad s^{-1}. The yield for γ-radiolysis[95] is ~ 10 molecules/100 eV, rising to 12.4 molecules/100 eV for radiolysis by powerful electron pulses[15,85,86]. For N_2O at 1 atm pressure, the change in yield occurs[86] in the range of dose rates 1.6×10^8–1.6×10^{11} rad s^{-1}. In pulse radiolysis, $G(N_2)$ is independent of N_2O pressure between 0.5 and 5.0 atm.[15] At 1 atm pressure the yield does not vary[85] if the temperature is raised to 200°. The yield is insensitive to dose up to 6.4×10^6 rad. According to Willis and coworkers[96], $G(N_2)$ equals 12.4 molecules/100 eV even at dose rates as high as $\sim 3 \times 10^{14}$ rad s^{-1}.

Boyd and coworkers[97] discovered an interesting feature of the dosimetry of pulsed electron radiation by means of gaseous systems. They studied the effect of pressure on the radiolysis yields of gaseous HCl, HBr, and N_2O at a dose rate of 1.6×10^{13} rad s^{-1}, and they found that below 0.5 atm the yield of H_2 in HCl and HBr is much higher than above 1 atm. (The same is true of the yield of N_2 in N_2O.) The effect is ascribed to the acceleration of secondary electrons in the transient electric field generated by the powerful electron pulses. A similar phenomenon occurs[96] in the radiolysis of N_2O and H_2S by electrons at a dose rate of $\sim 3 \times 10^{14}$ rad s^{-1}.[96]

Gaseous dosimetry at dose rates above 10^{12} rad s^{-1} is carried out in cells made of stainless steel. Lampe and coworkers[98] noticed a catalytic effect of this material in the decomposition of nitrous oxide of γ-radiolysis. The increase in the nitrogen yield due to this effect, $\Delta G(N_2)$, is described by the empirical formula

$$\Delta G(N_2) = \frac{4.2}{PI}, \qquad (3)$$

where P is the pressure of N_2O (atm) and I is the dose rate (Mrad h^{-1}).

It follows from formula (3) that for $P = 1$ atm and $I >$ 10 Mrad h^{-1} the quantity $\Delta G(N_2)$ is small in comparison with $G(N_2)$, which is usually 10–13 molecules/100 eV. Evidently, the effect can be ignored in pulse radiolysis, for which $I \gg 10$ Mrad h^{-1}.

10. OTHER DOSIMETRIC SYSTEMS

The output of the LiF thermoluminescent dosimeter is reported[99–101] to be independent of dose rate up to 2×10^{11} rad s^{-1}. It is also independent of dose[101] up to 10^5 rad.

Fielden and Hart[69] made a detailed study of the suitability of LiF single crystals for the dosimetry of pulsed radiation. They found that the response of this dosimeter is independent of dose rate between 0.9 and 1.5×10^6 rad s^{-1}. The measurements were made with γ-radiation from ^{60}Co and with X-ray pulses of different duration (10^{-6}, 9.5×10^{-8}, and 1.1×10^{-8} s). These authors stress that LiF can be used to measure extremely small doses (down to 10^{-2} rad per pulse).

Lithium fluoride has also been examined by Alsop and coworkers[102] as a possible thermoluminescent dosimeter for electron pulses at dose rates up to 10^{12} rad s^{-1}. These workers also considered the possibility of using CaF_2, activated with Mn, for the dosimetry of this type of radiation.

Schmidt and Buck[103] proposed a calorimetric method for the dosimetry of pulsed electronic radiation in which thermal changes are monitored conductimetrically. Their quartz cell, fitted with two parallel platinum foil electrodes, is filled with electrolyte and placed behind the collimator which defines an electron beam 2.5 cm in diameter. When the electron pulse strikes the cell, the

Table 3. Dosimetric systems for pulsed radiation.

System	Indicator reaction	Radiation-chemical yield (ions or molecules/100 eV)	Dose rate (rad s^{-1}) for constant radiation-chemical yield
10^{-3} M aq. Fe^{2+}, 0.4 M H_2SO_4, saturated with air	Formation of Fe^{3+}	15.6	$<10^8$
10^{-2} M aq. Fe^{2+}, 0.4 M H_2SO_4, saturated with oxygen	ditto	16.07	$<6 \times 10^9$
10^{-4}–10^{-3} M aq. Ce^{4+}, 0.4 M H_2SO_4	Reduction of Ce^{4+}	2.3–2.5	$<10^8$
10^{-3} M aq. Fe^{2+}, 10^{-2} M Cu^{2+}, 5×10^{-3} M H_2SO_4, deaerated	Formation of Fe^{3+}	0.65	$< 5 \times 10^8$
10^{-3} M aq. Fe^{2+}, 10^{-2} M Cu^{2+}, 5×10^{-3} M H_2SO_4, saturated with oxygen	ditto	0.75	$<10^8$
10^{-3} M aq. Fe^{2+}, 5×10^{-2} M Cu^{2+}, 10^{-3} M H_2SO_4, saturated with air	"	0.58	$<10^{10}$
10^{-3} M aq. Fe^{2+}, 0.1 M Cu^{2+}, 10^{-2} M H_2SO_4, saturated with air	"	0.58	$<3 \times 10^{10}$
5×10^{-2} M aq. $H_2C_2O_4$	Decompn. of $H_2C_2O_4$	4.9	$<2 \times 10^8$
0.1 M aq. $H_2C_2O_4$	ditto	4.9	$<2 \times 10^9$
0.2 M aq. $H_2C_2O_4$	"	4.9	$<2 \times 10^{10}$
10^{-2} M solution of NaOH, saturated with hydrogen	Formation of e^-_{aq}	6.6	$<1.5 \times 10^8$
10^{-3} M solution of CH_3OH (pH 9)	ditto	2.7	$<10^{10}$
aq. H_2SO_4 (pH 3–4)	Formation of H_2O_2 or H_2	$G(H_2O_2) = G(H_2) = 1.16$	$<2 \times 10^9$
Benzene	Formation of H_2	0.04	6×10^{12}–$1.3 < 10^{14}$
Cyclohexane	ditto	4	
Chlorobenzene in ethanol, containing 4 vol.% H_2O	Formation of HCl	4.5–5.5 (depending on concn. of C_6H_5Cl)	up to 10^9
Gaseous oxygen	Formation of ozone	12.8	10^{12}–3×10^{13}
Gaseous nitrous oxide	Formation of N_2	12.4	1.6×10^{11} and above
Polystyrene plates containing *trans*-stilbene	Stilbene isomerisation	0.73	up to 7.5×10^{13}
Polychlorostyrene plates containing the methoxide of Malachite Green	Colouration of plate	—	up to $\sim 10^{14}$
LiF single crystals	Thermoluminescence	—	up to 2×10^{11}–10^{12}

emperature of the electrolyte rises due to the absorption of the dose, and the electrical conductivity also changes by ~ 2% per degree). Changes in electrical conductivity are measured by a sensitive bridge method. This calorimetric cell can be used for doses of $\sim 10^3$ rad. The best electrolyte is a phosphate buffer (pH ~ 7), in which changes of electrical conductivity due to radiation-chemical reactions are negligible. A correction for the energy absorbed by the platinum foil electrodes must be made.

1. DOSE MEASUREMENT ALONG THE LIGHT BEAM DURING PULSE RADIOLYSIS WITH OPTICAL MONITORING OF SHORT-LIVED PARTICLES

As was pointed out earlier in this review, when optical monitoring of the short-lived particles is used in pulse radiolysis it is necessary to know the dose along the path of the light beam used as a probe. This is because the distribution of the dose is not usually uniform in these experiments (for example, only part of the solution is exposed to the radiation, the cross-section of the light beam is smaller than the cross-section of the electron beam, etc.). In these systems the dose is measured from observations of the optical absorption of any reaction product whose optical characteristics are known.

Dorfman and coworkers [104,105] suggest, for dosimetry under these conditions, measurement of the optical absorption of the Fe^{3+} ions produced during the irradiation of a solution of ferrous sulphate in sulphuric acid. In this system the kinetic curve shows a stationary period lasting several seconds after the application of the pulse. Adams and coworkers [106] used an aqueous solution of ferrocyanide, in which the plateau of the kinetic curve is reached in a few milliseconds. Fletcher and coworkers [107] used a $\times 10^{-3}$ M solution of KCNS saturated with oxygen, in which $(CNS)_2^-$ ion-radicals are formed by the reaction between OH radicals and thiocyanate ions. The molar extinction coefficient of this particle is 7350 litre $mole^{-1}$ m^{-1} at 475 nm, and $G[(CNS)_2^-] = G(OH) = 2.9$. [108,109]

Other workers [110–112] also used a CNS^- solution for this purpose. The formation of hydrated electrons (see Section 6) is a possible alternative approach to this problem.

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This review has highlighted a number of special features of chemical methods of dosimetry when applied to pulsed radiation as opposed to γ-radiolysis. The most important effect is a dependence of the yield of the radiolysis products upon the dose rate: hence, it is essential to choose a dosimetric system whose response is independent of dose rate within the expected range. Table 3 has been compiled to assist the reader in the choice of a suitable system.

The following conclusions can be made by inspection of Table 3. Liquid benzene is the most generally applicable dosimetric system. The yield of hydrogen during radiolysis of liquid benzene is constant over the entire range of dose rates likely to be available to present-day workers. With aqueous solutions, the range of dose rates over which the yield is constant usually increases with solute concentration. The most convenient gaseous system for the dosimetry of pulsed radiation is nitrous oxide, because the yield of N_2 varies only by 20% between γ-radiation and electronic radiation from an accelerator of the "Febetron" type. Lastly, chemical changes in some polymer systems can also be independent of dose rate between wide limits.

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Mechanism of the Action of an Electron Beam on Organic Photoresists

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The litereature dealing with the decomposition of positive and negative photoresists by actinic light and by electron bombardment is reviewed, and the action of a stream of electrons on other organic materials, metals, and inorganic dielectrics is discussed. A mechanism producing internal irradiation of the resist is considered: the incident electrons excite the resist molecules into fluorescence and phosphorescence.
The influence of the (metallic or dielectric) substrate on the achievement of the required line widths is discussed. It is shown that the cross-linking of a negative photoresist under the influence of an electron beam occurs by free-radical polymerisation.
65 references.

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I. INTRODUCTION

The basic components of integrated microcircuits (semiconductor diodes and transistors, capacitors, interconnections, and resistors) have simple geometric shapes of micron or sub-micron dimensions. The main requirement in the production of integrated circuits is the ability to reproduce a given pattern a large number of times and to register it very accurately on a pre-existing pattern. Even the production of discrete transistors requires the superposition of 4 or 5 patterns[1]. Photolithography is the only procedure by which this requirement can be met with acceptable yields.

The photolithographic process consists in coating the article with a layer of acid-resistant polymer, which protects the metal, dielectric, or semiconductor from the action of an etchant. The need for ever-greater miniaturisation of the components of microcircuits poses a number of difficult scientific and technological problems concerning the synthesis of improved photoresists and the development of new methods of exposure.

The resolving power of processes relying on exposure to light is, of course, limited by the wave length of the light. The smallest line widths so far reported[2] are of the order of 1 μm (0.65 μm windows and 0.35 μm stripes between windows). These dimensions coincide almost exactly with the theoretical limit of line width attainable by exposure to light of wave length 0.3–0.4 μm.

The use of an electron beam to produce lines and patterns of small dimensions is not subject to the same limitations. An electron beam can be focussed to a spot a few Ångstroms in diameter, and the effective wave length of the electrons can be decreased to one Ångstrom or less by using a sufficiently high accelerating voltage (see Table 1). This effect is of the utmost importance in minimising diffraction phenomena and increasing the resolving power.

The results achieved in practice by exposing photoresists with an electron beam fall very far short of theoretical predictions. Some data on the line widths obtained by irradiating photoresists with electrons are summarised in Table 2. Even the narrowest lines are wider than the electron beam by a large factor, whereas the most commonly reported results are orders of magnitude worse than the theoretical expectations.

Table 1. Relationship between electron wave λ and accelerating voltage U.[3]

U, V	1	10	100	1000	10000	30000	40000	50000
λ, A	12.26	3.88	1.23	0.388	0.123	0.0698	0.0601	0.0530

Table 2. Electron beam irradiation of photoresists.

Photoresist type	Accelerating voltage, kV	Charge, C cm^{-2}	Beam diameter, A	Line width, A	Edge roughness, A	Substrate material	Layer thickness, A	Ref.
KPR, KMER, KOR, KTFR	14,20	—	10000	—	—	Al	1500—2500	4
AZ-1350	7.5; 16; 30	—	2500	10000	—	SiO_2	3600	5
KTFR	7.5; 16; 30	—	2500	10000	—	SiO_2	—	5
KTFR, KPR	30		3000	10000	500	Al	3000	6
AZ-1350	30	$7\cdot10^{-5}$	1000	10000	—	SiO_2	3600	7
KTFR	30	—	1000	10000	—	SiO_2	—	7
AZ-1350	20—30	10^{-4}	—	20000	500	—	—	8
KTFR	20—30—	$7\cdot10^{-6}$	—	20000	500	—	4500	8
KTFR	6	10^{-5}	—	—	—	SiO_2	3800	9
—	—	—	1000	10000	—	Si	—	10
AZ-1350	—	10^{-5}	5000	10000	—	Si, SiO_2	—	11
KPR	—	10^{-6}	5000	10000	—	Si, SiO_2	—	11
KPR	25	$5\cdot10^{-5}$	100	2500	700	Au–Pt alloy	—	12
Siloxane SH-200	—	—	1000	4000	—	Si	3000	13
KTFR	—	$5\cdot10^{-6}$	—	10000	—	Cr	2000	14
KTFR	—	—	5000	15000	—	Ag	10000	15

Note. KPR (Kodak Photo Resist, Eastman Kodak, USA) is the vinyl ester of cinnamic acid; KOR (Kodak Ortho Resist, Eastman Kodak, USA) is a type of KPR improved by the addition of a sensitiser; KMER (Kodak Metal Etch Resist, Eastman Kodak, USA) is a polymer of modified natural rubber, improved by a diazide sensitiser; KTFR (Kodak Thin Film Resist, Eastman Kodak, USA) is similar to KMER but needs to be decanted before use; AZ-1350 (Shipley, Azoplate, USA); SH-200 (Japan) is a polysiloxane containing methyl radicals.

This divergence between theory and practice is explained by various factors, including the lack of resists specially designed for electron beam exposure, complex interactions between the stream of electrons and the layer of resist (or the substrate), the lack of monochromaticity of the beam, etc. A working theory of the interaction between an electron beam and the resist is needed before any attempt can be made to formulate resists of the required composition and structure.

The most important parameters from the point of view of device fabrication are the line width and the unevenness of the edge. Hence, this review will deal specifically with the factors which influence the technologically accessible line widths.

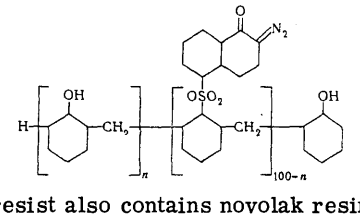
The interactions between high-energy electrons and polymers of various compositions have been discussed in detail by several workers (see, for example, Ref. 16, and the references quoted in the following Sections), particularly in the case of thin films [17,18].

Because of the complexity and multiplicity of the phenomena which accompany the passage of electrons through the photoresist and the substrate, a full discussion of the problem is not an easy matter. To facilitate the analysis, we shall deal first with the reactions accompanying the exposure of photoresists with light, the reactions induced by electron bambardment, and the interactions between a stream of electrons and the photoresist and substrate.

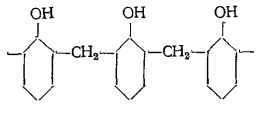
2. EXPOSURE OF RESIST BY A LIGHT BEAM

Positive resists are the most commonly used in the planar technology for the production of semiconductor devices [2]. Typical of this group of organic polymers are the compounds AZ-1350 (USA) and naphthoquinonediazide NKhDA (USSR). The two compounds have very similar compositions, differing only in some of the functional groups responsible for some specific properties.

The positive resist 1,2-naphthoquinonediazide(2)-5-sulphoester of novolak has the following structural formula [19]:

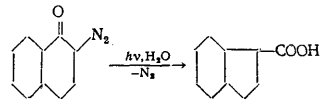


The photoresist also contains novolak resin as the film-forming component. Novolak consists of a complex mixture of products of different molecular weight, based on the polymer chain



When the resist is heated the photosensitive component decomposes with evolution of nitrogen. At first the thermoplastic film is converted into an insoluble compound which is very stable and adherent to the substrate. This reaction begins at 140–160°, i.e. below the temperature at which the novolak forms insoluble compounds. The reaction is assisted by the products of the decomposition of NKhDA. The most likely mechanism of this conversion is acylation of the hydroxy groups of the novolak by the ketens formed by thermal decomposition of the naphthoquinonediazido groups of the photoresist. Heating at temperatures above 250° is accompanied by heat evolution, characteristic of the condensation of the novolak units into a polymer of high molecular weight [20].

The application of NKhDA as a photoresist follows from the following change in the material under the influence of actinic light. Illumination with light of wave length shorter than 460–480 nm decomposes the NKhDA with evolution of nitrogen. The resulting indeneketen absorbs water present in the film, giving rise to indenecarboxylic acid which has hydrophilic properties and can dissolve in the aqueous developer. Addition of alkali to the developer helps to dissolve the exposed film. It should be noted that the novolak resin added to the resist is transparent to light of this wave length.



The quality and the sharpness of the image produced depend on a number of factors, including the completeness of the photochemical reaction and the avoidance of spurious polymerisation phenomena during the heating stage of the process.

One possible side reaction is acylation of the novolak by the ketens; other reactions include interaction of the ketens with the carbonium ions responsible for the photochemical reaction and decarboxylation of the decomposition products at high enough temperatures. The products of the side reactions are insoluble in organic solvents and in the alkaline developer. Tsirlin and coworkers [21] studied the effect of side reactions on the sharpness of the image obtained, and demonstrated the influence of resist composition and of the ratio of novolak to naphthoquinonediazide on the onset of negative resist behaviour.

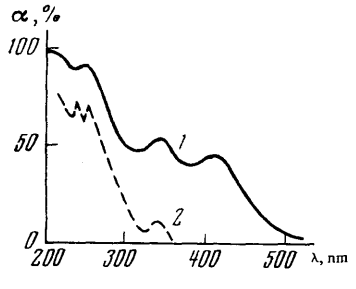


Figure 1. U.v. absorption spectra of (*1*) positive photoresist and (*2*) K-18 novolak resin [2].

Fig. 1 shows the absorption spectra of a layer of 1,2-naphthoquinonediazide(2)-5-sulphonate of novolak, and of the novolak resin K-18. The novolak resin absorbs at wave lengths below 370 nm.

The first and the second absorption band of phenol occur [22] at ~ 2780 Å and ~ 2380 Å respectively. The photolysis of phenol involves the series of reactions

$$ROH + h\nu \rightarrow ROH^* \overset{H_2O}{\rightleftarrows} RO^* + H_3O^* \rightarrow RO^- + h\nu' \overset{H_2O}{\rightleftarrows} ROH + OH^-.$$

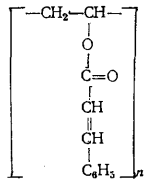
RO denotes a phenyl or a substituted aromatic system.

The most commonly used light source is a mercury lamp. The emission spectrum of the mercury lamp has a discrete line structure. The light of wave length 2537, 3650, 4050, and 4358 Å is active towards the photosensitive layers. The intensity distribution of these spectral lines in mercury lamps is 2:10:4:8. High-pressure lamps also emit a background radiation whose intensity amounts to 0.1–0.25 of the intensity of the main lines.

Negative photoresists, mostly based on poly(vinyl cinnamate), are known as PVTs in the USSR and KPR, KOR, etc. in the USA. These resists also are widely used in photolithographic processes for the production of electronic devices.

A very important feature of negative photoresists is their high stability—they are superior to positive resists in this respect.

PVTs is obtained by the etherification of poly(vinyl alcohol) and cinnamic acid, and has the following structural formula [2,23–25]:

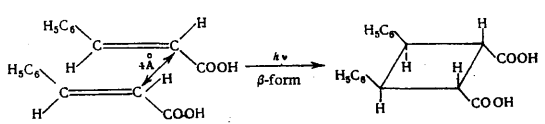


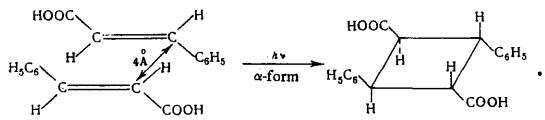
Irradiation of the resist with actinic light produces cross-linking of the molecules. Unsensitised PVTs has an absorption maximum at 270–320 nm and a long-wave absorption edge at 330 nm [26,27]. After irradiation, photoresist layers absorb more weakly in this region because of the decrease in the number of double bonds. Exposed resist contains up to 15% of three-dimensionally cross-linked groups [28]. The quantum yield of the cross-linking reaction can be as high as 50%.

The addition of a sensitiser shifts the absorption maximum to the region of 360–370 nm, and the absorption edge to 400–420 nm. Studies of absorption in the infrared region have shown [27] that the function of the sensitiser is to transmit to the double bonds of PVT's the energy of quanta of long-wave radiation. The quantum efficiency of the sensitiser (Michler's ketone) [29] does not exceed 0.76. This rather low efficiency is due to steric effects, which prevent intimate contact between the sensitiser and the PVTs molecules. The sensitiser is added in amounts of about 10% by weight. The loss of sensitiser is almost insignificant (0.04%): this is because the photon energy is insufficient to cause decomposition of the sensitiser.

According to Lyalikov and coworkers [27], the absorbed radiant energy is transmitted to the double bonds, which are converted into single bonds. The resulting biradicals interact to form cross-linkages, and the solubility of the photoresist in organic solvents decreases.

Robertson and coworkers [26] suggest that the cinnamoyl groups of PVTs form a four-membered ring. *Trans*-cinnamic acid is also believed [30] to form four-membered rings. It is known, from crystallographic studies, that effective photodimerisation is impossible unless the reacting centres are less than 4 Å apart. The dimer can be formed in two configurations, depending on the relative orientation of the constituent molecules:



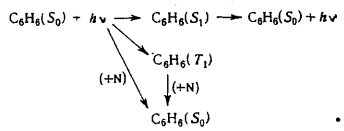


The probability of polymerisation increases when the molecules are excited to the triplet state. The sensitiser plays a special role in transmitting triplet–triplet energy to the PVTs molecules. Energy transfer is possible only when the triplet-state energy of the donor is greater than the triplet-state energy of the acceptor [31–33]. The height of the triplet level of the sensitiser affects the yield of the polymerisation products: for example, the efficiency of the dimerisation falls off steeply [30] when $E_T < 53$ kcal mole^{-1}. The triplet levels of some of the commonest sensitisers are listed below:

acetophenone	74 kcal mole^{-1}
benzophenone	69 kcal mole^{-1}
Michler's ketone	61 kcal mole^{-1}

Mention must also be made of the contribution of the benzene groups of the photoresist and of the sensitiser to the transfer of radiant energy.

High fluorescence yields are common [22] for aromatic hydrocarbons in solution at low concentration. Photodecomposition of aromatic molecules has a very low quantum efficiency in the first absorption band (0.01 to 0.0001 or less). In benzene, the primary processes induced by irradiation within the second or third absorption band (1849 Å) are very different from those induced by the first band (2537 Å). When benzene is excited to the S_2 and S_3 state, internal conversion to the S_1 state has a very low probability, but chemical reactions can occur very readily, including aromatic ring opening with formation of isomers and hydrogen:



The excitation of benzene groups is accompanied by the subsequent emission of light of greater wave length.

3. EXPOSURE OF RESIST BY AN ELECTRON BEAM

Thornley and Sun [4] exposed various kinds of photoresist to electron beams of 14 and 20 keV energy. In their view, electrons having these high energies must break all the chemical bonds in their path when they pass through a layer of resist: the resist molecules can then undergo a complete reorganisation. They found that 14 keV electrons are more effective than 20 keV electrons, and they ascribe this behaviour to the fact that the faster electrons can lose less energy than the slower electrons in collisions with resist molecules.

Matta [5] measured the dose needed for the exposure of negative and positive photoresists on a silicon substrate by electrons of various energies. The average current density required was found to be constant and independent of the thickness of the layer of resist. The optimum current densities are plotted in Fig. 2 as a function of accelerating voltage. A possible explanation of this phenomenon is that the exposure is due (at least partly) to the electrons reflected by the substrate). Matta also showed that the current density for optimum exposure with different depths of penetration of the primary electrons is

a function of the angular distribution of the electrons reflected by the silicon substrate. The positive resist required current densities 10 times greater than the negative resist.

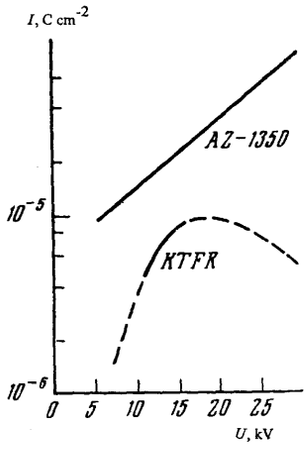


Figure 2. Variation of total charge needed with accelerating voltage.

Koichi and coworkers [6] studied the effect of an electron beam on negative resists. They concluded that the limitations on the obtainable line width are set by the reflection of electrons at the substrate interface and by the low sensitivity of photoresists to electrons. They considered the model for the interaction of the electron beam with the photoresist and the substrate shown in Fig. 3. The electrons, having passed through the resist, penetrate into the substrate material following a straight path up to a depth x_d equal to the mean free path of the electrons in that material. Beyond this point they suffer diffuse scattering in all directions. Formulae for x_r and x_d are given:

$$x_r = \frac{I^2 A}{8\pi q^4 N \rho Z} \bar{E}_i \left\{ 2 \ln \frac{2E_p}{I} \right\}; \quad (1)$$

$$r_0 = \sqrt{x_r (x_r - 2x_d)}; \quad (2)$$

$$x_d = \frac{C \cdot x_r}{Z + 8}; \quad (3)$$

where $\bar{E}i$ is an exponential integral, I is the mean excitation potential of the atom, A is the atomic weight, q is the electronic charge, ρ is the density of the substrate material, N is Avogadro's number, Z is the atomic number, E_p is the electron energy, and C is a constant depending on the atomic number of the material ($C = 8-12$).

When a beam of electrons having energies in excess of 20 keV interacts with a layer of resist most of the chemical bonds are broken, and a complete redistribution of the molecular bonds can take place. Analogous effects occur in positive resist. It can be shown that the line width is a sensitive function of the thickness of the resist: lines cannot be narrower than the sum of the resist thickness and the beam diameter. For example, with a beam diameter of 0.3 μm and a layer thickness of 0.1–0.2 μm we can produce lines 0.3–0.5 μm wide. Furthermore, the line width depends also on the radius of the back-reflection r_b, which is determined by the properties of the substrate material. Experiments using aluminium and copper substrates gave minimum line widths in the ratio of 2 to 5. The raggedness of the line edges was of the order of 0.05 μm.

Studies of the exposure of different polymers have also been described [34]. Ordinary resists are shown to be insensitive to electron bombardment, and the need to develop special electron resists is pointed out. When the polymer is bombarded with electrons, instantaneous cross-linking of neighbouring side-chains is induced, but some significant breaking of the main chains also takes place. These effects influence the size of the molecules and the solubility of the polymer. Depending on the predominance of one or other of these processes, polymers may be classified into cross-linking types and degrading types. The following materials were examined in detail: poly(vinyl cinnamate) (degree of polymerisation 500–1000), polydimethylsiloxane (degree of polymerisation ~7000), and polydimethylsiloxane containing vinyl radicals (degree of polymerisation 5000–10 000).

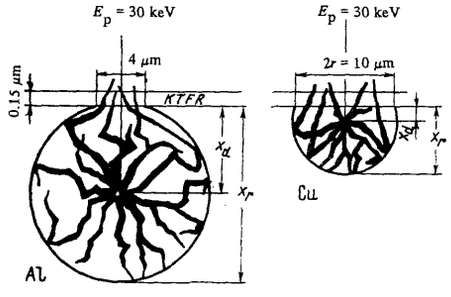


Figure 3. Schematic of the motion of electrons in a solid [6].

Miyauchi and coworkers [14,15] have published a study of the sensitivity to electron irradiation of several commercial grades of resist (KPR, KOR, AZ-1350, etc.). They obtained best exposures under the following beam conditions: beam voltage 10–30 kV, charge 5×10^{-6}–10^{-4} C cm^{-2}.

The sensitivity of the resist is constant within the stated limits of accelerating voltage. The optimum exposure time depends on the thickness of the layer of resist. The width of the resulting stripe is greater than the beam diameter: this effect is due to scattering of the electrons in the material and reflection at the substrate interface. The minimum width obtained after development is equal to the sum of the thickness of the layer and the diameter of the beam. Broyde has described some experiments on the exposure of negative [35] (KPR, KTFR) and positive [36] (AZ-1350) resists. He explained the cross-linking processes in negative resists by radiation-chemical considerations. The cross-linking energy of the resists was determined experimentally (2.5×10^{20} eV cm^{-3} for negative resists, 1.5×10^{20} eV cm^{-3} for positive resists). The cross-linking of KPR, in the presence of oxygen, is thought to be evidence for a free-radical polymerisation mechanism. The addition of sensitisers (benzotriazole, imidazole, indazole) to positive photoresist lowers the

threshold current of electrons by a large factor. Overexposure causes swelling in negative resists and loss of solubility in positive resists.

The main conclusions from this experimental study of the exposure of photoresists by an electron beam are: a) the exposure processes are influenced by the secondary electron emission characteristic of the substrate material; b) the use of terms such as "bond breaking" and "gel point" is quite inadequate as an explanation of the molecular restructuring produced by electron bombardment—Broyde's macroscopic explanation[35] in radiation-chemical terms is almost totally irrelevant to the mechanism of molecular conversion; c) there is no satisfactory explanation of the mechanism of the elementary polymerisation reactions in negative photoresist and of the degradation reactions in positive photoresists.

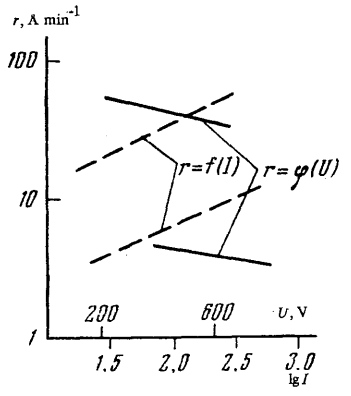


Figure 4. Rate of film growth against accelerating voltage and current density[39].

The molecular rearrangements induced by electron bombardment can be explained by using the results of work[17,18] on the deposition of polymer films from the gas phase. Workers are unanimous in their conclusion that film deposition occurs through the stages of adsorption of monomers by the solid surface, followed by electron-bombardment-induced polymerisation. Two mechanisms are considered: a) polymerisation by a radical mechanism[37], in which the radicals react with each other and with monomers; b) polymerisation by an ionic mechanism[38], in which the molecules dissociate into fragments which subsequently interact. The two polymerisation mechanisms lead to formally identical equations when detailed equilibrium [steady state condition (Ed. of Translation)] is assumed. The rate of growth of the film is

$$r = K_1 p \sqrt{I} \tag{4}$$

by the radical mechanism, and

$$r = K_2 p \sqrt{I}, \tag{5}$$

by the ionic mechanism, where K_1 and K_2 are constants, p is the monomer concentration (butadiene) in the gas phase, I is the current density. The form of the growth rate against current density relationship does not uniquely identify the polymerisation mechanism. Haller and White's experiments[38] with oxygen and hydrogen in the polymerisation vessel provide some evidence for an ionic mechanism of the polymerisation of butadiene.

Kolotyrkin and coworkers, after a critical assessment of a mass of published data, concluded that both polymerisation mechanisms may be operative in film formation, but one mechanism usually predominates, depending on the experimental conditions and on the nature of the starting material[17]. Tsapuk and coworkers[39] have described the deposition of polymers from the gas phase under the influence of electron bombardment. They find that the growth rate of the films decreases as the accelerating voltage increases, and increases with the power 0.5 of the current density. Plots of the growth rate of the polymer against accelerating voltage and current density are shown in Fig. 4. By solving simultaneously the equations $r = f(I)$ and $r = \varphi(U)$ we obtain a quadratic relationship between the current and the accelerating voltage:

$$I = -\alpha U^2 + \beta, \tag{6}$$

where α and β are constants, and I and U are the current density and the accelerating voltage respectively.

We note a qualitative agreement between this equation and the observed current density–accelerating voltage relation for the negative photoresist KTFR (see Fig. 2). On the other hand, the $I = f(U)$ relationship for positive resist is entirely different.

4. INTERACTION OF AN ELECTRON BEAM WITH SOLIDS

Many studies have been made[41,42] of the passage of electrons through solids, the energy loss of electrons per unit length of absorber, the magnitude of the secondary electron emission, etc. (A recent review of the literature[40] contains 1035 references.) In order to discuss the interaction of an electron beam with a photoresist and the substrate material we need to know the range of the electrons in the materials, the energy loss, the secondary electron emission coefficient (SE), and the inelastic scattering coefficient of the electrons (IS).

According to Bethe[42], the energy losses of moving electrons due to inelastic collisions are described by the equation

$$\frac{dE}{dx} = \frac{2\pi \cdot q^4 NZ}{E} \ln \frac{2E}{J} \tag{7}$$

whence we can derive, by integration, the range of the electrons in the material:

$$R = \frac{J^3}{8\pi q^4 NZ}\left[E_i\left(2\ln\frac{2E}{J}\right)\right] \tag{8}$$

where R is the electron range, T, q, and x are the energy, charge, and path length of the electron in the absorber, NZ is the number of electrons per cm^3 of the absorber (for a photoresist we can take $NZ = 3 \times 10^{23}$), $J = \frac{8}{e} I$ is the energy needed to produce an ion pair in the absorber, e is the base of natural logarithms, and $I = 26.4$ eV is assumed for gaseous ethylene irradiated with electrons. It is assumed that the value of I does not differ very much for other hydrocarbons ($I = 24.8$–27.1 eV), and is independent of the state of aggregation; $[E_i(2\ln\frac{2E}{J})$ is an exponential integral which can be expressed in the form

$$\left[\frac{e^{2\ln\frac{2E}{J}}}{2\ln\frac{2E}{J}}\right]\left(1+\frac{1}{2\ln\frac{2E}{J}}+\frac{2}{\left(2\ln\frac{2E}{J}\right)^2}\right)$$

Calculations by Eqn. (8) agree well with experimental data on the passage of electrons through the negative resists KPR and KTFR [35] (see Table 3).

Table 3. Experimental ranges and ranges calculated by Eqn. (8).

Electron energy, keV	Range, μm (exp.)	Range, μm (calc.)
5	0.65	0.66
10	2—2.5	2.3
15	—	4.8
20	—	8.3

Broyde also points out[35] that calculations by the Thomson–Widdington equations gives low results (by a factor of five). His expression for the energy transferred by collisions is

$$\Delta E_p = \frac{2\pi q^4 NZT}{2E}\left(\ln\frac{2\pi q^4 NZT}{I(1-\beta^2)} - \beta^2 - 0.34\right) \qquad (9)$$

where, in addition to the symbols defined above, T is the thickness of the layer of resist, and $\beta = v/c$ is the ratio of the electron velocity to the velocity of light.

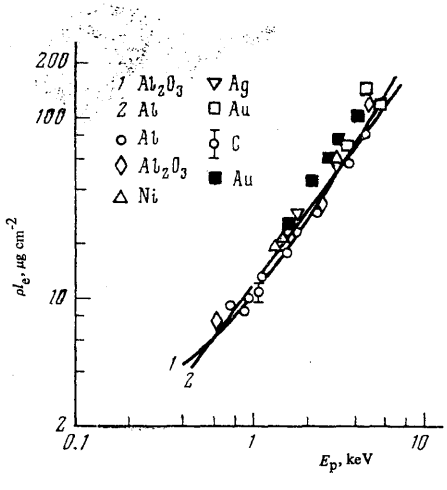


Figure 5. Depth of penetration against electron energy[43].

A great deal of experimental information on the transmission of electrons through matter is available in the literature. The most accurately measured quantity is usually the gravimetric depth of penetration (see Fig. 5), although the linear range is also quoted.

Plots of the secondary electron emission coefficient and the inelastic scattering coefficient for a number of materials are reproduced in Fig. 6.

The SE and the IS coefficient are related to the spectrum of secondary electrons (i.e. the relative proportions of fast and slow electrons). Fast electrons (energy > > 50 eV) include electrons emitted by the absorber and primary electrons reflected at 180°. The angular distribution of IS electrons for a massive metal target normal to the primary beam is closely approximated by the cosine law.

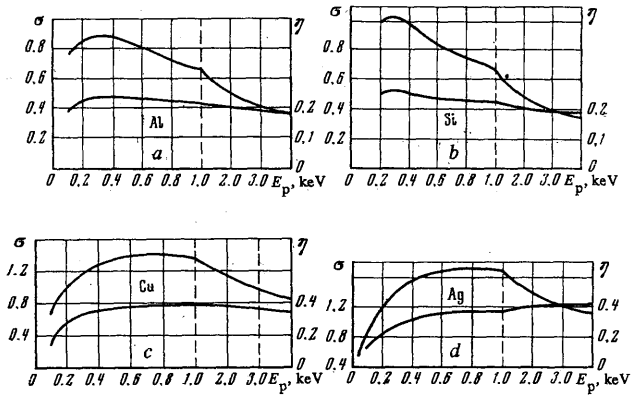


Figure 6. Secondary electron emission coefficients (σ) and inelastic scattering coefficients (η) for electrons in a number of materials[40].

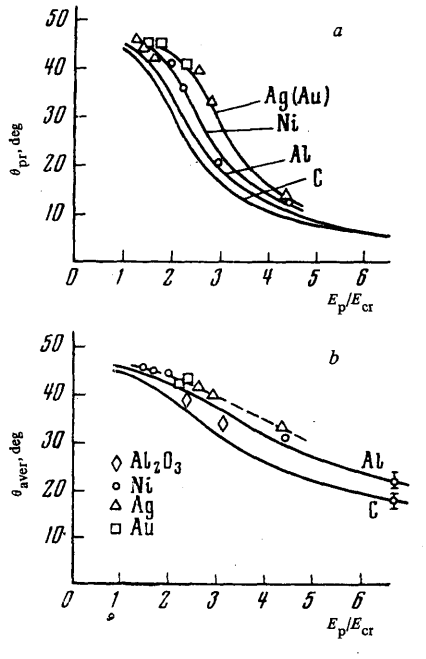


Figure 7. (*a*) Most probable and (*b*) average scattering angle of electrons[44].

Fig. 7 shows the most probable (*a*) and the mean (*b*) angle of scatter of electrons passing through films of various metals.

Irradiation of a solid by electrons is accompanied by a discrete energy absorption (called the characteristic

energy loss, CEL). Data on the CEL of various solids are summarised in Table 4.

The passage of electron beams through a carbon film and through films of various hydrocarbons [poly(vinyl formamide), poly(vinyl acetal), etc.] produces characteristic losses with very similar spectra[49]. The main difference noted[50] is that carbon has an additional absorption peak at 5.4 eV which is not found in poly(vinyl acetal).

Table 4. Characteristic energy losses of electrons in solids.

Material	CEL, eV					Reference	Remarks
	level I	level II	level III	level IV	level V		
Al	—	7.2	14.6	20.5	№	45	Arithmetic mean values
Cu	3.5	6.8	11.9	—	—	45	
Si	—	—	—	3	34	46	
C	—	—	—	23.0	46.0	46	Poly(vinyl acetate) films
Au	—	—	—	24.0	47.0	46	
Al_2O_3	—	—	—	23.0	46.0	46	
MgO	—	5.0	12.0	22.5	45.0	46	
SiO_2	—	5.2	—	21.3	—	46	
Ge	—	—	16.5	—	—	47	
Au	—	6.6	15.5	—	—	48	
C	—	7.5	—	—	—	49	Carbon films
C	—	5.4	—	—	—	50	

The origin of the characteristic energy losses of the electrons can be explained by two mutually exclusive hypotheses: one-electron interactions and collective interactions.

According to Sternglas[51], the CEL are associated with electron transitions from the inner shells to the uppermost levels, ultimately leading to escape from the atom. This suggestion is confirmed by the good agreement between the magnitude of the characteristic losses and the fine structure of the X-ray absorption edge.

A CEL mechanism involving the excitation of plasma waves in the metal cannot be excluded. This hypothesis was put forward by Watanabe[47].

The secondary electron emission of metals and semiconductors varies between relatively narrow limits (from 0.5 to 1.8 eV). Narrow-gap semiconductors (Ge, Si, and others) have secondary emission properties similar to those of metals. The most probable energy of slow secondary electrons in these materials is ~1.5–3.5 eV, and is almost independent of the primary beam energy above ~200 eV.

In dielectrics, the secondary electron emission coefficient and the secondary electron energy are quite different from the corresponding values for metals. For example, the number of secondary electrons decreases as the energy of the incident electrons increases, and the escape depth of secondary electrons is greater in dielectrics. In metals the internal secondary electrons interact strongly with the conduction band electrons, and therefore their energy is insufficient to overcome the surface barrier after a few collisions. Conversely, the internal secondary electrons in dielectrics are located in the conduction band with an energy less than 10 eV, which they cannot transfer to electrons in the filled band.

The secondary electron emission from glass and fused quartz[40,41] has a value of 2–3; values reported for paraffin oil and for diffusion pump oil are 3–4.8 and 2.8–2 respectively.

The anomalous secondary emission given by metallic emitters covered with a layer of dielectric consists in a large secondary emission coefficient coupled with an unusually high emitted electron energy. It follows from the above arguments that electron bombardment of such an emitter must result in the appearance of positive charge in the dielectric, due to the large difference in secondary emission coefficient between the metal and the dielectric.

By exploiting the analogy with a maintained gas discharge, Jacob (quoted in Ref. 40) analysed experimental data on the emission from magnesium oxide and showed that the average electron energy was 10–20 eV, with a field strength of 10^6 V cm^{-1} in the dielectric.

According to Fridrikhov and coworkers[52], these parameters have the values 11 eV and 5×10^5 V cm^{-1} in sodium chloride. Goetze[53] finds that the energy of secondary electrons emitted from potassium chloride reaches 4 eV. The calculations assume that the enhanced secondary emission and secondary electron energy in dielectrics is due to the positive space charge in the dielectric, and also to the presence of pores. In dense dielectrics the anomalous secondary emission parameters are not observed[40].

Polymers (including photoresists) may also contain gas-filled pores: experimental evidence for this assumption is given by Karasev[54].

5. MECHANISM OF INTERNAL IRRADIATION OF A POSITIVE PHOTORESIST

The essential facts concerning positive photoresists can be summarised as follows:

1. The changes in positive photoresist due to irradiation with light occur by two competing reaction paths: a) decomposition of the light-sensitive component and conversion of the resist into a water-soluble component (this reaction occurs when the resist is exposed to light of wave length shorter than 4600–4800, i.e. to a photon energy of 2.6 to 2.7 eV); b) deacylation of the NKhDA by ketens with formation of insoluble compounds (this reaction is observed when the resist is heated). Because the commonly used lamps do not emit radiation of wave length shorter than 3700 Å, and the photoresist layers are usually cooled during exposure, we may assume that the role of the novolak resin is an entirely passive one (film-forming ingredient).

2. The reaction products are the same after irradiation with electrons and with light. The exponential relationship between accelerating voltage and current suggests that the molecular rearrangement following electron bombardment involves neither a free-radical nor an ionic mechanism.

3. The electrons passing through a layer of photoresist lose fairly substantial amounts of energy. Calculations by Eqns. (8) and (9) indicate the following losses:

Energy of incident electrons, keV	Thickness of resist, Å	Energy loss, keV
15	3600	1.2
15	6000	2.4
15	12000	5.1
20	6000	1.6

The energy take-up by secondary electrons is relatively small (a few per cent). The large characteristic energy losses of electrons passing through organic compounds suggest electronic excitation of the molecules.

4. The secondary electron emission from a solid includes two characteristic groups of electrons: a) slow electrons, having an energy of a few electron-volts, and b) fast electrons, with energies higher than 60 eV. The energy of the fast electrons is high enough to cause excitation and ionisation of hydrocarbon molecules. The passage of fast electrons through a dielectric causes the appearance of positive space charge. The dielectric–metal combination of materials offers an enhanced secondary electron emission coefficient and slow-electron energy (up to 4, 10, or 20 eV).

Inelastic collisions between electrons and atoms or molecules lead to excitation and ionisation of the latter. An electron can excite a molecule provided that its energy exceeds that of the excited level of the molecule.

Electrons can excite different groups in the NKhDA molecule during their passage through a layer of resist: a) excitation of naphthyl groups causes decomposition of the photosensitive component, followed by typical photolytic changes in the NKhDA molecule; b) excitation of the electrons in the novolak and in the phenolic groups of NKhDA is accompanied by fluorescence, inter-state transition to the triplet state, and partial phosphorescence.

The photon energy of the phosphorescence is probably close to the u.v. absorption edge of the novolak (typically, 3.3–4 eV).

Lastly, the recombination of ion-molecules produced by electron impact can produce similar effects (i.e. fluorescence and phosphorescence). A rough estimate of the number of resulting ions from the measured secondary emission suggests that their role in the balance of internal radiation is very limited (a few per cent).

We shall now consider in detail the conditions which obtain when a photoresist is irradiated by a stream of electrons, the effect of the substrate material on the width of the resulting line and the sharpness of its edges, and lastly the optimisation of the resist composition from the standpoint of further miniaturisation of electronic devices.

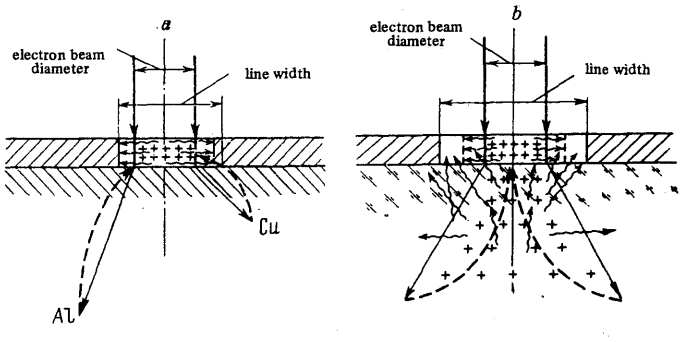


Figure 8. Passage of electrons through a layer of resist into a solid, and resulting diffuse irradiation: *a*) metallic substrate; *b*) dielectric substrate.

1. Irradiation of a positive photoresist on a metal substrate (Fig. 8*a*). We assume negligible divergence of the beam in the resist. The left-hand side of Fig. 8*a* depicts the penetration of the electrons into a light-metal substrate (Al), the right-hand side applies to a heavy-metal substrate (Cu). As a result of secondary electron emission, positive charges appear in the photoresist along the path of the primary electrons. The passage of the electron beam through the photoresist causes excitation and ionisation of the molecules. Both the NKhDA and the novolak resin molecules are excited.

The instability of electronically excited naphthyl groups in the NKhDA molecules results in decomposition by a reaction path indicative of excitation by photons of 2.7 to 2.8 eV energy.

The phosphorescence of the phenolic groups of the NKhDA molecule, of the novolak resin, and of the recombining ion-molecules gives rise to radiation in all directions (including the horizontal). This radiation is the main reason for the large difference between the line widths obtained in practice and the width of the electron beam.

The presence of positive space charge in the resist produces, on the one hand, an acceleration of the slow secondary electrons to energies at which they become able to excite molecules, and on the other hand it deflects the trajectories of inelastically scattered electrons, which therefore suffer a drift in the direction of the positive charge. Because of the shallower escape depth of the inelastically scattered electrons in heavy metals, and of their greater concentration, their interaction with the charge is less marked in heavy metals, and therefore the lines are broader (the comparison between copper and aluminium was given by Koichi and coworkers [6]).

The electrons which have passed through the resist are gradually slowed down, and they transfer their energy to the substrate. The temperature rise of the substrate favours competing reactions like the deacylation of the naphthyl groups by ketens and the condensation of the novolak resin. It is interesting to note that the roughness of the edges obtained in practice is of the same order as the grain size of thin metal films thermally evaporated in a vacuum. (The edge roughness is given [6] as 0.05 μm, the grain size [55–57] is 500–1000 Å.)

2. Irradiation of a positive photoresist on a dielectric substrate (Fig. 8*b*). The internal irradiation of the photoresist is similar to the case of a metal substrate, but there are some important differences. Because of the finite dielectric constant of the substrate material, the secondary and the inelastically scattered electrons suffer more marked interactions with the space charge (which now appears in the substrate as well as in the resist). Their trajectories will be drawn towards those of the primary electrons, and as a result the line width should be less dependent on the density of the substrate material.

However, if the substrate material is transparent to u.v. light (e.g., silicon dioxide) the radiation produced in the bulk of the substrate is propagated in all directions and can irradiate the resist from below. This effect also influences the line width which can be obtained, as compared with a metallic substrate (see Table 2). Many workers [4,6,14] have deposited metallic films on the transparent dielectric substrate in order to attenuate the u.v. light emerging from the substrate: the metal film acts as a screen to short-wave radiation. However, the use of a u.v. screen produces undesirable side effects, discussed above.

These variants include the whole range of experimental conditions quoted in the literature. It is evident from the above discussion that there are a number of reasons why the very narrowest lines cannot be obtained. The most important are: internal irradiation of the resist, bombardment of the resist by reflected and accelerated secondary electrons in the case of a metallic substrate, and irradiation from the substrate in the case of a dielectric substrate transparent to actinic light.

In spite of their different origin, all these effects lead to the same undesirable result: a broadening of the line. Procedures to localise phenomena conducive to line broadening have been suggested.

a) The use of photoresists containing ions and atoms which absorb light of 480 nm wave length and below (Cr^{6+}, V^{5+}, Cu, Au, etc.) minimises internal irradiation and prevents its lateral propagation from the exposed areas.

b) The use of thin screens of light metals protects the photoresist from the radiation emitted by the dielectric substrate.

c) The stream of short-wave radiation emerging from the dielectric substrate can be attenuated by providing a screen of glass containing heavy-metal ions and atoms (Cr^{6+}, V^{5+}, Cu, Au, etc.). The low thermal conductivity of glass and its high secondary electron emission coefficient should favour the production of narrow lines.

6. COURSE OF POLYMERISATION REACTIONS UNDER ELECTRON BOMBARDMENT

The internal irradiation phenomena observed in positive photoresists occur also in negative resists, for the following reasons: a) the presence of benzene rings, excited to the first singlet level by the beam of primary electrons, produces efficient fluorescence and phosphorescence effects—the excitation and deactivation of the sensitiser is accompanied by similar phenomena; b) inelastically scattered electrons are able to excite resist molecules; c) the generation of positive space charge in the bulk of the resist by the anomalous secondary electron emission results in the excitation of the resist molecules by secondary electrons which are accelerated to sufficiently high energies.

The deactivation of the resist molecules which are excited by primary electrons, by inelastically scattered electrons, and by accelerated secondary electrons is accompanied by radiation which is propagated into the bulk of the resist.

The procedures used to localise the radiation in positive resists (by adding absorbing ions) are applicable, in general, also to negative resists.

The excitation and the deactivation of the cinnamoyl groups in the photoresist molecules, and their subsequent polymerisation (both in the irradiated and in the adjacent areas), are the exact counterpart of the reactions which occur in the photoresist under the influence of light (i.e. biradical polymerisation). The energy of u.v. light is insufficient to extract electrons from the molecules.

The polymerisation mechanism involving excitation of the double bonds of the cinnamoyl groups is not the only one available to the resist. Electron irradiation produces, in addition to excitation, substantial ionisation of the molecules (up to 50% of the irradiated molecules): in other words, this form of irradiation gives rise to a greater number of primary processes than does irradiation with light. The subsequent deactivation and recombination of the molecules can take place by a great variety of possible reaction paths.

Thus, electron bombardment can activate other groups in the PVTs molecule, whilst also forming free radicals and ions. Hence, polymerisation reactions involving other groups of the PVTs molecule and of the sensitiser are possible, for example: a) bond formation between benzene ring, between a benzene ring and a linear chain, etc.; b) free-radical polymerisation; c) ion–molecule reactions.

Deactivation of the benzene rings, and also of radicals and ions, is accompanied by fluorescence and phosphorescence effects. The energy of transitions from the excited levels to the ground state is fairly high: in benzene, for example, it corresponds to the edge of the first absorption band, i.e. ~ 2537 Å. Light quanta of this energy can excite the cinnamoyl groups of the photoresist molecules, the sensitiser, etc. This stepwise utilisation of the energy of the electron beam partly explains the well known fact that the exposure of a negative photoresist with an electron beam requires less energy than exposure with light.

Several workers[27,35,58] have found that the energy needed to polymerise a poly(vinyl cinnamate) photoresist such as PVTs or KPR with an electron beam is smaller by a factor of 3 than the energy needed for exposure with light.

It must be stressed that electron irradiation can also lead to polymer degradation. According to Pshezhetskii, irradiation of poly(vinyl alcohol) causes evolution of hydrogen (95%), methane, carbon dioxide, and other radiolysis products[16]. The yield of gaseous products can be as high as 1.7 molecules per 100 eV of energy absorbed and increases with the dose of radiation. The optimum dose for the production of high-molecular products varies between 0.5 and 5 Mrad for different substances[59]. Negative photoresists have been irradiated with doses as high as 4.65 Mrad[35], 3.9 Mrad[11], 23 Mrad[6], 46 Mrad[12], etc.

As stated above, the irradiation of poly(vinyl alcohol) with high-energy electrons is accompanied by polymer degradation and gas evolution. Poly(vinyl esters) are also readily degraded by penetrating radiation[60]. PVTs is obviously an exception to this rule, at least within the range of electron energies and radiation doses of relevance to this review.

The polymerisation produced by electron bombardment is largely determined by the nature of the target molecules[61] and by the specific features of the reactions induced by the radiation.

Because of the difficulty of isolating individual products, and of defining conditions for the unambiguous identification of the polymerisation mechanism, contradictory results are often obtained. In spite of the generally adopted working hypothesis that radiation-induced polymerisation involves free radicals, the polymerisation is often accompanied by interactions between ions and molecules.

Irradiation with an electron beam can initiate a large number of reactions in a photoresist. None of the published papers deals specifically with the polymerisation mechanism of poly(vinyl cinnamate) resists: this is unfortunate, because a knowledge of the predominant reaction could be of great help in the choice of the best resist composition and of the best exposure energy. The cross-linking of separate molecules into blocks undoubtedly influences the resolution of the photolithographic process.

Press[2] has shown that the energy needed for exposure with light, assuming excitation of the double bonds in PVTs, obeys an exponential law. Even allowing for the stepwise, repeated utilisation of the energy of the primary electrons, transmitted through fluorescence and phosphorescence phenomena, this energy is insufficient to cause cross-linking of the resist. The ion–molecule reaction mechanism, or the free-radical mechanism, seems to be more economical in energy.

The system in which a film of resist on a metallic layer is irradiated by scanning a beam of accelerated

electrons in a vacuum behaves as a complex emitter. Electron bombardment of this two-layer structure (dielectric–metal) is accompanied by anomalous secondary electron emission. The appearance of positive space charge in the bulk of the resist can be treated as the addition of a large number of ions with a sufficiently long life time. These ions are not usually carbonium ions, though they may give rise to carbonium ions (possibly as intermediate products) during subsequent decomposition.

In the gas phase these ionic particles can be formed only at sufficiently low pressures, because the breaking of a covalent bond to give a carbonium ion requires a greater expenditure of energy than does the formation of radicals. It must also be remembered that the ions formed as a result of excitation have a life time of the order of 10^{-5} s, followed by decomposition. Ionisation with formation of carbonium ions is possible only when the required ionisation energy is compensated by solvation of the resulting ion in solution or by coulombic interaction in an ion pair (either in solution or in the gas phase) [62].

In the solid phase the course of the reaction is affected by heterogeneities, defects, etc., which enable the electrons to be captured and retained by the crystal lattice. This effect is responsible for the high stability of cations in solids.

Although the possibility of an ionic–molecular polymerisation mechanism is not entirely excluded, the most likely mechanism for the polymerisation of poly(vinyl cinnamate) photoresists under electron bombardment is a mechanism involving free radicals, for the following reasons:

1. Irradiation of PVTs with u.v. light gives rise to cross-linking even though the quantum energy of the light is insufficient to cause ionisation.

2. Addition of oxygen to the chamber in which KPR is irradiated with electrons does not affect the polymerisation [35]. Oxygen is the strongest known inhibitor of cationic polymerisation.

3. The fact that irradiation with a beam of 14 keV electrons is more effective than irradiation with 20 keV electrons [1] also suggests a free radical polymerisation mechanism. The beam of 14 keV electrons suffers considerably greater losses in the layer of resist, which is therefore heated to a higher temperature.

The cross-linking of negative photoresists by a free-radical polymerisation mechanism explains a number of previously surprising features of electron-beam exposure. The most important are: a) the energy needed for the cross-linking reaction becomes lower; b) the spatial resolution of the resist depends on the tendency of free-radical reactions to initiate chain growth, which can propagate sideways from the point of initiation; c) the roughness of the edge of the polymerised stripe depends both on the propagation of free-radical chains and on the properties of the substrate (thermal conductivity, thermal diffusivity, thickness, grain size, etc.).

7. DISCUSSION AND CONCLUSIONS

The many and complicated phenomena which accompany the passage of an electron beam through a photoresist have not yet been fully investigated. This is the main reason for the inconsistent results reported by different workers and for the contradictory explanations advanced to account for them.

Although some encouraging results have been obtained in attempts to decrease the size of the microcircuit elements, and in defining the optimum accelerating voltage, charge, and other technological parameters, many outstanding problems still stand in the way of a more general application of electron-beam exposure of photoresist. Some of these are: a) the inconstancy between theoretically expected and practically accessible dimensions of the microcircuit elements [6,11,13,63]; b) the low operating efficiency, due to the slow scanning speed of the beam—according to Thornley and coworkers [64], electron beam exposure can be profitable only if projection or multiple-beam apparatus is used; c) the difficulty of obtaining a spot of sufficiently small diameter.

Although the above problems have separate identities, they are by no means unconnected: a decrease in beam diameter is accompanied by a decrease in the flux of electrons, which makes the permissible scanning speed even slower and therefore lowers the operating efficiency of the process. The discrepancy between the calculated and the experimentally obtained line widths is explained by the lack of monochromaticity of the beam, by the lack of resists specially designed for exposure by electrons, and by the influence of the substrate material. The low productive capacity, and the difficulty of producing patterns of prescribed dimensions, stem from the use in electron lighography of materials which were designed as photoresists, although other materials could be used to better effect [13,64,65].

Detailed analysis of the problems is complicated by the large numer of commercial resists and by the wide variety of their properties [23].

The reactions considered in this review (changes in positive photoresist based on naphthoquinonediazide and changes in negative photoresist based on PVTs) are a convincing illustration of the problems underlying the use of an electron beam for exposure. We have deliberately chosen the most familiar and widely used resists, though many other types and grades are available. For the grades considered here, the following parameters of the layer of resist can be calculated with quite good accuracy: energy balance, resolving power of the beam, edge roughness of the resulting pattern, thickness of resist, and accelerating voltage. With other types of polymer (of both the cross-linking and the degrading type), based on different compounds, the phenomena and the rules discussed above should be applied with care, taking due notice of the structure and composition of the starting materials and of their reactions under electron irradiation.

The sequence of reactions in the polymers should be investigated in accordance with the nature of the chosen material: a) primary excitation and ionisation reactions; b) secondary reactions involving deactivation and recombination of the molecules.

It is important to consider first of all the physical processes associated with fluorescence, phosphorescence, triplet–triplet energy transfer, and secondary electron emission. The subsequent chemical reactions (intramolecular decomposition, degradation, or polymerisation) are critically dependent on the properties of the starting compound. In addition to the reactions of the main component of the resist, we must consider also the role of the various additives.

The main conclusion to be made from the present review is that the widespread penetration of electron-beam exposure into industrial practice must await the solution of the following problems:

1. The influence of the substrate material on the exposure and on the development of the film of resist (including the effect of secondary electron emission).

2. The effect of the radicals and ions formed by electron bombardment on the course of chemical reactions in photoresists.

3. Minimising the energy required for the exposure of the resists. Special interest attaches to the use of an electron beam for exposing negative photoresists, for the following important reasons: a) the energy required for exposure is lower by a factor of 6 as compared with positive photoresists; b) the energy required is lower by a factor of 3 as compared with exposure by light; c) negative resists are more stable towards etchants than positive resists.

The use of sensitisers to decrease the energy required for the exposure of positive photoresist has been convincingly demonstrated by Broyde[36].

4. The synthesis of new resists, more sensitive towards electron irradiation, and free from internal irradiation effects. The latter requirement is essential to the achievement of even smaller dimensions in microelectronic circuits.

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Reaction Mechanisms of the Direct Epoxidation of Alkenes in the Liquid Phase

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Reaction mechanisms for the liquid-phase epoxidation of alkenes are reviewed critically: the classical Prilezhaev reaction, catalytic epoxidation with participation of hydrogen peroxide and of organic hydroperoxides, reactions for the production of alkene oxides in the oxidation of unsaturated hydrocarbons, reaction of a combined oxidation of alkenes with aldehydes. The mechanism and prospects of the catalysed oxidation with oxygen of alkenes to epoxides are discussed in detail. 150 references.

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1. INTRODUCTION

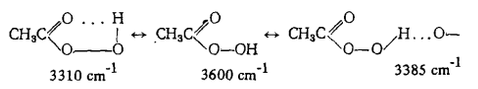
Alkene oxides are important intermediates in industrial organic synthesis. In addition to traditional uses—the production of antifreezes, solvents, and plasticisers for plastics and explosives—new ways of using them have appeared: the production of non-ionogenic surface-active substances, polyethers, polyurethanes, etc. In this connection the direct oxidation of alkenes now has a permanent place in the organic synthesis industry with an extremely promising future[1]. Processes for the oxidation of alkenic hydrocarbons are displacing such traditional and well-accepted processes as the synthesis of ethylene oxide through 2-chloroethanol. Almost all the ethylene oxide is obtained by the direct vapour-phase oxidation of ethylene on a silver catalyst. Monographs and reviews have dealt with this important process and the mechanism of the reactions on which it is based[2-5]. Although the direct vapour-phase oxidation of alkenes is used in all the works built in the last 10–15 years, there is a continuous search for new paths of liquid-phase oxidation of alkenes, since this allows the temperature at which the processes are conducted to be reduced and (especially important) their selectivity to be increased. For example, in addition to the classical method of epoxidising propene with peracids a new method of epoxidation with the hydroperoxides of such organic compounds which are readily oxidised by molecular oxygen has appeared. The combined oxidation of propene plus aldehydes lies at the basis of processes developed by the Institute of Chemical Physics of the

Academy of Sciences of the USSR and by the Institut francais du Pétrole. Very recently there have been extensive searches for catalytic systems activated by oxygen in the epoxidation of unsaturated compounds. Complexes of metals of variable valency (Mo, V, W, Ir, and Rh) with various ligands form such systems. An investigation of liquid-phase epoxidation processes is continuing and being extended. A special part is played by the study of the mechanisms of these reactions, which are of practical importance. The task of the present review is a critical examination of papers dealing with the reaction mechanisms of liquid-phase epoxidation—from the classical Prilezhaev reaction to the most recent investigations into the activation of molecular oxygen in the epoxidation of alkenes.

2. THE PRILEZHAEV REACTION

The Prilezhaev reaction[6,7] between a per-acid and an alkene is now reliable and has been studied in detail: methods of preparation of the per-acids and the reactions of many unsaturated compounds have been examined in detail[8,9]. However, the search for the most effective per-acids in particular reactions and for the most convenient paths for effecting epoxidations with a per-acid is still continuing[10-12]: for example, there is the use of *o*-sulphoperbenzoic acid as an epoxidating agent allows *trans*-1,2-cyclohexane-1,2-diol to be obtained at 25°C in yields of up to 88% from cyclohexene[12] via the oxide.

The per-acids exist in solutions in various forms depending upon the nature of the solvent[13-15]. When the solvent does not form hydrogen bonds the per-acid is a monomer with an intramolecular hydrogen bond[14]. The stretching frequency of the hydroxyl of the per-acid (3600–3750 cm^{-1}) is depressed to 3000–3500 cm^{-1} under the influence of a hydrogen bond. Below we show peracetic acid in various states with the corresponding vibration frequencies of the hydroxyl of the acid[15]:

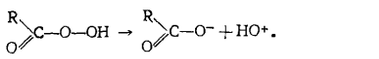


The reactivity of the per-acids is quite different in solvents which form a hydrogen bond—nitromethane, acetone, etc. Thus it is well known that perbenzoic acid which is formed in the oxidation of benzaldehyde can be isolated solely in acetone, since in solvents which do not form hydrogen bonds the per-acid reacts rapidly with benzaldehyde by the Bayer–Villiger reaction[16].

The per-acids are weaker acids than their analogues which do not contain a peroxide group[17]:

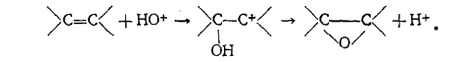
Acid	p*K*
HCOOH	3.7
HCO_3H	7.1
CH_3COOH	4.8
CH_3CO_3H	8.2

Organic per-acids are readily polarised and they have a tendency to heterolytic breaking of a weak O–O bond:



However, the hydroxy-cation HO^+ cannot exist in the free form, since it would be a species with a very high energy.

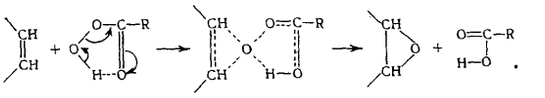
Even in the first kinetic investigations the Prilezhaev reaction[18,19] was found to be first order with respect to both components and it was shown that this reaction is bimolecular like other heterocyclic reactions of per-acids with amines, sulphides, phosphines, phosphites, azo-compounds, and aryl iodides[20]. In early studies it was suggested that the epoxidating species is the free hydroxy-cation HO^+, which attacks the alkene[21,22]:



But as stated above the cation HO^+ cannot be formed.

A study of the relative reaction rates of per-acids with various alkenes showed that per-acids are typical electrophilic agents[23]. The per-acids can be arranged in a series in order of decreasing electrophilic character in full agreement with the values of the Taft σ constant for the R groups: CF_3CO_3H (+2.6), $C_6H_5CO_3H$ (+0.6), HCO_3H (+0.49), CH_3CO_3H (0).

A systematic study of the rates of epoxidation of substituted alkenes by substituted perbenzoic acids[24] provided a basis for a molecular mechanism of the reaction of a per-acid with an alkene[25-28]:



This reaction mechanism, in which the π-bond of the alkene is attacked, is supported by experimental facts found in the epoxidation of *trans*-stilbene and its derivatives (4-OCH_3, 4-CH_3, 4-Cl, 4-NO_2, 3-Cl, 3-NO_2) with per-benzoic acid and its derivatives (4-NO_2, 4-Cl, 3-NO_2, 3-Cl, 4-CH_3, 4-OCH_3).[24]

1. As a result of a study of these reactions at 20–40°C in benzene the activation parameters ΔG^*, ΔH^*, and ΔS^* were determined and it was found that despite the small range, the variation in ΔH^* (14.0–16.0 kcal $mole^{-1}$) and ΔG^* (20.0–23.0 kcal $mole^{-1}$) by the effect of substituents on the electron density of the reaction centre.

Electron-donating substituents in *trans*-stilbene decrease ΔG^* and ΔH^*, but electron-withdrawing substituents increase ΔG^* and ΔH^*. On the other hand, electron-withdrawing substituents in perbenzoic acids decrease ΔG^* and ΔH^*, but electron-donating substituents in perbenzoic acid increase ΔG^* and ΔH^*. Hence the alkene behaves as a nucleophilic agent in the reaction, and the per-acid as an electrophilic one.

2. The addition of the salt $Mg(ClO_4)_2$ to the reaction has no effect whatsoever on the rate of the process, that is, it does not possess ionic limiting stages.

3. The reactivity of substituted ethylenes falls with decrease in the order of the double bond: styrene > *trans*-stilbene > triphenylethylene > tetraphenylethylene (Table 1).

4. The effect of solvent on the rate of epoxidation of the alkenes is completely connected with the formation of hydrogen bonds between the per-acids and molecules of the solvent (Table 2).

Hence all the above results show that the reaction of an alkene with a per-acid is bimolecular. The rate constant for the reaction of *trans*-stilbene with perbenzoic acid is, in the usual form[24]: $1.78 \times 10^8 \exp(-15\,850/RT)$ litre $mole^{-1}$ s^{-1}.

The intermediate formation of a π-complex has recently been demonstrated kinetically in the reaction of propene

with peracetic acid[29]. The reaction is effected in benzene solution at 20–60°C. The absence of radical stages in the reaction was shown by the introduction into the system of an inhibitor of radical processes—2,6-di-t-butyl-4-methylphenol; the inhibitor introduced had no effect on the reaction rate. A detailed kinetic investigation of the reaction of peracetic acid with propene allowed the following scheme to be suggested for the process:

$$CH_3CO_3H + n\,C_3H_6 \underset{k_2}{\overset{k_1}{\rightleftarrows}} [CH_3CO_3H \cdot n\,C_3H_6] \xrightarrow{k_3} C_3H_6O + CH_3COOH.$$

Table 1. Kinetic characteristics of the epoxidation of alkenes by perbenzoic acid in benzene at 20–40°C.[24]

Alkene	$10^4k^{20°}$, litre mole^{-1} s^{-1}	$\Delta H^{\neq}$, kcal mole^{-1}	$\Delta G^{\neq}$, kcal mole^{-1}	$-\Delta S^{\neq}$, cal mole^{-1} deg^{-1}
Styrene	6.12	14.2	21.7	24.8
cis-Stilbene	5.70	14.1	21.7	25.2
Triphenylethylene	—	15.7	22.6	22.7
Tetraphenylethylene	—	17.2	24.1	22.6
Cyclohexene	127	12.7	19.9	24.0
Cyclohexene*	3.72	15.3	22.0	22.0

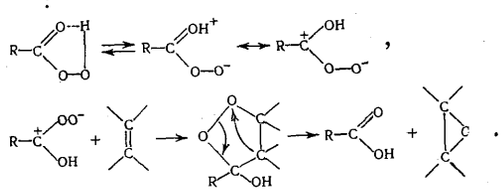
* Reaction in diethyl ether.

It was shown that one molecule of per-acid reacts with two molecules of propene ($n = 2$) and the equilibrium constant was determined: $K = k_1/k_2 = 3 \times 10^3 \exp(-5500/RT)$ litre^2 mole^{-2}. The rate constant of the decomposition of the π-complex is $k_3 = 6.7 \exp(-11\,600/RT)$ s^{-1}.

Table 2. Effect of the solvent on the epoxidation rate constant at 30°C.

trans-Stilbene + CF_3CO_3H (Ref.11)		Ethyl crotonate + *m*-chloroperbenzoate (Ref.24)	
solvent	10^4k, litre mole^{-1} s^{-1}	solvent	10^4k, litre mole^{-1} s^{-1}
CCl_4	14.6	CCl_4	0.115
$CHCl_3$	36.0	C_6H_6	0.173
CH_2Cl_2	36.1	$CH_3COOH+(CH_3CO)_2O$	0.0075
$ClCH_2CH_2Cl$	32.7		
$(CH_3)_3COH$	0.42	CH_3COOH (90%)+H_2O (10%)	0.053
C_6H_6	18.9		

A few papers have also suggested that per-acids react with alkenes by a bipolar 1,3-addition mechanism[30], which is well known[31] and is realised in the ozonation of alkenes[32–34]:



In support of the mechanism of bipolar 1,3-addition there is the low value of ρ in the Hammett equation (−0.8) for the reaction of per-acids with alkenes and the same effect of the solvent on this reaction as in the oxonation of alkenes[35]. However, there is no clear proof of the bipolar 1,3-addition mechanism in the reaction of alkenes and per-acids, whereas the reaction of an alkene and per-acid with the formation of a π-complex has been proved convincingly[24,29]. In the reaction of propene with peracetic acid the limiting stage is the decomposition of the π-complex[29]; in all the other instances studied the reaction is limited by the bimolecular reaction of the alkene with the per-acid. It is possible that the kinetic investigations of the reactions of alkenes and per-acids over wide ranges of concentration of the two components will give new examples of such reactions where the decomposition of an intermediately-formed complex of the per-acid with the alkene is limiting.

Table 3. Rate constants for the epoxidation of substituted cyclohexenes by perbenzoic acid at 5°C in benzene[38].

Compound	10^4k, litre mole^{-1} s^{-1}	Relative rate
Cyclohexene	63.3	1.0
3-Hydroxycyclohexene	34.5	0.55
3-Methoxycyclohexene	4.25	0.067
3-Ethoxycyclohexene	4.72	0.075
3-Acetoxycyclohexene	2.90	0.046
4-Hydroxycyclohexene	2.67	0.042

The reaction of per-acids with cycloalkenes is stereospecific[36–40]: when a cyclic alkene reacts, the oxygen atom of the epoxide that is formed occupies an axial position and the π-bond of sterically hindered molecules is attacked from the less hindered side. The formation of epoxides from cyclic allyl alcohols takes place in the *cis*-position to the OH group[38], which shows the strong accelerating action on epoxidation:

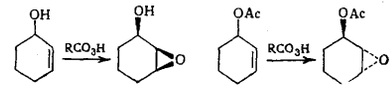


Table 4. Rate constants for the epoxidation of substituted cyclohexenes by *m*-chloroperbenzoic acid in ether at 25°C.[40]

Compound	10^3k, litre mole^{-1} s^{-1}	Relative rate
Cyclohexene	1.88	1.0
4-t-Butylcyclohexene	1.76	0.94
3-Methylcyclohexene	1.77	0.94
4-Methylcyclohexene	1.52	0.81
trans-4,5-Dimethylcyclohexene	1.49	0.79
cis-4,5-Dimethylcyclohexene	0.87	0.46
3,3-Dimethylcyclohexene	0.83	0.44
cis-4,5-(CH_2OCH_2)-Cyclohexene	0.94	0.50
trans-4,5-(CH_2OCH_2)-Cyclohexene	0.55	0.29

The epoxidation of 3-acetoxycyclohex-1-ene takes place much more slowly than reaction with cyclohexen-3-ol and is accompanied by the preferential formation of the *trans*-epoxide. Stereospecificity strongly affects the rates of epoxidation of cycloalkenes by per-acids (Table 3).

The introduction of alkyl groups into cyclohexene retards epoxidation, the action being purely steric, and not inductive, in nature[40] (Table 4).

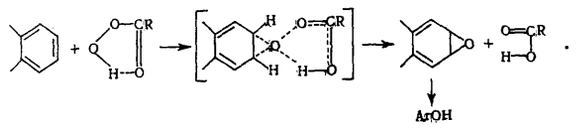
Stereoselectivity is pronounced in the epoxidation of substituted cyclohexenes:

Substituent in cyclohexene	% of *trans*-epoxide in reaction with *m*-chloroperbenzoic acid at 25°C
4-t-Butyl	39.5
4-Methyl	53.6
cis-4,5-Dimethyl	87.0

The electrophilic properties of per-acids were convincingly confirmed and used in the hydroxylation of aromatic compounds[41-50]. Use of such a strongly electrophilic agent as CF_3CO_3H with additions of BF_3 for the hydroxylation of mesitylene allowed mesitol to be obtained in 88% yield[48]. Hydroxylation of phenol with the system (H_2O_2 + HF) gives 54% hydroquinone and 42% pyrocatechol[49], and the use of performic and peracetic acids with additions of polyphosphoric acid and P_2O_5 gives 52.5% pyrocatechol and 16.6% hydroquinone[50]. There has been hardly any investigation of the kinetics and mechanism of hydroxylation of aromatic compounds by per-acids, although it has been clearly established that there are no radical steps in this reaction[46,47]. It has also been shown that the distribution of the isomers of substituted benzenes during hydroxylation with CF_3CO_3H is typical of electrophilic substitutions in the benzene nucleus[47]:

Compound	Phenols			Reactivity in relation to benzene
	ortho	*meta*	*para*	
Anisole	73.7	0	26.3	530
Toluene	78.2	2.3	19.7	11.7
Fluorobenzene	17.2	0	82.8	0.27

It was shown very recently that, in the combined oxidation of aromatic compound plus benzaldehyde, phenols are formed and the rate at which they accumulate does not alter when inhibitors of radical reactions are introduced into the system[51,52]. The formation of the phenols proceeds by the reaction of benzenes with perbenzoic acid formed in the oxidation of the benzaldehyde. The behaviour of an inhibitor confirms that the hydroxylation of aromatic compounds by perbenzoic acid does not proceed by a radical mechanism. We assume that the mechanism of the hydroxylation of aromatic compounds by per-acids is molecular by analogy with the epoxidation of alkenes:



The formation of epoxides of aromatic compounds, which rapidly isomerise into phenols is now not in doubt[53].

3. EPOXIDATION OF ALKENES WITH HYDROPEROXIDES AND WITH HYDROGEN PEROXIDE WITH PARTICIPATION OF CATALYSTS

Organic hydroperoxides possess the capability of heterolytic breaking of the O–O bonds to a lesser extent than per-acids. However, such breaking can be facilitated with the aid of catalysts—metals of variable valency, which can be divided into two groups according to their type of reaction with organic hydroperoxides. To the first group belong metals such as Fe, Co, and Cu, for which the lower and higher valence states differ by unity. These metals usually facilitate homolysis of the O–O bond in hydroperoxides and generate radicals in the reactions with them. The second group includes such metals as V, Mo, W, and Cr, which in their highest oxidation states can cause heterolysis of the O–O bond in organic hydroperoxides.

Investigation of epoxidation by t-butyl hydroperoxide (TBHP) with participation of the acetylacetonates of various metals showed that the epoxidation of 2,4,4-trimethylpent-1-ene, oct-1-ene, and 4-vinylcyclohexene is accelerated especially effectively by the acetylacetonates of Cr, V, VO, and MoO_2, whereas those of Co, Cu, and Fe are not effective[54]. Epoxidation of propene with ethylbenzene hydroperoxide lies at the basis of a method for obtaining propene oxide developed by the firm Halcon[55]. Salts and compounds (naphthenates, acetylacetonates, oxalates, nitrates, etc.) of molybdenum, tungsten, titanium, vanadium, niobium, tantalum, and rhenium that are readily soluble in the reaction medium are used as catalysts. Recently, not only various compounds of metals having variable valency but also various organic hydroperoxides have been widely used in the epoxidation of alkenes. TBHP and vanadium and vanadyl acetylacetonates are used for the epoxidation of cyclohexene[56], cumene hydroperoxide (CHP) and molybdenum naphthenate and also $MoCl_5$ are used for the epoxidation of cyclohexene[57] and of cyclohexen-3-ol[58]. The epoxidation of propene with molybdenum resinate and various hydroperoxides—TBHP, CHP, and ethylbenzene hydroperoxide (EBHP)—has been studied in special detail[59,60]. The epoxidation of 2-methylpent-2-ene[61] and various butenes[62] has been studied. The kinetics and mechanism of these reactions have been investigated[56,59,60,62,63].

Table 5. Epoxidation of oct-1-ene with t-butyl hydroperoxide in the presence of $Mo(CO)_6$.

Solvent	Conversion, %	Yield of epoxide, %
Benzene	75.0	92.0
Methylcyclohexane	72.0	84.0
Ethanol	40.0	37.0
t-Butyl alcohol	16.0	58.0
Acetone	39.0	5.0

The effect of the alkene structure, the hydroperoxide structure, the temperature, and the solvent on the epoxidation of alkenes and the kinetics of epoxidation of oct-1-ene and oct-2-ene with participation of TBHP and molybdenum hexacarbonyl $Mo(CO)_6$ have been investigated in detail[63]. It was found that out of a great number of various salts and coordination compounds of metals of various valency the greatest catalytic activity in epoxidations is exhibited by coordination compounds of molybdenum. The conversion of the alkene and the yields of the oxide are greater in non-polar solvents (benzene or cyclohexane) than in polar (Table 5).

We think that Sheng and Zajacek[63] were wrong in attributing the effect of the above solvents solely to their polarity, since the solvents, which in this instance are polar, can affect the reaction in various other ways; acetone and alcohols form hydrogen bonds with TBHP and reduce its activity, alcohols can enter the coordination

sphere of the catalyst and lower its effectiveness, as several investigations have confirmed[56,59].

For the epoxidation of oct-1-ene hydroperoxides (HP) can be arranged in the following sequence of decreasing activity: *p*-nitrocumene HP > cumene HP > t-butyl HP.[63]

Carrying out the reactions in an atmosphere of CO retards the epoxidation catalysed by $Mo(CO)_6$. The epoxidation of *cis*- and *trans*-but-2-enes shows the stereospecificity of the process, since the *cis*-epoxide is obtained exclusively from the *cis*-butene whereas *trans*-butene yields exclusively the *trans*-epoxide. In an investigation of the kinetics of the epoxidation of oct-1-ene with TBHP and $Mo(CO)_6$ it has been shown that the reaction is first order with respect to all three components. Oxygen does not affect the rate of epoxidation but influences the life of the catalyst.

The combination of such facts as the absence of an effect of O_2 on the epoxidation rate, the passivity of Co, Mn, and Fe complexes which react with the hydroperoxides with the formation of radicals, and the stereospecificity of epoxidation show that there are no radical steps in the epoxidation. The proposed mechanism of epoxidation is[63]:

$$ROOH + Mo^{n+} \rightarrow Mo^{n+}_{cat} , \quad (1)$$

$$ROOH + Mo^{n+}_{cat} \rightleftarrows \left[\begin{matrix} ROOH \\ \vdots \\ Mo^{n+}_{cat} \end{matrix}\right] \quad (2)$$

$$\left[\begin{matrix} ROOH \\ \vdots \\ Mo^{n+}_{cat} \end{matrix}\right] + >C=C< \rightarrow >C-C< + ROH + Mo^{n+}_{cat} .$$
$$\qquad\qquad\qquad\qquad\qquad\quad O$$

In the first reaction the catalyst is activated, in the second a complex of the catalyst and ROOH is formed, the reaction of which with the alkenes limits the rate of the whole process. The drawback of this scheme is the absence of specific indications of the activation and regeneration of the catalyst. In addition, according to the above scheme at high ROOH concentrations the rate of epoxidation should be independent of [ROOH], as has been noted in several instances[63], but this fact is interpreted as the consequence only of the decomposition of ROOH by a side-reaction. It was subsequently shown[56,59,60,64] that the kinetics of epoxidation are more complex and ways of regenerating the catalyst were also demonstrated.

As an example we will consider the mechanism of the epoxidation of cyclohexene with participation of TBHP and V and VO acetylacetonates[56].

t-Butyl hydroperoxide oxidises (activates) the catalyst:

$$VO(acac)_2 \xrightarrow{TBHP} -\overset{|}{\underset{|}{V^{V}}}- .$$

The activation is rapid and irreversible. The active form of the catalyst rapidly forms a complex with TBHP by the reverse reaction:

$$-\overset{|}{\underset{|}{V^{V}}}- + BuO_2H \overset{K_{equil}}{\rightleftarrows} -\overset{|}{\underset{|}{V^{V}}}-O-\overset{Bu}{\underset{OH}{}} .$$

The equilibrium constant is $K_{equil} = 10.3$ litre mole^{-1} at 50.6°C.

The complex reacts with cyclohexene; this determines the rate of the entire process:

$$-\overset{|}{\underset{|}{V^{V}}}-O-\overset{Bu}{\underset{OH}{}} + \bigcirc \xrightarrow{k} HO-\bigcirc + -\overset{|}{\underset{|}{V^{V}}}-O-\overset{Bu}{\underset{}{}} .$$

The following two reactions then occur rapidly:

$$HO-\bigcirc + -\overset{|}{\underset{|}{V^{V}}}-OBu \rightarrow O=\bigcirc + -\overset{|}{\underset{H}{V^{V}}}-OBu ,$$

$$-\overset{|}{\underset{|}{V^{V}}}-O-\overset{Bu}{\underset{H}{}} + BuO_2H \rightleftarrows -\overset{|}{\underset{|}{V^{V}}}-O-\overset{Bu}{\underset{OH}{}} + BuOH .$$

The last reaction is confirmed by the retarding action of alcohols on the epoxidation of cyclohexene[56]. The above scheme agrees with all the experimental results; an equation typical for such schemes is obtained for the initial rate of accumulation of epoxide:

$$W_0 = \frac{k \cdot K_{equil}[TBHP][V_0][ol]}{1 + K_{equil}[TBHP]}$$

where $[V_0]$, and [ol] are the concentrations of VO acetylacetonate and cyclohexene respectively, and k is the velocity constant of the rate-limiting step. The activation parameters of the rate-limiting process of the reaction are:

$$\Delta H^{\neq} = 12.7 \text{ kcal mole}^{-1}, \Delta S^{\neq} = -19.8 \text{ e.u.}$$

An analogous mechanism is proposed for the epoxidation of propene by various hydroperoxides with participation of a molybdenum-containing catalyst[59,60]. In the epoxidation of propene, alcohols can be arranged in the following order according to their inhibiting action[59]: MeOH > EtOH > Pr^nOH > n-octanol > 1-phenylethanol. The reactivity of hydroperoxides is determined by a combination of electronic and steric factors: in the epoxidation of propene the hydroperoxides can be arranged in the series: EBHP (2,4), TBHP (1,3), and CHP (1). CHP is the least effective in the reaction with propene. For the rate-limiting reaction between the complex of the hydroperoxide with the molybdenum catalyst and propene the rate constants in the temperature range 50–80°C and the activation energy of this reaction were determined:

Hydroperoxide	Activation energy, kcal mole^{-1}
EBHP	15.2
TBHP	15.0
CHP	15.6

In the technological realisation of the epoxidation of propene by ethylbenzene hydroperoxide with the participation of a molybdenum-containing catalyst it was shown that above 90°C the selectivity of the process is reduced significantly, since the hydroperoxide is destroyed by undesirable side-reactions[64]. A study of the reaction at 76–120°C aimed at obtaining equations for the optimisation of the process yielded the multistage mechanism:

$$R_1(R_2)(R_3)COOH + Mo \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} [R_1(R_2)(R_3)COOH \cdot Mo] , \quad (I)$$

$$X + C_3H_6 \xrightarrow{k_2} C_3H_6O + [R_1(R_2)(R_3)COH \cdot Mo] , \quad (II)$$

$$[R_1(R_2)(R_3)COH \cdot Mo] + R_1(R_2)(R_3)COOH \xrightarrow{k_3} R_1(R_2)(R_3)COH + X , \quad (III)$$

$$X + R_1(R_2)(R_3)COOH \xrightarrow{k_4} 2R_1(R_2)C{=}O + 2R_3OH + Mo , \quad (IV)$$

$$X + R_1(R_2)(R_3)COOH \xrightarrow{k_5} [R_1(R_2)(R_3)COH \cdot Mo] + R_1(R_2)(R_3)COH + O_2 . \quad (V)$$

The distinguishing features of this mechanism are the irreversibility of stage (III) and the side-reactions (IV) and (V) for decomposition of the hydroperoxide. On the basis of this scheme differential equations describing the consumption of the hydroperoxide and accumulation of propene oxide (PO) were written. Having used the experimental results on the rates of consumption of hydroperoxide w_{HP} and the rates of accumulation of the epoxide w_{PO} and having solved the equations by the Runge–Kutta method the investigators obtained a set of constants, the values of which were approximated to the Arrhenius equation. The coefficients of the Arrhenius equation were found by the least squares method.

The resulting equations for the rate of consumption of hydroperoxide and accumulation of the epoxide had the following form:

$$w_{HP} = K_I[Mo][HP](2K_{II}[HP] + k_2[propene])/(1 + K_{III}[HP]),$$

$$w_{PO} = K_1 \cdot k_2 \cdot [HP][Mo] \cdot [propene]/(1 + K_{III} \cdot [HP]),$$

where $K_I = \kappa_1/k_{-1}$, $K_{II} = k_4 + k_5$, $K_{III} = k_4/k_{-1}$.

The following values of the constants were obtained for the temperature range 76–120°C:

$$K_I = 49.6 \exp(-3480/RT) \text{ litre mole}^{-1};$$

$$K_{II} = 2.19 \cdot 10^5 \exp(-5960/RT) \text{ litre mole}^{-1} \text{ min}^{-1};$$

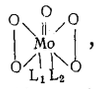
$$K_{III} = 113 \exp(-15800/RT) \text{ litre mole}^{-1};$$

$$k_2 = 5.7 \cdot 10^7 \exp(-10500/RT) \text{ litre mole}^{-1} \text{ min}^{-1}.$$

The results obtained can serve as the basis for the optimisation of the epoxidation of propene by ethylbenzene hydroperoxide in various types of reactor [64]. It is noteworthy that stage II, the rate-limiting step for the entire process has an activation energy of 10.5 kcal mole^{-1}, which differs significantly from the activation energy for this stage obtained in the epoxidation of propene by the same hydroperoxide with a molybdenum-containing catalyst at 50–80°C, 15.2 kcal mole^{-1}. [59,60] The various butenes can be arranged in the following series according to reactivity in their epoxidation by hydroperoxides in the presence of a molybdenum catalyst [62]: *cis*-but-2-ene : *trans*-but-2-ene : but-1-ene = 36.6 : 14.2 : 1.0. This ratio shows the effect of steric factors on the reaction rate in the epoxidation by hydroperoxides with participation of catalysts.

A characteristic feature of catalysed epoxidations with hydroperoxides is that the catalyst oxidised at the start of the process is not reduced at the end but is regenerated in an active form by exchanging an alcoholic ligand for hydroperoxide [56,59]. There remains a series of unexplained details in the mechanism of these reactions: the activation step of the catalyst, the chemistry of the limiting reaction, etc. Evidently these problems cannot be solved with the aid of kinetic investigations alone. An important part in the explaining of the details of the mechanism of these reactions should be played by the use of physicochemical methods of investigation of intermediate complexes formed during the course of the process and also a study of the reactions of the complexes themselves with alkenes. Such a type of investigation of the covalent peroxo-complexes of Mo^{VI} has been made [65].

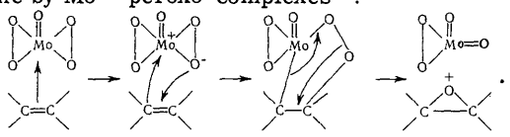
The epoxidation of alkenes by peroxo-complexes of Mo^{VI} of the following structure:



where L_1 and L_2 are aromatic amines, amides, phosphoramides, or phosphines, has been studied in various solvents at various temperatures.

The selectivity of the epoxidation with participation of such complexes reaches 50–95%, depending upon the conditions. The epoxidation of cyclohexene in dichloroethane at 10–30°C by the complex $[Mo(O_2)O]$–HMPTA (where HMPTA is hexamethylphosphorictriamide) proceeds through the intermediate formation of an associate of this complex with cyclohexene, the decomposition of which limits the rate of the process. The reaction was followed by the decrease in active oxygen (1 mole of the complex gives 2 atoms of active oxygen) and the process characterised by the effective first-order rate constant; the effective activation energy is 15.9 kcal mole^{-1}, very close to the values of E_{act} obtained for the epoxidation of propene by hydroperoxides in the presence of molybdenum-containing catalysts [60].

Solvents with various dielectric constants do not markedly affect the rate of epoxidation of a peroxo-complex although some of them can act on the reaction, by entering into the coordination shell of the complex. The coordination ability of some of the solvents used decrease in the order: HMPTA > DMF > tetramethylurea. The accumulated experimental results allowed a bipolar 1,3-addition mechanism to be proposed for the epoxidation of an alkene by Mo^{VI} peroxo-complexes [65]:



In addition to organic peroxides, hydrogen peroxide can be used in the epoxidation of alkenes [66–72]. The reaction of hydrogen peroxide with alkenes is catalytically accelerated by the addition of tungstic acid and tungstates [66–70], molybdenyl acetylacetonate [71], and isocyanate [72]. The mechanism of the catalytic action of tungstic acid and tungstates has now been well studied [68,70]. The epoxidation of allyl alcohol in an aqueous medium by hydrogen peroxide with addition of H_2WO_4 or Na_2WO_4 is characteristically zero order with respect to peroxide, and first order with respect to allyl alcohol and tungstate. The effective activation energy of this reaction is 14.6 kcal mole^{-1}. The following results have been obtained on the reactivity of alkenes in epoxidation by hydrogen peroxide (40°C) in the presence of tungstate:

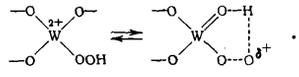
Hydrocarbon	$10^6 k$, s^{-1}
Cyclohexene	4.0
Allyltrimethylsilane	2.7
Allylmethylether	1.6
Allyl bromide	1.0
Allyl chloride	0.9

The logarithm of the constant is related linearly with the Taft σ constant, the coefficient ρ in the Taft equation being −0.44.

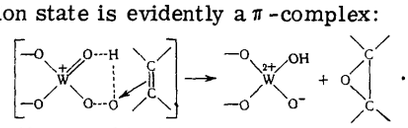
On the addition of tungstic acid or a tungstate to the peroxide the anion of pertungstic acid is formed rapidly:

$$HWO_4^- + H_2O_2 \rightleftarrows HWO_5^- + H_2O.$$

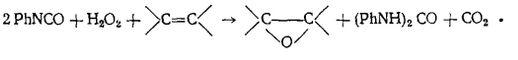
The actual anion HWO_5^- is the active species in the epoxidation of alkenes [70]; it exists in cyclic form owing to the formation of an intramolecular hydrogen bond and has an oxygen atom capable of electrophilic attack at the double bond:



The transition state is evidently a π-complex:



An interesting combination of epoxidation by hydrogen peroxide with the use of isocyanate has been described [72]. At 20°C cyclohexene, styrene, and hex-2-ene are epoxidised with 33–69% yield in reaction with hydrogen peroxide and phenyl isocyanate. The stoichiometry of the reaction is:



Two molecules of phenyl isocyanate and hydrogen peroxide form a complex (maximum absorption corresponds to a wavelength of 314 nm), which is also an epoxidising agent. It was found that under these conditions peroxocarbamic acid does not epoxidise alkenes.

Hence whereas in several instances the reaction mechanism is clear, for example, in the epoxidation of alkenes by hydrogen peroxide and tungstates, many problems of the reaction mechanism in the catalytic epoxidation by hydroperoxides have still not been settled. It is not clear whether the metal in the complex with hydroperoxide undergoes valency changes during the reaction or regeneration of the catalyst is effected solely by exchange of ligands[56,59]. The oxidation of a catalyst by hydroperoxides with the formation of active species has not yet been investigated, and the reaction between the complex of a metal with hydroperoxide and an alkene has not been studied at the level of the physical chemistry of the elementary act. Complexes of hydroperoxides with metals are not always capable of epoxidating an alkene, and in several instances such complexes generate radicals from the hydroperoxides and accelerate the autoxidation of the alkene, for example, in the autoxidation of oct-1-ene with participation of t-butyl hydroperoxide and Cr^{III} acetylacetonate[73]. In isolated instances an important part is played by the catalytic decomposition of the peroxides with participation of the metals, which becomes an undesirable side-process in epoxidation[60].

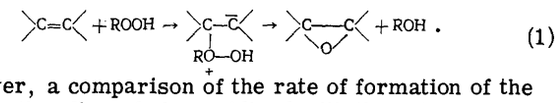
Despite a series of unsolved problems in the catalytic epoxidation of alkenes with hydroperoxides, requirements which are presented to the catalysts by this reaction can be formulated: (1) the central atom should be present in a high oxidation state; (2) the metal atom should have vacant *d*-orbitals capable of adding a pair of electrons; (3) one-electron redox reactions should be absent; (4) the metal should be employed in the form of a complex with labile ligands.

Clearly, all these requirements are not unique, are general in nature, and are typical for many catalytic reactions of coordination compounds.

4. NON-CATALYSED OXIDATION OF ALKENES WITH OXYGEN

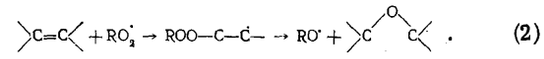
The mechanism of non-catalysed oxidation of unsaturated hydrocarbons has been studied in detail and described in several monographs and papers[74-76]. There can now be no doubt as to the radical-chain nature of the oxidation of unsaturated hydrocarbons by oxygen. This is confirmed by the photochemical sequence in the oxidation of alkenes[77], by the initiating action of peroxides[78], by the accumulation during the reaction of hydroperoxides, aldehydes, ketones, and acids. However, in addition to the above products in the oxidation of alkenes by oxygen, epoxides are formed. The aim of the present section will be to consider the mechanisms by which the alkene oxides are formed. Comparison of the oxygen absorbed with the amount formed in the oxidation of alkenes by peroxides showed that the alkenes absorb oxygen more than is observed with peroxides[79]. It appeared that in addition to hydroperoxides alkene oxides are formed; they were observed in the oxidation by oxygen of di-isobutene[80], styrene[81], methylstyrene[82], methyl elaidate[83], 2,4,4-trimethylpentene[84], cyclohexene[84], but-1-ene and but-2-ene[85], propene[86-90], and 2-methylpent-2-ene[91]. In isolated instances[87-91] alkene oxides can be obtained with yields which are of practical value (40–50% on the alkene which has been oxidised).

By which reactions are the epoxides formed in the oxidation of the alkenes by oxygen? One of the first reactions was proposed by Farmer and coworkers[92]:



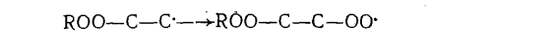
(1)

However, a comparison of the rate of formation of the epoxide in the alkene being oxidised with the rate of conversion of the hydroperoxide showed that in the initial period of reaction the epoxide is formed in parallel with the hydroperoxide and is one of the primary products of the oxidation of the alkene[81]. A mechanism by which the epoxide is accumulated in parallel with the hydroperoxide has therefore been proposed[93]:



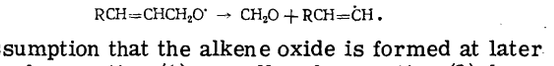
(2)

This reaction has been studied by the example of styrene[81] and methylstyrene[82]. In addition to reaction (2) in the oxidation of styrene the intermediate radical is converted into a peroxide radical:



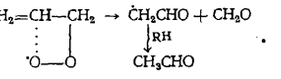
and a polymeric peroxide is formed[81]; in the oxidation of di-isobutene a polymeric peroxide is not formed: only the oxide and hydroperoxide accumulate. This allowed Mayo[80] to suggest that reaction (2) proceeds in a single step. Others have expressed similar opinions[94,95]. However, as further investigations showed, this reaction does not agree with several experimental facts[86].

The common oxidation of isopropylbenzene or ethylbenzene with propene at 80–90°C in the presence of an initiator is not accompanied by the formation of propene oxide, although a sufficiently high concentration of peroxide radicals was observed in the oxidation of cumene and ethylbenzene by EPR[96]. The formation of epoxide by reaction (2) should be accompanied by the accumulation of an equivalent amount of alcohol, but in the oxidation of cyclohexene, for example, alcohol is not observed in the early stages of reaction[94]. A second difficulty can be avoided by assuming that the RO· radical decomposes before the formation of alcohol, according to the scheme adopted for the oxidation of di-isobutene[80]:

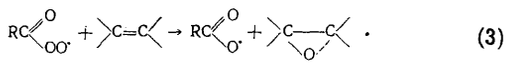


The assumption that the alkene oxide is formed at later stages than by reaction (1) as well as by reaction (2) does not agree with the experimental facts: the rate of formation of the alkene oxides by reaction (1) in an atmosphere of nitrogen is many times less than under oxidation conditions[94].

These difficulties can be avoided by postulating that in the oxidation of an alkene the epoxidising species is not the radical $RO_2^{\cdot}$ but the acyl peroxide radical RCOOO·, which is formed in the oxidation of aldehydes[86]. Actually, at 120–145°C during the oxidation of propene the accumulation of propene oxide precedes the formation of acetaldehyde[86]. The relation of the rates of accumulation of acetaldehyde and hydroperoxide tend towards a constant value at $t \to 0$ that is, the aldehyde accumulates in parallel with the hydroperoxide. Therefore the reaction proposed for the formation of the aldehyde is the unimolecular decomposition of the peroxide radical by analogy with the gas-phase oxidation of aldehydes[97]:



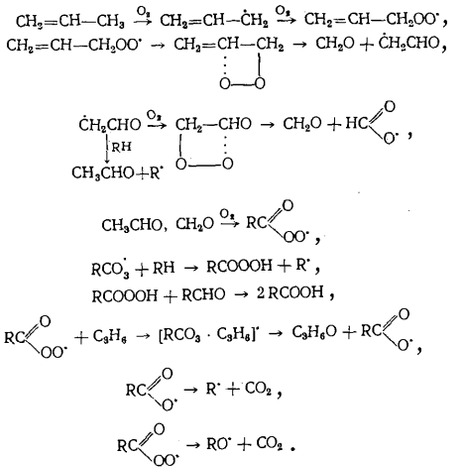
The oxidation of the aldehydes which are formed leads to acylperoxy-radicals, which are more reactive towards a double bond than the alkenylperoxy-radicals, and form oxides by the reaction:



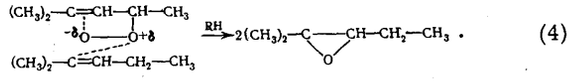
(3)

Reaction (3) can be one of the main paths for the formation of an alkene oxide, since aldehydes almost always accumulate in the oxidation of an alkene[85,86,90]. A detailed study of the liquid-phase oxidation of propene in non-metallic reactors (Teflon) showed that the intermediate products of the oxidation are formaldehyde and acetaldehyde, by way of which ~ 90 mole % of the propene reacts[87-90].

A scheme for the oxidation of propene in non-metallic reactors has been proposed[90]:



In the oxidation of 2-methylpent-2-ene at 120°C in a stainless steel reactor it was shown quite recently[91] that the rate of formation of the epoxide is much greater than the rate of accumulation of the conversion products of the acyl and alkenyl peroxide radicals, that is, reactions (2) and (3) cannot be explained by the accumulation of 2-methylpent-2-ene oxide in the quantities which are obtained experimentally (42% oxide in the conversion of methylpentene). A new reaction scheme for the epoxidation of alkenes was therefore proposed:



(4)

During the interaction of the unpaired electron of the radical with the π-bond the O–O bond in the radical is polarised, which facilitates the transfer of oxygen to the double bond and the detachment of a second oxygen atom by the neighbouring alkene molecule.

On making an overall examination of the epoxidations of alkenes during their oxidation it can be stated that hydroperoxides hardly participate at all in the epoxidation processes; during the epoxidation of the lower alkenes an important part is played by reaction with acylperoxy-radicals (3), but reaction of the double bond with alkenylperoxy-radicals (2) cannot be excluded completely. However, evidently there are also other paths of epoxidation, for example, reaction (4): the structure of the alkene plays a large part in the epoxidation.

5. MECHANISM OF COMBINED OXIDATION OF ALKENES AND ORGANIC COMPOUNDS OF OTHER CLASSES

It is well known that the combined oxidation of alkenes with aldehydes gives the possibility of increasing the yield of epoxide compounds to 50% or over[98-104]. This fact was used to create a new method of preparing alkene oxides[101,104]. Blyumberg and coworkers proposed to use the active oxygen of peroxide radicals formed during the oxidation of organic compounds for the epoxidation of alkenes. In one stage of the combined oxidation alcohols, ketones, acids, etc. are formed simultaneously with the alkene oxides. Substances which are carriers of active oxygen can be ketones or aliphatic and aromatic hydrocarbons in addition to aldehydes[105]. The best results are achieved by use of acetaldehyde and ethyl methyl ketone. The process is carried out in an inert solvent and air serves as oxidant. In the oxidation of propene plus acetaldehyde the optimal temperature is 55–60°C, the pressure 50 atm, the ratio acetaldehyde:propene = 1–2 : 8–9. 0.05 wt.% cobalt acetate is introduced as a catalyst. An excess of propene, benzene, ethyl acetate, acetone, dichloroethane, or acetic acid is used as solvent. Table 6 gives the results for the combined oxidation of alkenes with other organic compounds[105]. An analogous process was proposed by the Institut français de Pétrole[104]: the epoxidation of propene, but-1-ene, hex-1-ene, or 2-ethylhex-1-ene is effected at a partial pressure for the alkene of 22–30 atm in the presence of acetaldehyde, propionaldehyde, or butyraldehyde. Benzene, chlorobenzene, dichlorobenzene, toluene, or xylene is used as solvent. The temperature for the process is determined by the nature of the alkene being oxidised. Azo-compounds, organic peroxides, or salts of metals of variable valency are used as initiators of the epoxidation.

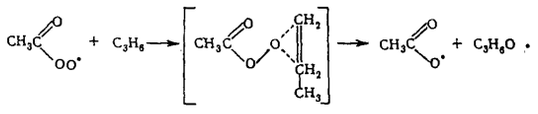
Table 6. Characteristics of the combined oxidation of alkenes and other compounds[105].

Conjugated pair	Temp., °C	Concn., wt.%	Yield of oxide, kg per 100 kg first component
Acetaldehyde + propene	55—80	34.0	70.0
Propionaldehyde + propene	70	12.0	50.0
Ethyl methyl ketone + propene	145	10.0	96.0
Butane + propene	145	3.0	11.0
Isopropylbenzene + propene	130	3.0	13.4
Ethylbenzene + propene	120—140	3.0	15.0
Acetaldehyde + 2-methylpropene	80	12.0	82.0
Acetaldehyde + ethylene	80	8.5	13.0

The problems of the combined oxidation of alkenes and aldehydes were investigated using the pair propene plus acetaldehyde[106-108]. A study of the kinetics and mechanism of oxidation of this pair of substances at 70–80°C and 50 atm in an inert solvent (benzene) showed that the main epoxidating species is the acylperoxy-radical formed in the oxidation of acetaldehyde by oxygen[106]. At the moment of reaching the maximum rate of accumulation of propene oxide in the reaction mixture an inhibitor of radical reactions was introduced—2,6-di-t-butyl-4-methylphenol. After the introduction of the inhibitor the propene oxide concentration rose very slightly, that is, the bulk of the oxide is accumulated from the reaction of propene with free radicals, and a smaller part by reaction with the per-acid.

A study of the epoxidation of propene with peracetic acid under the same conditions made it possible to estimate the contribution of this reaction to the total accumulation of

propene oxide[29]. It was found that at 70–80°C only ~ 15% of the propene oxide is formed by reaction with peracetic acid and the rest comes from the reaction with acylperoxy-radicals[106]:



In addition to the epoxide, methanol, methyl acetate, biacetyl, and methyl formate are formed in the combined oxidation of acetaldehyde and propene[106]. The composition of the oxidation products is greatly dependent upon the oxygen partial pressure[107].

The principal reactions which occur during the combined oxidation of acetaldehyde and propene are[107]:

$$CH_3CHO + O_2 \xrightarrow{k_1} CH_3\dot{C}O + HO_2^{\cdot},$$

$$CH_3\dot{C}O + O_2 \xrightarrow{k_2} CH_3COOO^{\cdot},$$

$$CH_3COOO^{\cdot} + CH_3CHO \xrightarrow{k_3} CH_3COOOH + CH_3\dot{C}O,$$

$$CH_3CHO + CH_3COOOH \xrightarrow{k_4} 2\,CH_3COOH,$$

$$\left.\begin{array}{l} 2\,CH_3CO^{\cdot} \xrightarrow{k_5} (CH_3CO)_2 \\ CH_3CO^{\cdot} + CH_3COOO^{\cdot} \xrightarrow{k_6} \\ 2\,CH_3COOO^{\cdot} \xrightarrow{k_6} \end{array}\right\} \text{chain breaking,}$$

$$CH_3COO\dot{O} + C_3H_6 \xrightarrow{k_7} CH_3COO^{\cdot} + C_3H_6O,$$

$$CH_3COO^{\cdot} + CH_3CHO \xrightarrow{k_{2'}} CH_3COOH + CH_3\dot{C}O\ .$$

The rate of oxidation of CH_3CHO (RH) in the absence of propene is described by the formula:

$$w_0 = \frac{k_2[RH]\sqrt{w_i}}{\sqrt{k_6}}\left\{1 + \frac{k_5 k_2[RH]}{k_6 \cdot k_1[O_2]} + \frac{k_4}{k_6}\left(\frac{k_2[RH]}{k_1[O_2]}\right)^2\right\}^{-1/2}.$$

When the rate of oxidation is independent of $[O_2]$:

$$w_\infty = \frac{k_2[RH]\sqrt{w_i}}{\sqrt{k_6}}.$$

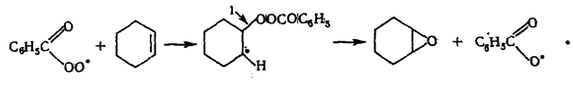
The validity of the above formulae is confirmed by the linear relation between $[(w_\infty/w_0)^2 - 1][O_2]$ and $[O_2]^{-1}$ obtained from experimental results[107].

From the above scheme, clearly a change in O_2 concentration will affect the composition of the radicals participating in recombination and also affect the composition of the reaction products. Actually when the O_2 concentration is reduced there is an increase in, for example, the quantity of biacetyl formed.

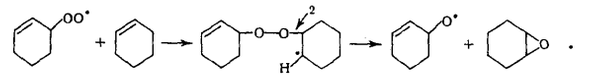
In an investigation of the common oxidation of propene and acetaldehyde in dimethyl phthalate solution (70–90°C, 55 atm air) the effective rate constants for the consumption of acetaldehyde and the effective activation energy (9.6 kcal mole^{-1}) were determined[109,110].

In some studies the combined oxidation of benzaldehyde and unsaturated compounds was investigated[111,112].

In studying the oxidation of cyclohexene and benzaldehyde with participation of cobalt acetate, which reacts rapidly with per-acids, it was noted that only ~ 3% of perbenzoic acid reacts with cyclohexene with the formation of epoxide; all the remaining epoxide is formed by the reaction of cyclohexene with peroxide radicals[111]:

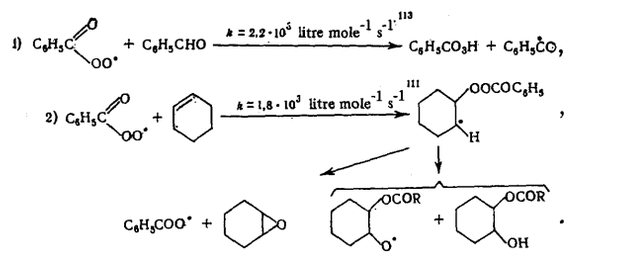


It is suggested[111] that cyclohexenylperoxy-radicals also participate in the epoxidation:



This reaction is quite possible, since the energy of bond 2 is greater than the energy of bond 1.

It is known[102,103] that alkenes retard the oxidation of aldehydes. This is easy to understand on considering that the rate constant for chain propagation in the oxidation of benzaldehyde at room temperature is close to the rate constant for the reaction of acylperoxy-radicals with a double bond:



Clearly, either stable products or radicals with little activity in chain propagation are obtained in the second reaction.

The kinetic results examined above obtained in the combined oxidation of propene with plus aldehydes[105–107] and of cyclohexene plus benzaldehyde[111] show that the principal reaction in epoxidation is the interaction of radicals with the double bond and the per-acids—oxidation products of the aldehydes—make a relatively small contribution to epoxidation. Only in isolated instances, for example, in the oxidation of α-methylstyrene and benzaldehyde does non-radical epoxidation of the double bond by reaction with a per-acid amount to more than 10–15%.[112]

6. CATALYSED OXIDATION OF ALKENES BY THE OXYGEN IN AN OXIDE

The use of catalysts in processes of liquid-phase oxidation of alkenes allows the temperature of the reaction to be significantly reduced and the selectivity of the processes to be increased. In the oxidation of propene suspensions in dibutyl phthalate of finely ground copper, silver, or their oxides are used as catalysts. The yield of propene oxide on these catalysts reaches 87%. It has also been proposed to use Co, Cu, Mn, V, or Cr promoted with Ba or Pb salts for these purposes[114,115]. Various catalysts based on Cu and Ag are used in the oxidation of butenes. A special copper catalyst containing alkali metal halides has been developed[116]. In addition, it is thought that in the oxidation of butenes to the epoxide it is not necessary to employ catalysts but it is quite sufficient to use initiators to shorten the induction period[117].

The catalysts used until now for the liquid-phase oxidation of alkenes to epoxide are usually heterogeneous and selected by analogy with the catalysts for the gas-phase oxidation of alkenes. The mechanism of action of the heterogeneous catalysts in the epoxidation will not be examined in the present review. We will concentrate attention on the use of homogeneous catalysts in the oxidation of alkenes to epoxides, since there have been many recent studies in this direction and in several instances

alkene oxides have been obtained in high yields under comparatively mild conditions. An investigation of the liquid-phase oxidation of propene with oxygen with participation of chelates of MoO_2^{2+}, WO_2^{2+}, Co^{2+}, Cr^{3+}, and Cu^{2+} (various azo-compounds obtained by diazotisation of substituted phenols and naphthols were used as chelating ligands) showed that the complexes of MoO_2^{2+} and WO_2^{2+} are the most selective in the oxidation of propene to its oxide, and allow the oxide to be obtained in up to 70% yield in the conversion of ~ 7% of the propene (temperature: 150°C; solvent: benzene; total pressure: 45 atm).[118,119] The remaining cations with the same ligands are less selective in this reaction and give a lower yield. A detailed investigation of the catalysis of the oxidation of propene with participation of chelates obtained from MoO_2^{2+}, $MoCl^{4+}$, and $OMo(OH)_2^{2+}$ and the study of the magnetic properties of these chelates suggested that the catalyst in this reaction takes up a molecule of oxygen and activates it[120-126].

In a study of the mechanism of activation of oxygen in the oxidation of propene to its oxide with participation of molybdenum chelates, the effect of a large number of chelating azo-compounds on the state of the central ion, on the magnetic properties of the chelate which adds to oxygen, and on the activity of the chelate in the epoxidation was investigated[120-126]. For each of the inorganic cations MoO_2^{2+}, $MoCl^{4+}$, and $OMo(OH)_2^{2+}$, chelates were obtained with compounds of the azonaphthoquinone type containing various substituents; for all the chelates their magnetic susceptibility was measured and their magnetic moments calculated[121]. For each of the three inorganic cations a linear relation was found between the magnetic moment and the Hammett σ constant for the ligand:

$$\mu - \mu_0 = R - S\sigma_{lig},$$

furthermore,

$$R = U + T\sigma_{cation},$$

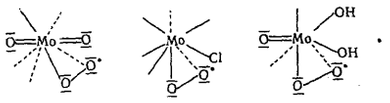
where σ_{cation} is the characteristic of the donor–acceptor capability of the cation with inorganic ligands. Hence:

$$\mu = \mu_0 + U + T\sigma_{cation} - S\sigma_{lig},$$
$$U = 1.83, \quad T = 1.15\ \mu_B.$$

The values of the other constants in these equations are:

Constants	MoO_2^{2+}	$MoCl^{4+}$	$OMo(OH)_2^{2+}$
σ_{cation}	1.00	0.23	−0.24
R, μ_B	3.00	1.47	2.20
S, μ_B	0.57	0.57	0.40

Hence the effect of the ligands and the state of the central atom were connected and characterised quantitatively. All three series of molybdenum chelates were used as catalysts for the epoxidation of propene and it was found that the selectivity of this reaction is linked with the state of the complex. For all three series of complexes the most selective were the chelates in which 0.7 of an unpaired electron is localised on the molybdenum. A departure from this optimal figure to one side or the other decreases the selectivity of the chelate in the epoxidation of propene. An investigation of the magnetic properties of the complexes and the parameters for the activation of oxygen by the complexes in relation to their selectivity in epoxidation suggested[122-126] that the epoxidating species are paramagnetic associates of the chelates with oxygen having the following structure:



In all three species the molybdenum is sexivalent.

In the homogeneous-catalytic reactions complexes of other metals which add an oxygen molecule in the coordination sphere were also employed: thus the complexes $IrX(CO)(PPh_3)_2$ and $RhX(CO)(PPh_3)_2$ (where X = Cl, Br, or I), first prepared by Vaska[127,128] were used in the oxidation of styrene[129,130], cyclohexene[131], and ethylbenzene[132]. Before turning to an examination of the mechanism of epoxidation of alkenes with participation of metal complexes which activate oxygen, we will consider the characteristic properties of these complexes. Complexes have recently been obtained that are capable of adding a molecule of oxygen and have as central atom iron, cobalt[133,134], iridium[127,128], rhodium[127,128], or ruthenium[135].

An oxygenated complex of a metal necessarily has a central atom which exhibits redox activity:

$$Co^{II} \rightarrow Co^{III};\quad Ir^{I} \rightarrow Ir^{III};\quad Fe^{II} \rightarrow Fe^{III},$$

and oxygen, which also exhibits redox activity as a ligand. Here the concept of valency loses significance and one can speak only of partial charges on the partners in the bond, when the total molecular orbital is predominantly localised at the metal or the ligand. The internuclear distance in the O–O group is a reliable measure of these partial charges. In the complex $[(Cl)Ir(CO)(PPh_3)_2]$ (I), which adds oxygen reversibly, both oxygen atoms are equivalent and at equal distances from the iridium. The distance between the oxygen atoms is 1.30 Å, which is greater than in molecular oxygen (1.21 Å) but significantly less than in O_2^{2-} (1.49 Å), and corresponds to the distance in $O_2^{\cdot-}$ (1.28 Å). Despite this it cannot be assumed that the oxygen in the iridium complex is the radical-anion $O_2^{\cdot-}$ since this complex is diamagnetic.

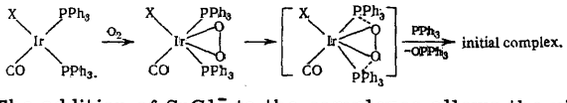
A characteristic feature of complex (I), extremely significant from the standpoint of the catalysis of the epoxidation of alkenes, is the capability of this complex to add ethylene reversibly[136]; an analogous complex is formed with tetrafluoroethylene[137]. A comparison of the bonding of oxygen with the bonding of the alkenes in these complexes is quite permissible, since the electronic structure of the oxygen molecule in the ligand field corresponds to the electronic structure of ethylene[138].

We will consider yet another property of the complexes which bond oxygen—the strength of the bonding of the oxygen with the central atom. If the Cl in complex (I) is replaced by iodine, the strength of the bonding of O_2 with the metal increases and the complex $[(O_2)Ir(CO)(I)(PPh_3)_2]$ (II) bonds oxygen irreversibly. An X-ray diffraction analysis of complex (II) gave an interesting result: the change from reversible (I) to irreversible (II) oxygen-containing complex is associated with an increase in the length of the O–O bond from 1.30 Å to 1.47 Å, but the equidistance of the oxygen atoms is retained. This distance corresponds to the anion O_2^{2-} (1.49 Å), hence the transfer of electrons from the metal to the O_2 ligand increases when chlorine is replaced by iodine[139]. Replacement of chlorine by phosphine also leads to the stabilisation of the compound of oxygen with $Ir[(PPh_2-[CH_2]_2-PPh_2)_2]^+$.[128,140] The addition of O_2 to the phosphine complexes of nickel, palladium, and platinum is irreversible[141]. In these complexes an intramolecular

redox reaction rapidly takes place, leading to the oxidation of the phosphine. In peroxo-complexes, such as the derivatives of Cr^{V}, Cr^{VI}, CrO_5, or $[CrO_8]^{3-}$, there should be preferential transfer of charge from O_2^{2-} to the central atom (a strong acceptor) and as a consequence of this the O–O bond length is 1.40 Å.[142]

Hence there is a continuous increase in the bond strength and the O–O internuclear distance in the series: labile compounds of oxygen → compounds with reversible addition of oxygen → peroxo-complexes.

Vaska complexes have been used as catalysts for the epoxidation of styrene with oxygen[129–130]:



The addition of $SnCl_3^-$ to the complexes allows the yield of epoxide to be increased 477% relative to the catalyst used. Iridium and palladium chlorides ($IrCl_3$ and $PdCl_2$) are also used as catalysts of the epoxidation of styrene. At 110°C they give 51 and 184% styrene oxide respectively[129]. The use of $RhCl_3$ as catalyst enables 1232% styrene oxide to be obtained after reaction for 8 h at 110°C.[130] It is noteworthy that Takao and coworkers[129,130] did not suggest any reaction mechanism for the epoxidation and oxidation of styrene. A great drawback of these Japanese studies is that the reaction was investigated in the most inappropriate solvent (toluene). Under the conditions employed (110°C, 1 atm oxygen, presence of the catalysts $IrCl_3$, $PdCl_2$, etc., there must be oxidation of the toluene with formation of benzaldehyde and other reaction products. Actually, the main product of the oxidation of styrene in toluene is almost always benzaldehyde[129]. The benzaldehyde which is formed, on being oxidised in combination with styrene can give styrene oxide, as was shown by the example of the oxidation of α-methylstyrene plus benzaldehyde[112]. Undoubtedly, toluene should be oxidised under the experimental conditions of the Japanese investigators, as was confirmed by the success in using Vaska complexes for the oxidation of ethylbenzene at 130°C and *p*-xylene at 120°C with the formation of acetophenone (90%) and *p*-tolylaldehyde respectively[132]. The unfortunate choice of solvent hinders the interpretation of the results of the Japanese investigators: possibly the catalytic epoxidation of styrene actually takes place but undoubtedly benzaldehyde—the oxidation product of toluene when any catalyst is used—plays an important part in the epoxidation.

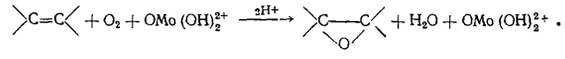
Only kinetic investigations of the epoxidation of alkenes with participation of Vaska complexes in an inert solvent will make it possible to judge their true catalytic activity in this reaction and its mechanism. An investigation of the catalytic influence of Vaska complexes on the oxidation of cyclohexene in benzene and CH_2Cl_2 at 25–60°C showed that the main oxidation product is cyclohexen-3-one[131]. Hence the catalytic activity of Vaska complexes—transporters of the oxygen atom—is certain[131,132] but it is difficult to judge to what extent these complexes are selective in epoxidations on the basis of the results that have been published.

We will now return to the problems of the activation of oxygen in the epoxidation of propene with participation of molybdenum chelates. As already noted, the epoxidating species is a paramagnetic associate of the chelate with an oxygen molecule[122]. In this associate the molybdenum is in the highest oxidation state. After the act of epoxidation has occurred or during the course of this act the molybdenum should be reduced to the quinquevalent state.

Various investigations[118–126] did not show any specific reduction paths for the molybdenum, that is, the regeneration of the catalyst during the course of the reaction. We can presume that in the reduction of molybdenum reaction products participate, for instance acetaldehyde formed in parallel with propene oxide by the non-catalysed oxidation of the latter:

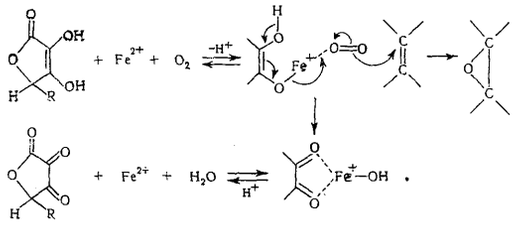
$$CH_3CHO + Mo^{VI} \rightarrow CH_3\dot{C}O + Mo^{V} + H^+ .$$

We represent the epoxidation itself as follows:



Such a type of transfer of an oxygen atom from an O_2 molecule to a substrate is known to be effected by oxidases with mixed functions[143,144], which epoxidise alkenes, oxidise aliphatic compounds to alcohols, and hydroxylate aromatic compounds to phenols.

Several systems which can be regarded as models of oxidases with mixed functions have been studied recently[53,145]. The study of such models helps to answer the problem of how many electrons are transported on the O_2 molecule and how this transport is linked with the epoxidation of the substrate. A scheme of epoxidation of an alkene with participation of one of the oxidase models with mixed functions—the Fe^{2+} + O_2 + ascorbic acid system—is given below[53]:



As this scheme shows, the epoxidising agent is a complex, the function of the ferrous ion in which is to unite with the reducing agent and oxygen and to convey to the latter electrons to form the transition state. The iron ion allows a singlet oxygen atom to be transferred from the combined O_2 molecule to the substrate in such a manner that the intermediate biradical compound is unnecessary. If a triplet oxygen atom were transferred the process would be less favourable energetically owing to the formation of a triplet reaction product, which is less stable than the singlet. The transfer of a proton of ascorbic acid into the complex with O_2 is evidently simultaneous with the transfer of electrons through the ferrous ion leading to the reduction and stabilisation of the oxygen atom which is not passed on to the substrate. The other oxygen atom, which has 6 electrons (hence the analogy with carbenes and nitrenes, which also have 6 electrons around the carbon or nitrogen and are extremely reactive) is introduced into the substrate. In this way four-electron exchange is effected with minimal motion of the nuclei.

If it is assumed that the reduction of the molybdenum is brought about by the ligand (which is not excluded) then the scheme for the epoxidation of propene with participation of molybdenum chelates does not differ from that discussed above. If the reduction of molybdenum is effected in interactions with the oxidation products of propene—acetaldehyde, etc.—then we have a new example of models of oxidases with mixed functions, distinguished by the fact that the reducing agent does not enter the coordination sphere of the complex, but reacts with the oxidised complex after the act of epoxidation has been completed. Unfortunately,

the most interesting studies of epoxidation with participation of molybdenum chelates[118-126] do not provide results on the regeneration of the catalyst, and we cannot now choose between these two possibilities. It is very significant that it could be shown which of the forms of active oxygen:

$$[Mo^{5+} \ldots O_2] \leftrightarrow [Mo^{6+} \ldots \dot{O}_2^-] \leftrightarrow Mo^{6+} + \dot{O}_2^-$$
(I) (II) (III)

is the main one in the epoxidation of propene.

It is form (II). However, this does not signify that in all other instances this form of the reacting species will be predominant. As Hamilton thinks[53], the nature of the attack of the substrate in different model systems can vary from radical to electrophilic and even nucleophilic. It all depends upon which state of the attacking species predominates. And this state is in turn determined by the type of metal and especially the ligands which are around it. In general there can be several forms of attacking species and the determination of the valence state of the metal or oxygen in it has no significance in itself. It is necessary to know which of the resonance forms is the most important because this will determine the nature of the attack of the substrate. The difficulty in determining the nature of the bonding in oxygen complexes was descriptively characterised by Alfred Werner, founder of the chemistry of complexes, 70 years ago, but his words are still true today: "The labile bonding of oxygen .... is so peculiar, that it is very difficult to give a satisfactory answer to the question of whether there is a valence bond or simply addition of the oxygen as a molecule, if this question has meaning at all".[146]

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Not all the epoxidations that we have considered can at present be characterised by rate constants of the limiting stages. However, for several epoxidising agents the energetic characteristics of the limiting reactions have been determined—the enthalpies of activation or the energies of activation. Table 7 gives the values of these energetic characteristics.

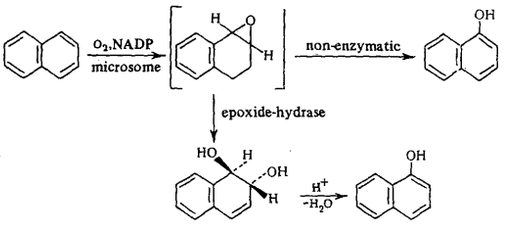
Table 7. Energetic characteristics of limiting reactions in the epoxidation of alkenes.

Epoxidising agent	Alkene	$\Delta H^{\times}$ or E_{act}, kcal mole^{-1}	Reference
Perbenzoic acid and its substituted derivatives	*trans*-stilbene and its substituted derivatives	$\Delta H^{\times}=14.0+16.0$	24
Perbenzoic acid	cyclohexene	$\Delta H^{\times}=12.7$	24
Peracetic acid	propene	$E=11.6$	29
HWO_5^-	allyl alcohol	$E=14.6$	70
TBHP + Mo-cat.	propene	$E=15.0$	60
CHP + Mo-cat.	propene	$E=15.6$	60
EBHP + Mo-cat.	propene	$E=15.2$	60
EBHP +Mo-cat.	propene	$E=10.5$	64
TBHP + $VO(acac)_2$	cyclohexene	$\Delta H^{\times}=12.7$	56
$[Mo(O_2)_2O]L_1L_2$	cyclohexene	$E=15.9$	65

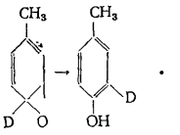
From Table 7, the activation energies or activation enthalpies for various epoxidising species are rather similar. This fact is not unexpected, since in almost all the reactions considered the epoxidating agent is an electrophilic species which attacks the π-bond of the alkene.

The nature of the alkene naturally affects the activation energy of the epoxidation: thus $\Delta H^{\times}$ in epoxidation with perbenzoic acid varies from 12.7 kcal mole^{-1} for cyclohexene to 17.2 kcal mole^{-1} for tetraphenylethylene (see Table 1). The epoxidation of a single alkene, for example, cyclohexene or propene by different agents leads to a change in the energetics within the limits of 2–4 kcal mole^{-1} (see Table 7), from which it seems that epoxidating agents are close to one another in their electrophilic properties. Unfortunately, there are no results on the energetics of the reactions in the epoxidation of alkenes by acylperoxy-radicals and molybdenum complexes which activate oxygen. In these two instances the epoxidating agents evidently exhibit a smaller electrophilic capacity than per-acids or complexes of hydroperoxides with ions of metals of variable valency.

A study of the mechanisms of epoxidation of alkenes helps a deeper understanding of the processes in the hydroxylation of aromatic compounds, since in several instances it has been reliably shown that arene oxides are intermediate products in the formation of phenols[53,147,148]. In the oxonation of benzene, for example, benzene epoxide is isolated but rapidly isomerises at room temperature into phenol[53]. Microsomal oxidation of aromatic compounds showed that arene oxides can play a part in the metabolism of aromatic substrates[147,148]:



3,4-Epoxy[4-^{2}H]toluene has been synthesised[148] and is converted into 4-hydroxy[3-^{2}H]toluene, with displacement of the deuterium:



Without the intermediate formation of the epoxide this fact cannot be explained. The unity of the mechanisms of epoxidation of alkenes and hydroxylation of aromatic compounds is confirmed by the fact that most of the epoxidating agents are simultaneously hydroxylating agents for aromatic substrates. Per-acids effectively epoxidate alkenes and hydroxylate aromatic compounds to phenols[41-50], oxidases with mixed functions and their models are also active in these two reactions[53,145]. It is quite possible that acylperoxy-radicals are not only epoxidating agents but can also hydroxylate aromatic compounds[51,52].

The practical significance of epoxidation is particularly great: new technological processes have now been developed on the basis of epoxidations with hydroperoxides with participation of catalysts[149,150]. An investigation of catalysts which activate oxygen and the study of their mechanism of action will undoubtedly open new prospects of direct epoxidation of alkenes with molecular oxygen under mild conditions. This direction of investigation of epoxidation seems to us to be the most important now.

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Methods of Chemical Synthesis of Aminoacid and Peptide Esters of Nucleosides, Nucleotides, and Oligonucleotides†

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The review gives a systematic account of the literature data for and the methods of synthesis of aminoacid esters of nucleosides, nucleotides, and oligonucleotides. The principle of the selection of protecting groups, the methods of activation of aminoacids, and the reaction conditions necessary for the synthesis of specific compounds are discussed.
A separate section is devoted to the discussion of methods for the preparation of peptide derivatives, in particular peptidyl-tRNA on the basis of natural aminoacyl-tRNA derivatives.
The bibliography includes 93 references.

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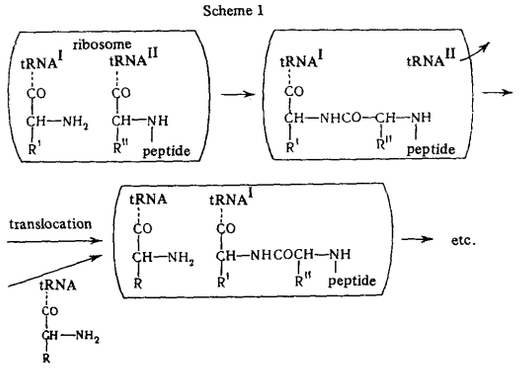
I. INTRODUCTION

Aminoacyl-tRNA and peptidyl-tRNA are always involved in the synthesis of each peptide bond during the matrix biosynthesis of protein on ribosomes. The peptide bond is formed as a result of electrophilic attack by the C-end of the peptide residue of peptidyl-tRNA on the amino-group of aminoacyl-tRNA (Scheme 1). At the present time this process can be achieved *in vitro* both in the form of a continuous cycle in which ribosomes act upon an endogenic or synthetic RNA-matrix, with formation of a polypeptide chain containing at least several peptide bonds [1,2], or stepwise with control of each succeeding stage in ribosomal activity [3].

Apart from the natural participants in the biosynthesis of a polypeptide on a ribosome (aminoacyl-tRNA and peptidyl-tRNA), aminoacid esters of nucleosides [4], nucleotides [5], and oligonucleotides [6] (as acceptors of the peptide, i.e. as analogues of aminoacyl-tRNA) and peptidyl-(or acylaminoacyl)oligonucleotides [7] (as donors of the peptides, i.e. analogues of peptidyl-tRNA) are employed successfully in single model steps involved in the formation of the peptide bond.

Scheme 1



The use of such compounds helped demonstrate the location of the peptidyl transferase centre of the bacterial ribosome on the 50 S-subunit [7] and also yielded some information about the substrate specificity of this centre [5-7,8].

Bearing in mind that the ribosomal synthesis of peptides and individual proteins in *in vitro* systems is widely used to investigate the functioning of the ribosome, it is of interest to develop methods for the chemical synthesis of aminoacyl- and peptidyl-tRNA.

Such methods would enable investigators to acquire all kinds of "Hybrid" variants in which the aminoacid of peptide [9] would be joined to tRNA which is non-specific in relation to them.

Despite the considerable advances achieved in the chemistry of natural products in the synthesis of amino-acid nucleotide derivatives and related compounds, the search for new methods of synthesis remains an urgent task. Derivatives of this kind will find application in the study of ribosomes and possibly of many enzymes involved in nucleotide synthesis. We believe that development of new methods of synthesis is a [necessary] stage on the path to non-enzymatic synthesis of aminoacyl-tRNA.

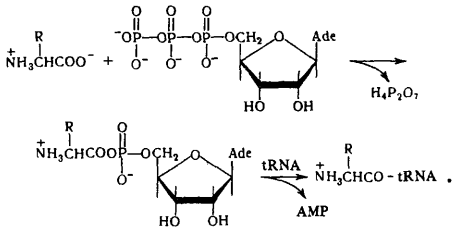
†List of abbreviations employed: tRNA = transfer ribonucleic acid, ATP = adenosine 5′-triphosphate, AMP or pA = adenosine 5′-monophosphate, pG = guanosine 5′-monophosphate, pC = cytidine 5′-monophosphate, pU = uridine 5′-monophosphate, pI = inosine 5′-monophosphate, A = adenosine, G = guanosine, C = cytidine, U = uridine, Ade = adenine, Gua = guanine, Cyt = cytosine; Ura = uracil, DMF = dimethylformamide, DMSO = dimethyl sulphoxide, THF = tetrahydrofuran, DCC = *NN′*-dicyclohexylcarbodi-imide, Z = benzyloxycarbonyl, BOC = t-butyloxycarbonyl, NPS = *o*-nitrophenylsulphenyl, Trit = trityl (triphenylmethyl), Mtrit = monomethoxytrityl, Ac = acetyl, F = formyl, and Im = imidazolyl. Residues of activating esters: OSu = hydroxysuccinimide, ONp = *p*-nitrophenyl.

The aminoacids and nucleic acid components have been named in accordance with the nomenclature adopted by IUPAC.

II. SYNTHESIS OF 3′(2′)-*O*-AMINOACYLNUCLEOSIDES

In protein-synthesising systems, aminoacyl-tRNA is formed from the aminoacid, tRNA, and ATP (Scheme 2) on special enzymes: aminoacyl-tRNA synthetases[2]. In the first stage of this enzymatic reaction, ATP is hydrolysed to AMP and inorganic pyrophosphate with coupled formation of aminoacyladenylate in which the aminoacid residue exhibits electrophilic properties. Next, this aminoacid residue is transferred to the 3′-hydroxyl of tRNA, which results in the synthesis of aminoacyl-tRNA with an ester linkage between the aminoacid residue and tRNA. The chemical nature of this linkage was established[10] in 1960 and it was shown to be a high-energy bond.

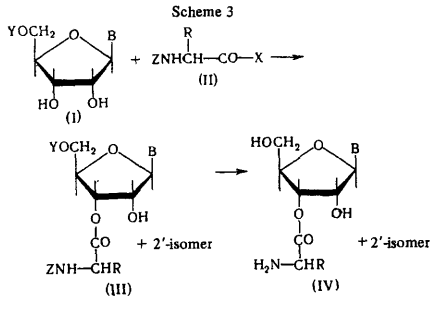
Scheme 2



In the development of approaches to the synthesis of aminoacylnucleosides and their more complex analogues, investigators have employed the principle of the biological process. In all cases the aminoacid residue was activated initially and then allowed to interact with the nucleoside component. Various methods of activation available in the chemistry of peptide synthesis were employed for this purpose. In terms of types of compounds and intermediate activated aminoacids, they can be classified as based on anhydrides, amides, and esters. The reactivities of the aminoacids or peptides activated in this way are different and moreover depend on reaction conditions to different extents. One must also bear in mind the possibility of the acylation of the amino-groups of the bases.

Numerous studies have been made on the synthesis of 3′(2′)-*O*-aminoacylnucleosides(IV).[11-18] The principle of the synthesis, which is common to all these investigations, consists in the reaction of 5′-*O*-protected nucleosides (I) and aminoacids (II) protected at the amino-groups and activated at the carboxyl (Scheme 3).

Scheme 3



where Y = triphenylmethyl or monomethoxytriphenylmethyl and Z = benzyloxycarbonyl, t-butyloxycarbonyl, or *O*-nitrophenylsulphenyl.

Since 5′-*O*-trityl or 5′-*O*-monomethoxytrityl-nucleosides(I) are insoluble in water, all the syntheses were performed in organic solvents such as pyridine, DMF, dioxan, and THF. It was shown that selective synthesis of aminoacid esters of nucleosides under these conditions without side reactions involving *N*-acylation of the bases is possible for adenosine, uridine, and guanosine. In the case of cytidine, the first step is the aminoacylation of the amino-group of the heterocyclic base, which necessitates a preliminary protection of this group.

Among the known methods for the activation of carboxy-groups of aminoacids for the synthesis of 3′(2′)-*O*-aminoacylnucleosides (IV), condensation with the aid of DCC,[4-7] symmetrical anhydrides of *N*-protected amino-acids[11,12], and imidazolides of *N*-protected[17] and *N*-protonated amino-acids[18] have been successfully employed. In the most fundamental study on the preparation of esters of all four main nucleosides (adenosine, guanosine, cytidine, and uridine) the synthesis was carried out by the method of symmetrical anhydrides[12]. As a result of all the stages in the synthesis, the yields of the phenylalanine esters of these nucleosides were respectively 36, 5.3, 19.3, and 33.6%.

3′-*O*-Aminoacid esters of 2′-deoxynucleosides (deoxyadenosine[12] and deoxythymidine[15]) were synthesised by a procedure similar to that used for the aminoacid esters of nucleosides, involving condensation with the aid of DCC or symmetrical anhydrides. The yields of these esters were close to those of ribonucleoside esters.

Among the *N*-protecting groups for aminoacids employed in the syntheses of 3′(2′)-aminoacylnucleosides, the benzyloxycarbonyl (Z),[11-16] t-butyloxycarbonyl (BOC),[4,19] and *o*-nitrophenylsulphenyl (NPS)[17,19] protecting groups have been used. It is not always a simple matter to make rigorous recommendations concerning the choice of a particular group when a new synthesis is planned. Each laboratory where aminoacylnucleosides were synthesised used a new set of protecting groups. However, we believe that the Z-protecting group, which can be eliminated by catalytic reduction without loss of purines, is most suitable for the preparative synthesis of aminoacyladenosine and aminoacylguanosine. Moreover, the comparatively low solubility of 5′-*O*-trityladenosine in the majority of the usual solvents, apart from pyridine and DMF, hinders the employment of the NCS group. For the aminoacid esters of uridine and cytosine, a wide-scale employment of BOC and NPS protecting groups is possible, their elimination being achieved by mild acid treatment—either with anhydrous trifluoroacetic acid or with ethereal hydrogen chloride—and does not lead to the cleavage of the ester linkage[19]. In one of the proposed methods of synthesis of 3′(2′)-*O*-aminoacyladenosines, the imidazolides of *N*-protonated aminoacids were employed[18]. This method does not require a preliminary introduction and subsequent elimination of a protecting group and is therefore suitable for microsyntheses, for example of radioactive esters. However, owing to the difficulty of dissolving the imidazolides of aminoacid trifluoroacetates, this procedure is fairly inconvenient for preparative syntheses.

Having described various methods for the synthesis of *O*-aminoacyl derivatives of nucleosides, a further important question must be discussed, namely their structures.

When nucleosides and nucleotides are aminoacylated, one may expect the formation of a mixture of the 2′- and 3′-isomers. The questions of the preferential aminoacylation of one of the hydroxy-groups of ribose and the migration of the aminoacyl residue between the 2′- and 3′-hydroxyls are not only of independent chemical interest but are also closely related to the determination of

the true position of the aminoacyl residue in aminoacyl-tRNA. It is important to know this in order to understand the mechanism of the formation of aminoacyl-tRNA on aminoacyl-tRNA synthetases [11] and the mechanism of the synthesis of the peptide bond on ribosomes [20].

In order to establish the location of the aminoacyl residue, a number of studies have been made both on synthetic aminoacyl derivatives of nucleosides and nucleotides [4,11,12,21-28] and on aminoacyladenosine isolated from aminoacyl-tRNA. [29,30] The conclusions arrived at proved to be extremely contradictory but considered together they demonstrate that, even if the synthetic methods for the preparation of *O*-aminoacyl-nucleosides and -nucleotides lead to a mixture of isomers, the 3′-isomer greatly predominates as the final product, although in some cases the aminoacylation reaction yielded both the pure 3′-isomer (Z-phenylalanyladenosine) [12] and the almost pure 2′-isomer (*O*-BOC-L-leucyladenosine) [4].

Apart from positive data on the aminoacylation of nucleosides under specified conditions (organic solvents, room temperature, several hours), negative results are also important. For example, it has been shown that the *p*-nitrophenyl, *N*-hydroxysuccinimide and 5-chloro-8-hydroxyquinolinyl esters of *N*-protected aminoacids do not react with the nucleoside hydroxyls, while *p*-nitrophenyl and *N*-hydroxysuccinimide esters react slowly with the amino-group of cytosine [31,32].

Concluding the discussion of the methods of aminoacylation of nucleosides, the following two conclusions may be reached:

1. For reaction with the hydroxyls of the riboside residue, the activation of the *N*-protected aminoacid must be fairly powerful; the imidazolides and anhydrides of aminoacids are capable of reacting with the hydroxyls (the synthesis using DCC probably also involves intermediate anhydrides).

2. Apart from the ribose hydroxyls, in anhydrous solvents only the NH_2 group of the cytosine residue reacts with the anhydrides, amides, (imidazolides), and esters of *N*-protected aminoacids. (Here and henceforth only the four main heterocyclic bases—adenine, guanine, uracil, and cytosine—are considered as part of the composition of nucleosides or nucleotides).

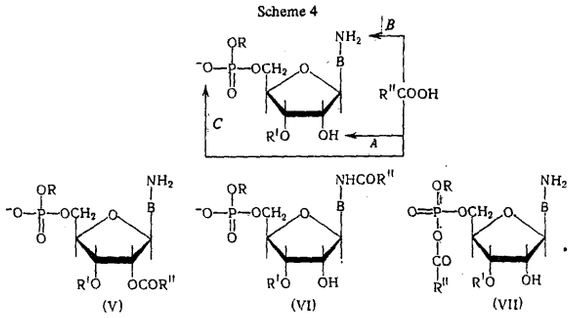
Like the synthesis of 3′(2′)-*O*-aminoacylnucleosides, the method using DCC makes it possible to introduce *N*-protected peptides into 5′-*O*-tritylnucleosides with formation of 3′(2′)-*O*-peptidylnucleosides [15]. Unfortunately, in this case, owing to the intrinsic features of the chosen scheme, appreciable racemisation of the *C*-terminal aminoacid of the peptide is bound to occur, and its extent remains unknown.

III. SYNTHESIS OF 3′(2′)-*O*-AMINOACID ESTERS, NUCLEOTIDES, NUCLEOSIDE 5′-DIPHOSPHATES AND 5′-TRIPHOSPHATES, AND OLIGONUCLEOTIDES

The difficulty of selective aminoacylation of ribose hydroxyls greatly increases on passing from nucleosides to nucleotides. Here the hydroxyls of the phosphate residue are added to the existing groups with nucleophilic properties—the ribose hydroxyls and the amino-groups as the bases. As a result, there is a possibility of the formation of three types of compounds on aminoacylation—esters (V), amides (VI), and mixed anhydrides (VII) (Scheme 4).

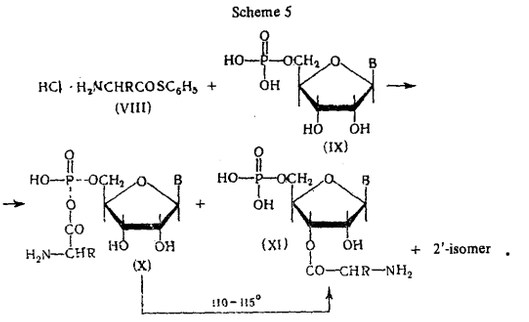
Indeed, the first attempts to extend the method of symmetrical or mixed anhydrides in anhydrous solvents or to carry out a condensation with the aid of DCC under the same conditions led exclusively to mixed anhydrides of type (VII). This showed that it is necessary to find conditions suitable for the aminoacylation of nucleotides in which the reactivity of the phosphate group is negligible.

Scheme 4



In 1958–1960 the first method was developed for the aminoacylation of nucleotides, consisting of the reaction of the thiophenol esters of aminoacid hydrochlorides (or hydrobromides) (VIII) with the nucleotides (IX) at 110 to 115°C in DMSO (Scheme 5). [33,34]

Scheme 5



The authors of the method showed that, when the reaction is carried out at 40°C, a mixture of the anhydride (X) and the ester (XI) is formed; when the temperature is raised to 110–115°C, the anhydride (X) rearranges to the ester (XI).

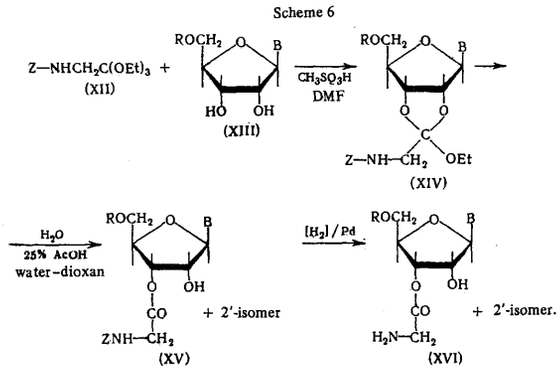
Aminoacid derivatives of (XI) were obtained by the thiophenol ester method in yields of 12–18% for pA esters, 9–10% for pU and pG esters, and 2–3% for 3′(2′)-*O*-aminoacyl-pC. In terms of aminoacids, the synthesis has been extended to valine, leucine, alanine, and methionine. It has been claimed that 3′(2′)-*O*-leucyladenosine 5′-triphosphate has also been obtained by this procedure [35], but the yield of this ester did not exceed 2% and convincing evidence for the structure of the compound obtained was not adduced.

The syntheses of 3′(2′)-*O*-aminoacylnucleotides by the thiophenol ester method, which are the first examples of the synthesis of such compounds, were in addition very important as models for the determination of the type of linkage between the aminoacids and tRNA. [10] It was found that the properties of the ester linkage between the aminoacid and the nucleotide in these compounds are very similar to the properties of the bond between the aminoacid and tRNA, which proves that the latter is also an ester linkage.

However, for preparative purposes the thiophenol ester method suffers from one major disadvantage in addition to low yields. Under the condensation conditions, the nucleotide is appreciably broken down, as a result of which at the end of the reaction the reaction medium contains a mixture of compounds from which the required substance is difficult to isolate. For example, when one of the syntheses by the thiophenol ester method was repeated in our laboratory, at least eight side products in appreciable amounts and several minor admixtures were obtained in addition to the 3′(2′)-*O*-aminoacyl nucleotides, but its yield was the same as that quoted in the literature.

From 1965, a series of studies were published in which a general method was proposed for the synthesis of glycine esters of nucleosides[22], nucleotides[36], and dinucleoside phosphates[37,38]. It is based on a selective reaction of the Z-glycine orthoester (XII) with the *cis*-hydroxy-groups of the nucleoside, nucleotide, or oligonucleotide (XIII). The resulting cyclic orthoester (XIV) hydrolyses to the corresponding Z-glycylnucleoside or its derivative (XV), from which the Z-protecting group is then removed, yielding 3′(2′)-*O*-glycylnucleoside (XVI) or its derivative (Scheme 6).

Scheme 6



(R = H, PO_3H_2, $P_3H_4O_9$, or nucleoside 3′-phosphate)

In the method described the transesterification involves exclusively the *cis*-glycol group: single hydroxyls do not react with the orthoester (XII). The yields of products are fairly high at all stages (60–80%). However, the method has two significant limitations. Firstly, hitherto it has been applicable exclusively to the synthesis of nucleoside or nucleotide esters of glycine, since the orthoesters of other L-α-aminoacids have not been described. Secondly, the conditions governing the interaction of the orthoester (XII) with the nucleoside (or the nucleotide) (XIII) and also the subsequent hydrolysis of the orthoester (XIV) are fairly severe (transesterification in DMF for 1–3 days in the presence of large amounts of methanesulphonic acid, hydrolysis in 25% acetic acid in aqueous dioxan over a period of several hours). Probably these disadvantages precluded the employment of the method for the synthesis of glycyl-tRNA.

Here mention should be made of yet another application of this method, in which the orthoester of benzyloxycarbonylglycine and $N_{(6)}$-dimethylaminomethyleneadenosine 5′-phosphate was used for condensation with $N_{(4)}$-dimethylaminomethylene-5′-*O*-tritylcytidine with the aid of DCC, which resulted in the formation of the corresponding orthoester of the nucleoside diphosphate; after hydrolysis and hydrogenolysis, it yielded CpA-Gly.[39] CpI-Gly was obtained by a similar procedure. This synthesis shows that the orthoester of the aminoacid can be used successfully to protect the *cis*-glycol group in the synthesis of oligonucleotides and thus gives rise to the possibility, in principle, of synthesising the glycine esters of oligonucleotides.

The first report of a series of studies in which a general method was proposed for the synthesis of aminoacid esters of pA, pU, pG, and pC using aminoacid imidazolides, was published in 1967. In the development of this method, the authors began with the following two conditions. Firstly, either water or a water–organic solvent mixture with water predominating was chosen as the condensation medium. The use of water made it possible to reduce sharply the nucleophilicity of the phosphate hydroxyls owing to their dissociation: $pK_a^I = 0.7–1$ and $pK_a^{II} = 5.9$ to 6.0 for pA, pU, pG, and pC. Moreover, it was found that, under these conditions, the reactivity of the amino-group of cytidylic acid, which does not react at all with activated aminoacids, is significantly reduced.

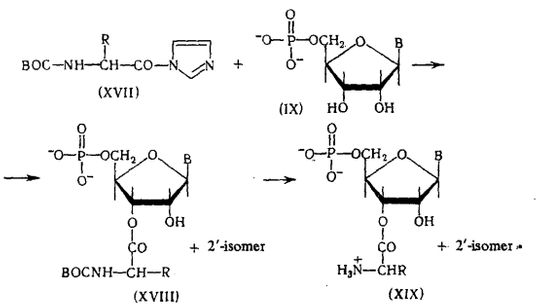
These characteristics of the behaviour of phosphates and amino-groups were known earlier. For example, whereas in acetylation with acetic anhydride in anhydrous solvents the *N*-acetyl derivative of cytidylic acid is always synthesised and the mixed anhydride of the nucleotide and acetic acid is formed[40,41], in an aqueous medium nucleotides or oligonucleotides are acetylated by acetic anhydride[42,43] exclusively at the ribose hydroxyls.

However, the hydroxyls of the riboside residues in nucleotides are also less nucleophilic in an aqueous medium than in anhydrous organic solvents. For example, in organic solvents the symmetrical anhydrides of *N*-protected aminoacids react vigorously with the hydroxyls of the riboside residues of nucleosides[11,12], while in an aqueous medium the same anhydrides altogether fail to react with nucleotides[19,44]. Furthermore, DCC has been widely used as the condensing agent for the synthesis of the ester linkages between *N*-protected aminoacids and nucleosides[45], while a water-soluble carbodi-imide {*N*′-cyclohexyl-*N*″-[β-(*N*-methylmorphilinium)ethyl]-carbodi-imide} is incapable of forming an ester linkage with the similar hydroxyls of tRNA.[46] Therefore successful condensation in water requires the choice of a powerful activating agent, which would make possible reaction with weak nucleophilic groups.

Imidazole was chosen as such activating agent. The imidazolides of *N*-protected aminoacids were used earlier to form the amide linkage in the synthesis of peptides[47,48] and also the ester linkage in depsipeptides[48]. The imidazolides of *N*-protected aminoacids were obtained by the reaction of *N*-protected aminoacids with *NN*′-carbonyldiimidazole by a standard method[47,48]. The condensation of BOC-alanylimidazolide with all the principal components of ribonucleic acids in a 5:1 water–DMF mixture at 20°C over a period of 3.5 h yielded 3′(2′)-*O*-BOC-alanylnucleotides in acceptable yields, ranging from 25 to 60% with respect to the initial nucleotide[19,49] (Scheme 7). In all cases the amides or anhydrides of type (VI) and (VII) (see p. 824) were completely absent from the reaction products. Virtually the only products were 3′(2′)-*O*-BOC-alanylnucleotides (XVIII, R = CH_3). Apart from them, the initial nucleotides (IX) and aminoacids were isolated from the reaction mixture. The yields of the esters with respect to the nucleotide which had reacted were 80–98%.

The BOC protecting group in (XVIII) was then removed by treatment with anhydrous trifluoroacetic acid (15 min at 0°C), which gave high yields of 3′(2′)-*O*-alanylnucleosides (XIX, R = CH_3). In the case of 3′(2′)-*O*-alanyladenosine 5′-phosphate, partial loss of the purine (sometimes to the extent of 15%) was observed.

Scheme 7

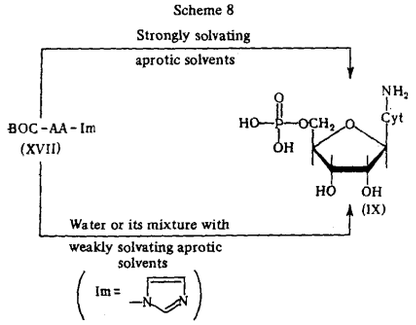


However, it was found that in this version the method is satisfactory only for alanine and glycine. The imidazolides of other BOC-aminoacids cannot be dissolved to a sufficient extent in a medium with 80% of water. Other readily removed *N*-protecting groups (for example Z, Trit, Mtrit, and NPS) only reduce further the solubility of aminoacid imidazolides. Therefore subsequently a large number of various solvents in 1 : 1 mixtures with water were investigated and it was found that the *O*-acylation of all nucleosides can be achieved in 1 : 1 mixtures of water with weakly solvating solvents such as acetonitrile, THF, and acetone. If the amount of strongly solvating aprotic solvent (DMF, DMSO, formamide, and pyridine) reached 30% of the total volume of the reaction medium, the reaction also involved the amino-group of pC (Scheme 8). [50] Thus esters involving the 3′(2′)-hydroxy groups of nucleotides with phenylalanine, lysine, aspartic acid, valine, proline, asparagine, etc. were obtained in such mixtures (the water–acetonitrile mixture was best) [19, 50, 51, 52].

One should note that 3′(2′)-*O*-aminoacylnucleotides of adenylic and uridylic acids are formed in high yields in anhydrous solvents, for example in a 5 : 1 DMSO–DMF mixture. However, this involves also the formation of a certain amount of impurities by side reactions, including 2′,3′-di-*O*-aminoacylnucleotides [19].

The imidazolide method also makes it possible to introduce into nucleotides fragments larger than aminoacids. The applicability of the method to all four nucleotides has been demonstrated for two peptides—BOC-Leu-Gly-Trp-OH and BOC-Ala-Ala-OH. [53] The BOC-protecting groups were removed by treatment with trifluoroacetic acid.

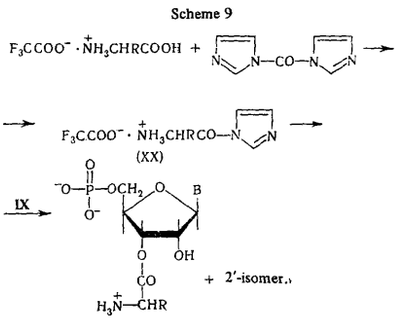
Scheme 8



It is noteworthy that the racemisation of the *C*-terminal aminoacid is not ruled out in this procedure.

The next version of the imidazolide method [19, 54, 55] involved the use of the imidazolides of *N*-protonated aminoacids (XX) in which the amino-group was protected by protonation. Aminoacid trifluoroacetates (or hydrochlorides) were converted into aminoacid trifluoroacetate imidazolides, which were then condensed with nucleotides in an aqueous medium at pH 7. Here the synthesis of 3′(2′)-*O*-aminoacylnucleotides (XIX) takes place virtually in only one stage (Scheme 9).

Scheme 9



It was found that the nucleotide (IX) reacts in different ways with the imidazolides of the *N*-protonated aminoacids (XX). Under the same conditions (for example with the same molar ratio of the reactants, dilution, time, and temperature), the imidazolides of valine and alanine trifluoroacetates reacted best with pA (yields 15–20%), less satisfactorily with pU and pG (yield 4–5%), and altogether failed to react with pC. In the last case all the pC was recovered unchanged from the reaction. (It is noteworthy that in the reaction with pA, pU, and pG the substances isolated contained, apart from the reaction products, mainly the initial nucleotides and only small amounts of side products.)

If the differences between the reactivities of nucleotides are represented by an inequality, the following formulation is possible:

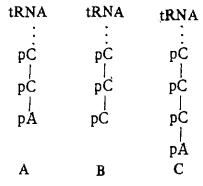
$$pA \gg pU = pG \qquad pC = 0.$$

A similar sequence was observed in the synthesis with thiophenol esters, where *N*-protonated aminoacids were also employed [33, 34]:

$$pA > pU = pG > pC.$$

These data are of interest from the standpoint of the aminoacylation of tRNA *in vivo*. Regardless of the type of tRNA or its origin [2], the end of tRNA carrying the aminoacid (the acceptor end) is known to contain always the same polynucleotide fragment —pCpCpA (A). Among cellular enzymes, there is a special enzyme which builds this fragment into tRNA, namely ATP(CTP)-tRNA nucleotidyltransferase [56]. In its usual form (A), tRNA is capable of being aminoacylated on the corresponding type of aminoacyl-tRNA-synthetase, forming aminoacyl-tRNA. However, if the terminal pA nucleotide is removed with the aid of ATP(CTP)-tRNA nucleotidyltransferase and pC is introduced instead, then the resulting molecule (B) is no longer capable of being aminoacylated. On the other hand, if one obtains with the aid of the same enzyme under

anomalous conditions a type of molecule, modified in relation to natural tRNA, in which one superfluous pC residue is present



(C), then the latter are capable of being aminoacylated on aminoacyl-tRNA synthetase [57] although they are larger than (A). This emphasises the role of the pA residue in enzymatic aminoacylation.

One must stress that the preferential chemical aminoacylation of pA has been demonstrated in both methods where the aminoacid is introduced into the synthesis with the amino-group protected by protonation, i.e. as under the natural conditions on the enzyme. On the basis of these data, one may suppose that the structure of pA makes it most reactive in relation to aminoacylation when two pC residues before the terminal pA in tRNA rule out the erroneous aminoacylation of the incomplete tRNA molecule.

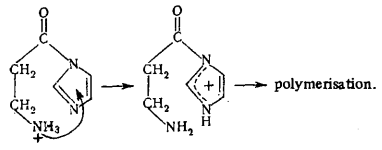
A study of the scope and limits of the applicability of the imidazolides of *N*-protonated aminoacids showed that anhydrous solvents may be used to synthesise *O*-aminoacyl-pA and *O*-aminoacyl-pU. In this case the yield increased to 30–35% for aminoacyl-pA and to 10% for aminoacyl-pU. However, in anhydrous solvents (DMSO, DMF, hexamethylphosphoramide), a number of impurities are formed together with aminoacylnucleotides; when pC is aminoacylated under these conditions, a mixture of side products is formed exclusively in a high yield [19].

Since it was not known from the available literature data whether the optical purity is retained in the synthesis of activated forms of *N*-protonated aminoacids and in their subsequent reaction, the stereospecificity of the synthesis of 3′(2′)-*O*-aminoacylnucleotides obtained with the aid of the imidazolides of *N*-protonated aminoacids was investigated. pA-Phe and pA-Val, obtained from pA, L-Phe, and L-Val, were hydrolysed with hydrochloric acid; next the aminoacids were purified and converted by reaction with salicylaldehyde into *N*-salicylidene derivatives. In the form of their copper complexes, such Schiff bases were investigated by circular dichroism (CD). The CD spectra of the copper complexes of the Schiff bases of salicylaldehyde and α-aminoacids show an anomalous rotation at 360–370 nm, the molecular ellipticity depending on the structure of the aminoacids and its sign on the configuration of the asymmetric carbon atom [58]. It was shown by this method that, within the limits of its sensitivity (up to 3%), the aminoacid is not racemised.

Further development of the aminoacylation method with the aid of the imidazolides of *N*-protonated aminoacids showed that the protection of the amino-groups by protonation is possible solely for α-aminoacids. If the amino-group is separated from the carboxy-groups by more than one carbon atom [for example in $NH_3(CH_2)_n$ COOH, $n > 1$ (2–10)], the formation of imidazolides involves a very rapid polymerisation:

$$\overset{+}{N}H_3(CH_2)_n\text{—CO—Im} \rightarrow \text{H—[NH}(CH_2)_n\text{CO]}_m\text{—OH}.$$

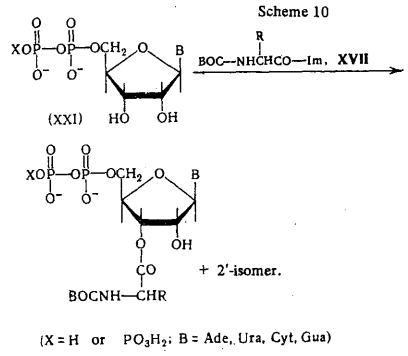
From the standpoint of the formal p*K* values for amino-groups, such a process appears unlikely. Thus, whereas the p*K* for the NH_2 group of glycine (the imidazolide of which is comparatively stable) is 9.6, for $n = 2$ and above the p*K* for the NH_2 group increases to 10 and above; therefore in this case the protection of the amino-group should be unreliable. A tentative explanation of this phenomenon involves a probable intramolecular proton transfer from the $\overset{+}{N}H_3$ group of the aminoacid imidazolide to N(3) of the imidazole ring. For α-aminoacids, such transfer is impossible due to steric hindrance, while for aminoacids with $n > 1$ it is theoretically (according to Stuart models) quite feasible. For example,



With α-aminoacids, the polymerisation reaction also occurs but its rate is very low. Probably here it involves an intermolecular mechanism, the dipeptide imidazolides formed undergoing a rapid further polymerisation, since their α-amino group is separated from the imidazole ring by more than four atoms. In an aqueous medium, the formation of oligopeptidylnucleotides takes place to a very small degree. In absolute solvents, dipeptidylnucleotides are formed in amounts up to 10%, their yield depending on the nature of the initial carbonyldi-imidazole.

A report of the use of the imidazolides of *N*-protected aminoacids for the synthesis of 3′(2′)-*O*-aminoacylnucleoside 5′-diphosphates and 5′-triphosphates (XXI) [59] under conditions resembling those in the aminoacylation of nucleotides (Scheme 10) was published in 1968.

Scheme 10

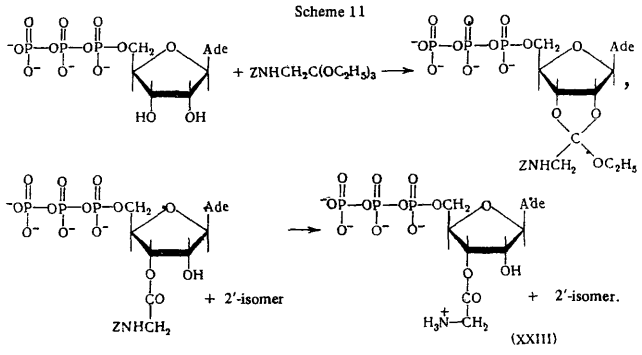


(X = H or PO_3H_2; B = Ade, Ura, Cyt, Gua)

3′(2′)-*O*-Peptidylnucleoside 5′-triphosphates were obtained similarly [60].

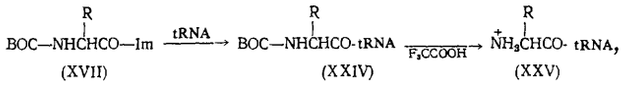
The applicability of the orthoester method in the synthesis of 3′(2′)-*O*-glycyl ATP (XXIII) was demonstrated in the same year [61] (Scheme 11).

Scheme 11



Investigators encountered the greatest difficulty in attempts to carry out a chemical aminoacylation of tRNA. tRNA is known to comprise 70–80 nucleoside units bound by (3′-5′)-phosphodiesters linkages. In such polymeric molecules (molecular weight about 25 000) there are on average 80 intermediate 2′-hydroxyls of the riboside residues, one 2′,3′-*cis*-diol group (to which the amino-acid in fact adds in enzymatic aminoacylation), a phosphomonoester group at the 5′- end of tRNA, and about 60 amino-groups of the bases. Under certain conditions, all these groups are capable of reacting with the activated aminoacid. Therefore it is not fortuitous that none of the methods, which are not distinguished by a high selectivity of the reaction with respect to the hydroxyls or by the mildness of the conditions of synthesis, yielded aminoacylated tRNA. The first and so far the only hope of developing a method for chemical aminoacylation arose in connection with the imidazolide method. A report concerning the interaction of the imidazolide of formylphenylalanine and BOC-glycine with a preparation of total tRNA from bakers' yeast was published in 1967.[62] The possibility, in principle, of the aminoacylation of tRNA in a mainly aqueous medium at 20°C over a period of several hours was demonstrated. Under the reaction conditions, compounds with ester type linkages and not anhydride or amide linkages are formed. Stable and high yields of aminoacyl-tRNA were achieved when the reaction was carried out in 1 M imidazole buffer. The BOC protecting group was removed from compound (XXIV) by treatment with anhydrous trifluoroacetic acid (Scheme 12).[63]

Scheme 12

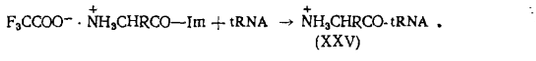


(XVII) (XXIV) (XXV)

where R = H (glycine) or $C_6H_5CH_2$ (phenylalanine).

In the process of elimination of the protecting group from the molecule, the aminoacyl-tRNA lost their adaptor function, i.e. the capacity to combine specifically with information RNA on ribosomes and thus participate in the biosynthesis of protein. Therefore it was necessary to eliminate this severe stage of the synthesis. This was achieved by employing the imidazolides of *N*-protonated aminoacids, which react with tRNA forming aminoacyl-tRNA in one stage (Scheme 13).[64]

Scheme 13

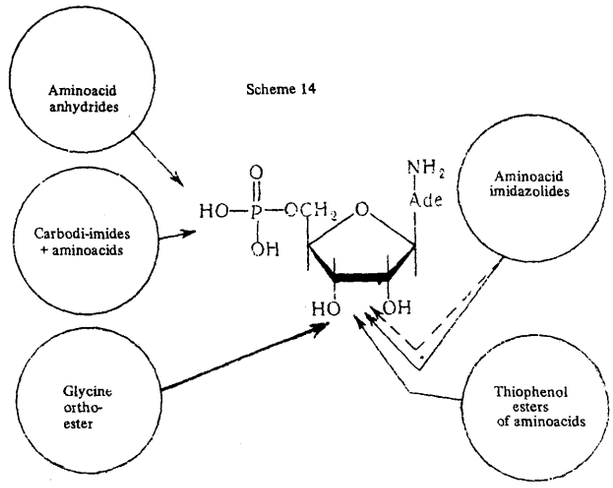


(XXV)

This reaction took place under very mild conditions—in 1 M imidazole buffer in water at pH 7 and 4°C over a period of several hours. The aminoacyl-tRNA separations obtained in this way are being studied at present.

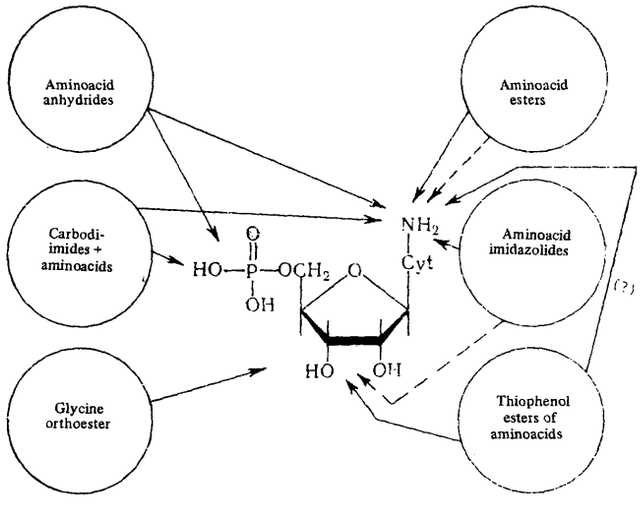
In conclusion, we shall attempt to summarise the data on the mode of the aminoacylation reaction as a function of the conditions and the reactivity of the activated aminoacid (Schemes 14 and 15). The nucleotides in the examples are adenylic acid (pA), the esters of which are widely employed in biochemistry, and cytidylic acid (pC) which has the most reactive amino-group. The properties of *p*-nitrophenyl and *N*-hydroxysuccinimide esters of *N*-protected aminoacids, which do not react either with the phosphate groups or with the ribose hydroxyls, should be considered separately. As regards their interaction with the amino-group of pC, the available data are contradictory: on the one hand, it is asserted that in water–organic solvent media such a reaction does not occur[65]; on the other hand, other investigators[32] did observe the reaction. Whatever the actual state of affairs, the unreacted nucleotides are isolated from the reaction mixture when the nucleotides are treated in a water–organic solvent medium at 20°C. These data served as a foundation for a large series of investigations which led to the discovery of methods for the selective acylation of the amino-group in aminoacylnucleotides and also aminoacyloligonucleotides (including aminoacyl-tRNA) (Section IV).

Scheme 14



The reactions designated by continuous arrows are carried out in organic solvents and those designated by broken arrows are carried out in solvents where water predominates.

Scheme 15



The reaction designated by continuous arrows are carried out in organic solvents and those designated by broken arrows are carried out in a medium where water predominates.

IV. SYNTHESIS OF ACYLAMINOACYL AND PEPTIDYL DERIVATIVES OF NUCLEOSIDES, NUCLEOTIDES, OLIGONUCLEOTIDES, AND tRNA

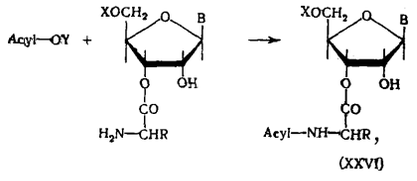
The last section of the review deals with the selective aminoacylation of aminoacyl derivatives of nucleosides, nucleotides, oligonucleotides, and tRNA. Above it was already stated that a rational approach to the search for aminoacylating agents of this type consists of the following steps: (a) the choice of activated forms of aminoacids the reactivity of which is insufficient for the interaction with ribose hydroxyls but permits condensation via the amino-group of the aminoacid residue of the aminoacylnucleoside and (b) the choice of conditions ruling out the reaction via the amino groups of the heterocyclic bases and via the phosphate groups.

Among the activated forms of carboxylic acids (including *N*-protected aminoacids), attention has been concentrated on activated esters. Activated esters such as the *p*-nitrophenyl and *N*-hydroxysuccinimide esters are most widely employed in peptide synthesis. These esters were in fact investigated in the first place as possible activating agents for aminoacylnucleosides and aminoacyl-tRNA.

Activated carboxylic acid esters (acetates, benzoates, etc.) were first allowed to interact with pC in anhydrous solvents, which gave high yields of $N_{(4)}$-acetyl-[66] or $N_{(4)}$-benzoyl-cytidine[67]. (As mentioned above, the amino-groups of adenine and guanine resist acylation by more reactive acylating agents such as anhydrides). However, it was shown in 1967[65] that in a mixture of water and an organic solvent the *N*-hydroxysuccinimide esters of acetic, formic, and other acids do not react with pC. On the basis of these data, a rational synthesis of acylaminoacyl-tRNA and peptidyl-tRNA was developed and is described below.

In 1967–1970 two reports were published[31,32] where it was shown that acyloxysuccinimides and acyl-*p*-nitrophenols can react in a water-organic solvent medium with the amino-group of pC at 24°C, and the yields of *N*-acylcytidylic acid can reach more than 35–45% in 24 h. In order to avoid this process, the authors suggested milder acylating agents, namely 5-chloro-8-hydroxyquinoline esters[32], which do not react with pC in a water–organic acid medium but do acylate the amino-group of the aminoacid residue. The acylation (aminoacylation) of the aminoacid esters of tRNA components or tRNA itself is shown in a general form in Scheme 16.

Scheme 16



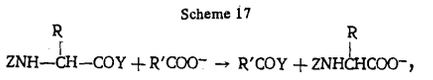
(XXVI)

where Y is the alcoholic component of the activated ester and X = H (nucleosides) or H_2O_3P (nucleotides or oligonucleotides).

A-(AcGly), A-(Val-Gly), A-(Lys-Gly), CpA-(AcGly), and CpA-(Lys-Gly) have been synthesised by activation with N-hydroxysuccinimide according to Scheme 16.[68,69]

Aminoacylation of aminoacylnucleosides and their analogues should not be carried out in acetate or formate buffer solutions. On the basis of the final results, one may suppose that in the presence of acetates of formates in organic solvents or in water there is an exchange of the activating group between the acylamino-acid and acetate or formate (Scheme 17).[70,71]

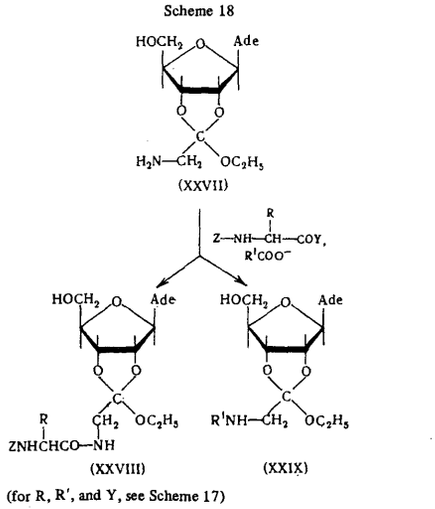
Scheme 17



where R = $CH(CH_3)_2$ or $(CH_2)_4NHZ$, Y = OSu or ONp, and R′ = H or CH_3.

The overall reaction, between the glycyladenosine orthoester (2′,3′-*O*-aminomethylethoxymethyleneadenosine) (XXVII) (Scheme 18) and the *p*-nitrophenyl or *N*-hydroxysuccinimide esters of benzyloxycarbonylvaline or $N_{(\alpha)}N_{(\epsilon)}$-dibenzyloxycarbonyl-lysine in the presence of acetate or formate in both anhydrous DMF or DMSO and in their mixtures with water results in the formation of a mixture of 2′,3′-*O*-(*N*-acyl)aminomethylethoxymethylene-adenosines. Apart from the main products, 2′,3′-*O*-(*N*-benzyloxycarbonylvalyl)- and 2′,3′-*O*-(*N*-dibenzyloxy-carbonyl-lysyl)-aminomethylethoxymethyleneadenosines (XXVIII), 2′,3′-*O*-(*N*-acetyl)- and 2′,3′-*O*-(*N*-formyl)-aminomethylethoxymethyleneadenosines (XXIX) were isolated from the reaction mixtures, their yield in a mixture of DMF and 2 M aqueous acetate buffers amounting to 39–42%.

Scheme 18



(for R, R′, and Y, see Scheme 17)

However, few examples of the synthesis of peptidyl-nucleosides or oligonucleotides have been described so far. The acylation of aminoacyl-tRNA has been investigated to an incomparably greater degree. Acylaminoacyl-tRNA is of particular interest for the investigation of the mechanism of the biosynthesis of protein on ribosomes. Acylaminoacyl-tRNA initiates the formation of the polypeptide chain in ribosomes (for example, FMet-tRNA in the protein synthesising system of *Escherichia coli*[72], AcPhe-tRNA in a model system with ribosomes and polyuridylic acid as the matrix[73], and in other cases).

FMet-tRNA was synthesised for the first time in 1964 by the reaction of *p*-nitrophenyl formate with Met-tRNA.[74] Acetic anhydride has been employed similarly[73] for the acylation of aminoacyl-tRNA, but this reaction does not

follow a single pathway: there is partial acylation of certain other parts of tRNA.[75,76] A convenient general method was developed in 1967–1970 using *N*-hydroxysuccinimide esters[75,76]. The condensation of *N*-hydroxysuccinimide esters of carboxylic acids with aminoacyl-tRNA is carried out in a mixture of water and organic solvents at 20°C and pH 5–6.

Among the numerous organic solvents employed, DMSO proved to be the most convenient. The yields of a number of acylaminoacyl-tRNA (FPhe-tRNA, AcPhe-tRNA, capryloyl-Phe-tRNA, lauroyl-Phe-tRNA, palmitoyl-Phe-tRNA, AcVal-tRNA, and AcMet-tRNA) were nearly qualitative and the yield of $N_{(\alpha)}N_{(\epsilon)}$-diAcLys-tRNA was about 90%. The acylaminoacyl-tRNA obtained did not lose their adaptor properties, i.e. in the presence of the corresponding codons they are capable of binding to ribosomes[76] and of initiating polypeptide synthesis[77,78].

The synthesis of oligopeptidyl-tRNA was first achieved using a water-soluble carbodi-imide[43,73]. Above it was already stated that this condensing agent in an aqueous medium is incapable of forming ester linkages between aminoacids and the hydroxyls of the ribose residues of tRNA; the amino-groups of the heterocyclic bases and the phosphate residues also fail to react under these conditions. This made it possible to develop with the aid of *N'*-cyclohexyl-*N''*-[β-(*N*-methylmorpholinium)ethyl] carbodi-imide (CME-carbodi-imide) the first method for the synthesis of formylpeptidyl-tRNA. Gly-Val-tRNA[46] and FGly-Gly-Val-tRNA[79] were obtained in this way. However, this method has not found wide application, possibly partly owing to the difficulty of removing the formyl protecting group without disrupting the structure of formylpeptidyl-tRNA.

A method employing *N*-hydroxysuccinimide esters, which nowadays makes it possible to synthesise derivatives up to deca- and trideca-peptidyl-tRNA, was developed more thoroughly. The synthesis of Gly-Phe-tRNA was achieved for the first time by the condensation of the *N*-hydroxysuccinimide ester of Mtrit-glycine (XXX) with Phe-tRNA to form Mtrit-Gly-Phe-tRNA (XXXI) followed by elimination of the protecting group (Scheme 19).

Scheme 19

$$\underset{\text{(XXX)}}{\text{MtritGlyOSu}} + \text{Phe-tRNA} \rightarrow \underset{\text{(XXXI)}}{\text{MtritGly-Phe-tRNA}} \rightarrow \underset{\text{(XXXII)}}{\text{Gly-Phe-tRNA}} .$$

The choice of the protecting group in (XXX) and of the conditions for the condensation of (XXX) with tRNA is not trivial, since the protecting group must be removed subsequently from compound (XXXI) under very mild conditions. Otherwise the labile peptidyl-tRNA bond might be easily broken. t-Butyloxycarbonyl (BOC), trityl (Trit), and monomethoxytrityl (Mtrit) *N*-protecting groups were tested for this purpose, but the attempts to eliminate the BOC and Trit protecting groups under mild conditions were unsuccessful. The Mtrit group was removed from (XXXI) with 5% dichloroacetic acid at 4°C in 5 min; the Gly-Phe-tRNA (XXXII) obtained as a result of such treatment possessed the adaptor function and was capable of functioning as a peptide donor on ribosomes[78].

Tests of this method of synthesis on a large group of dipeptidyl-tRNA showed[80] that the condensation of *N*-hydroxysuccinimide esters of Mtrit-aminoacids with aminoacyl-tRNA takes place just as satisfactorily at pH 5–8 in a 4 : 1 DMSO–aqueous buffer mixture. Among the organic solvents tested (DMSO, DMF, ethanol, THF, and ethyl acetate), DMSO was found to be most convenient. In this solvent the reaction takes place under the most homogeneous conditions and as a result has the highest yield.

The structure of the aminoacid in compound (XXX) (Scheme 19) also affected the yield of (XXXI). Whereas for the *N*-hydroxysuccinimide esters of Mtrit-glycine and Mtrit-alanine the yields were nearly quantitative[80–84], for the *N*-hydroxysuccinimide esters of Mtrit-phenylalanine and Mtrit-valine the yields did not exceed 55–85%.[80] This decrease of the yield can be accounted for by the steric hindrance of the aminoacid component to the synthesis of compound (XXX), since both the *N*-protecting group and the side group of the aminoacid are in this case fairly bulky. In order to overcome this difficulty, the NPS *N*-protecting group, which is readily removed from NPS-peptidyl-tRNA with a 0.4 M solution of sodium thiosulphate in water at 30°C in 2 h, was employed. Val-Gly-Phe-tRNA[85] and many other derivatives[86,87] were obtained in this way in nearly quantitative yields.

Peptidyl-tRNA with larger peptide residues were synthesised according to a scheme which is similar in principle but involves both stepwise and block procedures in the formation of the peptide chain[82]. The synthesis of penta-alanyl-tRNA (XXXV, Scheme 20) may be quoted as an example.

Scheme 20

$$\underset{\text{(XXXIII)}}{\text{Ala-tRNA}} \xrightarrow{\text{MtritAla-AlaOSu}} \text{Mtrit-(Ala)}_2\text{-tRNA} \rightarrow$$

$$\underset{\text{(XXXIV)}}{\text{(Ala)}_2\text{-tRNA}} \xrightarrow{\text{MtritAla-AlaOSu}} \text{Mtrit-(Ala)}_5\text{-tRNA} \rightarrow \underset{\text{(XXXV)}}{\text{(Ala)}_5\text{-tRNA}} .$$

According to this scheme, the pentapeptide (XXXV) is formed from 1 + 2 + 2 aminoacid units. The yield of (XXXIV) relative to (XXXIII) employed in the reaction was 93% and the yield of (XXXV) relative to (XXXIV) was 80%. Several tri- and tetra-peptides containing valine, phenylalanine, alanine, leucine, and methionine as aminoacids introduced by an enzymatic procedure and glycine or alanine introduced synthetically were obtained by a similar method[83]. $(Gly)_n$-Phe-tRNA, $(Gly)_n$-Val-tRNA, $(Ala)_n$-Phe-tRNA and $(Ala)_n$-Ala-tRNA, where $n = 4–12$, were also synthesised in 4–5 stages[84]. In the synthesis of such relatively large peptidyl-tRNA, the condensations were carried out at 30°C over a period of 12 h.

The use of the NPS-protecting group permitted the extension of this method to hydroxyl-containing aminoacids (serine, tyrosine, threonine[86], and phenylalanine[87]). In the case of these aminoacids, the condensation of NPS-peptidyl-OSu with aminoacyl-tRNA was carried out at 30°C in 2 h in a mixture of an aqueous buffer at pH 8.1 and DMSO in proportions of 1 : (1–4) by volume; there was then no need to protect the hydroxyls of serine, tyrosine, and threonine. The yields of the peptidyl-tRNA were nearly quantitative.

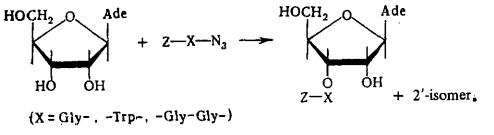
Activation of the formation of *N*-hydroxysuccinimide esters is now beginning to find application in the synthesis of special variants of acylaminoacyl-tRNA and peptidyl-tRNA for the solution of specific biochemical problems. For example, phenoxyacetyl-Phe-tRNA (forming part of the overall tRNA) was synthesised from the *N*-hydroxysuccinimide ester of phenoxyacetic acid and Phe-tRNA (forming part of the overall tRNA). This made it possible to develop a method for the isolation of the individual phenylalanyl-tRNA[88]. A similar method has been

developed also for Val-tRNA[89]. A series of acylamino-acyl-tRNA ($tRNA^{Phe}$, $tRNA^{Val}$), with a stable radical attached to the amino-group of the aminoacyl-tRNA, were obtained by the formation of the *N*-hydroxysuccinimido-ester of 2,2,5,5-tetramethylpyrroline-3-carboxylic acid N-oxide containing the stable radical[90,91]. The tertiary structures of the above compounds were investigated with the aid of ESR spectra.

A number of peptidyl-tRNA have been employed as substrates for the enzyme peptidyl-tRNA hydrolase[92], which hydrolyses selectively aminoacyl-tRNA.

In conclusion we must point out that the possibilities of the synthesis of the aminoacid esters of nucleosides, nucleotides, and polynucleotides have still been comparatively little investigated. This is illustrated by a recent study in which 3′(2′)-*O*-benzyloxycarbonylglycyl-, 3′(2′)-*O*-benzyloxycarbonyltryptophanyl- and 3′(2′)-*O*-benzyloxycarbonyldiglycyl-adenosines were obtained[93] (Scheme 21).

Scheme 21



(X = Gly-, -Trp-, -Gly-Gly-)

The synthesis was achieved by the condensation of benzyloxycarbonylaminoacid and benzyloxycarbonyldipeptide azides with adenosine in 3 : 1 aqueous dioxan at pH 9 and 8°C. This method is interesting from several points of view. Firstly, it does not require the protection of the 5′-hydroxyl. Secondly, it will probably make it possible to prevent the racemisation of the *C*-terminal aminoacid in peptides, provided that it can be extended to optically active peptides. Thirdly, the unusual behaviour of the azides of *N*-protected aminoacids and peptides in a medium containing mainly water at a high pH has been demonstrated in this case. It is known from experimental peptide chemistry that the use of aminoacid and peptide azides is possible solely for reactions involving the amino-group, since the hydroxyls of serine, threonine, and tyrosine do not react with azides under these conditions.

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Recyclisation Reactions of Heterocyclic Compounds Involving Hydrazine and Its Substituted Derivatives

O.P.Shvaika and V.N.Artemov

In the review an attempt is made for the first time to give a systematic account of the available literature data for the recyclisation reactions of heterocyclic compounds under the influence of two-centre nucleophilic agents-hydrazine and its derivatives. The recyclisation reactions are classified taking into account the capacity of heterocycles to undergo such reactions as a function of the structure and the distribution in the heterocyclic compounds of reaction centres determining the mode of recyclisation. Particular attention has been devoted to heterocyclic rearrangements involving the hydrazine moiety of the molecule. The mechanisms of the recyclisation processes are discussed. The importance of these reactions in organic synthesis has been demonstrated.
The bibliography includes 255 references.

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I. INTRODUCTION

The recyclisation reactions of heterocyclic compounds involve a rearrangement of the heterocyclic skeleton in which the ring heteroatom is replaced and the heterocyclic nucleus is contracted or expanded or undergoes isomerisation. From the theoretical point of view, these reactions are complex transformations involving ring opening and ring closure. Nevertheless for preparative purposes they are single-stage processes. In practice, recyclisation reactions can yield compounds which are frequently difficult to obtain in other ways and allow the transformation of one ring into another in complex molecules, giving rise thereby to a powerful and discriminating synthetic procedure. In their analytical aspect, as a method for the identification of heterocycles, such reactions have been used in biological chemistry.

Recyclisation reactions are a result of the interaction between heterocyclic compounds and other chemical agents or are a consequence of a rearrangement under the influence of temperature, light, or catalysis by acids or bases. Nucleophilic, electrophilic, and dipolar substances can serve as the chemical agents. A number of reviews have been devoted to the transformations of rings under the influence of dipolar agents[1]. The recyclisation reactions under the influence of electrophilic agents are characteristic only of specific heterocyclic systems. However, one frequently encounters ring rearrangements under the influence of nucleophilic agents. The latter must always be binucleophilic. This is because the ring rearrangement—its opening and reclosure—always requires the participation of two reaction centres in the heterocyclic molecule with which the binucleophilic agent interacts. The binucleophilic nature of the substance involved in recyclisation reactions can concern only one or two of its atoms. In the first case we are dealing with one-centre nucleophilic agents such as ammonia, 1,1-disubstituted hydrazines, primary amines, and sulphide and hydroxide ions. In the second case we have two-centre nucleophilic agents—hydrazine, hydroxylamine, and their derivatives. Ring rearrangements under the influence of one-centre nucleophilic agents usually reduce the replacement of the ring heteroatom via an intermediate ring opening step. The recyclisation reactions under the influence of two-centre nucleophilic agents, which involve nucleophilic additions and eliminations and obey the relations for the nucleophilic reactions of polar double bonds, are more complicated. For example, the two-centre nucleophilic agents involved in reactions with heterocycles containing polar double bonds (C=X, X=O, S, N, or P) have a higher reactivity than one-centre agents, due to the so-called α-effect[2,3]. Therefore they are also referred to as supernucleophilic agents[3]. This factor may affect significantly the rate-determining stages in the recyclisation reactions and can influence the mode of rearrangement. Moreover, two-centre nucleophilic agents can be involved in the ring rearrangement via one or both heteroatoms. Among supernucleophilic agents, the effect of hydrazine and its derivatives on heterocyclic systems has been particularly widely investigated, primarily in connection with the search for medicinal substances among heterocyclic derivatives of hydrazine.

Recyclisation reactions with hydrazines take place in both polar and non-polar solvents or in an excess of hydrazine in the temperature range 0 – 250°C.

One should bear in mind that the interaction of heterocycles with hydrazines can stop at the stage involving the substitution of labile groups in the heterocycle and the formation of ring-opening products or can be completed by a recyclisation the mode of which may be varied depending on structural factors and the reaction conditions. The expected reaction products may be isomeric. Hence one can understand the difficulties which frequently arise in the interpretation of the addition of hydrazines to heterocycles when a rearrangement of the latter is possible. This is reflected by frequent revisions of the mechanisms of such reactions initially suggested in the literature.

Despite this considerable number of published studies concerning the rearrangement of heterocycles, attempts to give a systematic account of the available data have not so

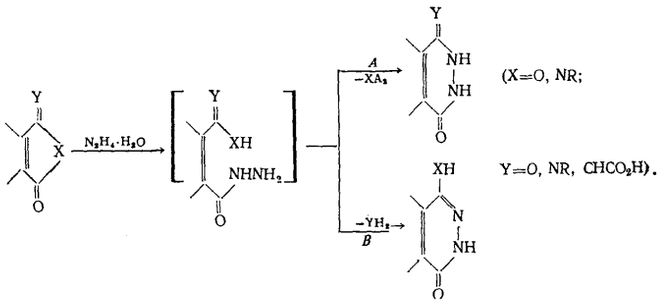
far been made. Although studies on the quantitative interpretation of recyclisation reactions have not been carried out, the available literature data based on synthetic investigations nevertheless permit definite generalisations and allow a systematic arrangement of the results. The present review includes the literature published in 1970 and partly in 1971.

II. RECYCLISATION REACTIONS OF HETEROCYCLES WITH TWO CENTRES IN THE RING SUSCEPTIBLE TO NUCLEOPHILIC ATTACK

1. FIVE-MEMBERED HETEROCYCLES

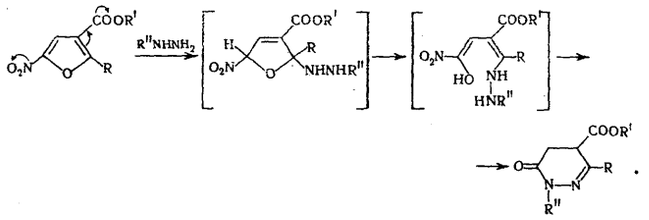
Five-Heterocycles with a Single Heteroatom

Recyclisation reactions with hydrazines are not typical for unsubstituted five-membered heterocycles with a single heteroatom in the ring. The presence of electron-accepting substituents in the ring renders both saturated and unsaturated and aromatic heterocyclic systems susceptible to nucleophilic attack. The rate of recyclisation is influenced by the electronic nature of the ring heteroatom (S > O ≫ NH), the presence of double bonds (cf. Feuer et al.[4]), and the position of activating substituents relative to the centres susceptible to attack. The outcome of the recyclisation reaction depends significantly on the positions of the centres susceptible to nucleophilic attack in the heterocycle. If they are in the α-positions relative to the ring heteroatom, then rearrangement to the pyridazine system usually takes place under the influence of hydrazines. Unsaturated five-membered heterocycles, including condensed heterocycles, containing exocyclic polar multiple bonds in both α-positions, react in this way:



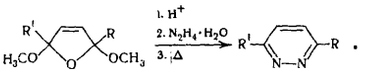
The mode of ring rearrangement—with elimination of the ring heteroatom (pathway *A*) or the α-substituent (pathway *B*)—depends on the nature of the substituent in the α-position. The occurrence of the reaction via both pathways has been noted only in the series of imino-oxoisoindolines [X = NH and Y = NR].[5] In other cases, where X = O or NR and Y = O or CHCOOH, the ring heteroatom is split off and a type *A* pyridazine structure is formed. The method of synthesis of type *A* cyclic hydrazides by the recyclisation of the corresponding cyclic anhydrides, which occurs when the reactants are simply mixed, is well known[6]. The anhydrides of 5,6-dihydro-*p*-dithi-in-2,3-dicarboxylic acids readily undergo a similar reaction, in particular with methyl- and *syn*-dimethyl-hydrazines[7,8]. Among reactions of this type, that of phthalidylideneacetic acid (X = O and Y = CHCOOH) with methylhydrazine to form oxophthalazineacetic acid has been used in the synthesis of physiologically active compounds[9].

Substituted furans, in which the $\alpha\alpha'$-centres susceptible to nucleophilic attack are activated by electron-accepting groups in the 2,4-positions of the ring, are recyclised under the influence of hydrazines into pyridazines[10], which resembles the ring rearrangement via pathway *B*:

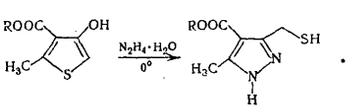


When R = H, the reaction takes place even at room temperature, but with R = alkyl it becomes strongly inhibited, which the authors believe is due to steric hindrance.

Recyclisation reactions with hydrazines in the furan series, where the $\alpha\alpha'$-centres of nucleophilic attack are activated saturated carbon atoms, have been described; they yield 3,6-substituted pyridazines which are otherwise difficult to obtain[11,12]:



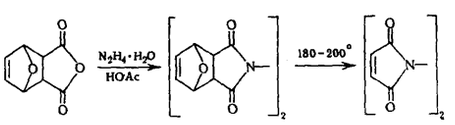
The thiophen ring with polar substituents in the $\beta\beta'$-positions is readily transformed into the pyrazole system[13]:



Nitrogen-containing heterocycles undergo recyclisation with somewhat greater difficulty than their oxa- and thia-analogues. Nevertheless a modification of the Gabriel synthesis (the Ing – Manske reaction)[14,16], based on the addition of hydrazines to cyclic dicarboxylic acid imides (X = NR and Y = O), is known.

The rearrangements into pyridazine systems of a number of pyrrole derivatives (X = NH), in which the $\alpha\alpha'$-centres of nucleophilic attack are activated by substituents in the β-position of the ring, are also known[17,18]. 3-Benzoyl-4-isonitrosopyrrole undergoes recyclisation into the bicyclic isoxazolopyridazine system under these conditions[19].

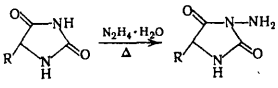
In the above reactions, the hydrazine molecule enters the ring via both nitrogen atoms, which results in the expansion of the initial ring. However, hydrazine can also enter the ring via only one nitrogen atom, which apparently depends to a considerable degree on the nature of the substituent in the hydrazine and on the medium. In acetic acid, cyclic dicarboxylic acid anhydrides give rise to the corresponding cyclic *N*-aminoimides on heating with hydrazine, phenylhydrazine, and acid hydrazides[20,21]:



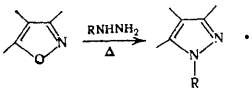
There are also literature data on the interconversion of cyclic hydrazides and imides[22–24]. Their formation depends sometimes on very slight changes in the structure of the anhydride[21,25]. Probably some of these reactions require further investigation.

Five-Membered Heterocycles with Two Heteroatoms

Five-membered heterocycles containing two nitrogen atoms in the ring (pyrazoles, imidazoles, and their hydrogenated analogues) do not undergo recyclisation reactions with hydrazines under the usual conditions. The presence of exocyclic heteroatoms appreciably activates such heterocycles. A simple preparative synthesis of aminohydantoins from hydantoins is known[26]:

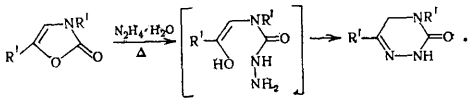


The capacity of five-membered heterocycles with two different heteroatoms to undergo recyclisation reactions depends on the relative positions of the heteroatoms in the ring. On heating with hydrazines, isoxazoles are converted into pyrazoles[27-30], but together with the latter other ring-transformation products were also detected:

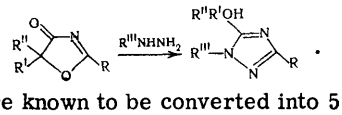


When the β-position of the isoxazole ring contains a powerful electron-accepting group (for example R″ = NO_2),[31-33] recyclisation with hydrazines, including even arylhydrazines, takes place particularly readily.

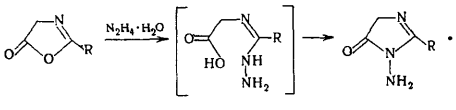
1,3-Oxazoles without activating substitutents are sensitive to hydrazinolysis but subsequent ring closure does not occur[34,35]. However, isomeric oxazolones and their derivatives containing an oxo group in addition to the multiple bond in the ring are capable of recyclisation when acted upon by hydrazines. Under these conditions, the outcome of the reaction depends significantly on the relative positions of the oxo-group and the ring multiple bond, which determine the mode of nucleophilic attack in the heterocyclic nucleus. On refluxing with hydrazine hydrate, 2-oxazolones yield triazinones[36]:



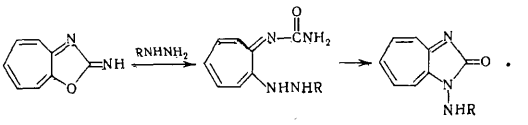
4-Oxazolones react vigorously with hydrazine forming triazoles[37]:



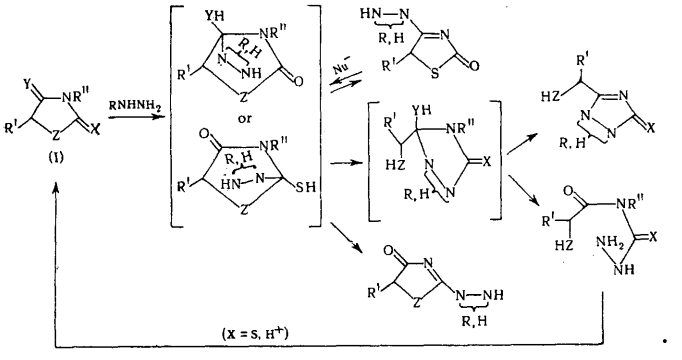
5-Oxazolones are known to be converted into 5-imidazolones when acted upon by hydrazine hydrate[38,39]. In contrast to both previous transformations, in this case hydrazine enters into the ring via only one heteroatom:



This difference in the behaviour of oxazolones probably depends on the activity of the nitrogen atoms of the hydrazine group in relation to the secondary electrophilic centre. If the latter is a carbonyl group, as in the first two cases, the interaction with the more basic β-nitrogen atom is preferable. On the other hand, the more strongly polarised α-atom interacts with the carboxy-group. The possibility of an interachange of the sites of attack in the heterocycle by the hydrazine molecule cannot be ruled out; this has been observed in the recyclisation of 2-imino-2*H*-cycloheptoxazole derivatives[40], in which *N*-amino-heterocycles are formed:



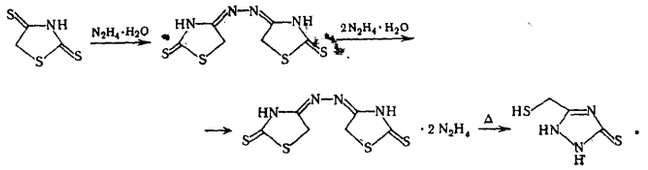
The oxa- and thia-zolidine rings activated by exocyclic heteroatoms in the 2- and 4-positions readily react with hydrazines with recyclisation into triazolones or triazolethiones[41]. Alkyl substituents in azolidinones (I, Z = S) inactivate them with respect to the addition of hydrazines, while *N*-arylated azolidinones are readily degraded[41,42]. The mode of reaction depends on the nature of the exocyclic heteroatoms in (I)[43,44] and also on the substituents in the hydrazine molecule, which determines the site of primary attack in the heterocycle by the hydrazine[45]. Depending on the reactivity of electrophilic centres in the azolidinone and the rate of removal of the XH_2 or YH_2 fragment, a hydrazonoazolidinone or triazolone (triazolethione) is formed. In isorhodanine (I, X = O, Y = Z = S), for example, the rate of elimination of hydrogen sulphide is much higher than the rate of reaction involving the 2-position in the ring and the rate of dissociation of the C — Z bond, which results in the formation of 4-hydrazinoazolidinone as the primary product. If conditions favouring such interaction are created (in the presence of nucleophilic agents), recyclisation into triazolone takes place. In rhodanines (I, X = Z = S, Y = O), the outcome of the reaction depends on the medium to an even greater extent[43,46]. 2-Hydrazinoazolidinones are formed only in an alcoholic medium, while in aqueous and alkaline media recyclisation into triazolethiones takes place:



When hydrazine acts upon rhodanines, it is possible to isolate an acyclic hydrazinolysis product, which is converted, depending on the conditions determining the competitive cyclisation reaction[47,48], into 2-hydrazinoazolidinone (in neutral solvents, on heating) or into a triazolethione (in alkaline media) or is reconverted into the initial rhodanine (in acid media). Recyclisation of substituted rhodanines into benzylidenehydrazonoazolidinones[49] and thiadiazine structures[46,50] has also been described.

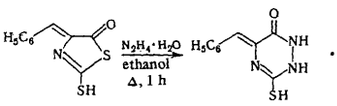
The recyclisation in the series of thiorhodanines has an unusual feature[43]. The presence of the reactive 4-thione group in the ring leads to the initial formation of an azine which reacts further with hydrazine in the presence of an

excess of the latter to form a saltlike adduct, which is converted on heating into a triazolethione:

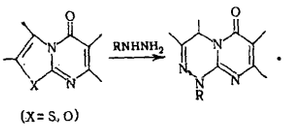


The recyclisation reaction of azolidine systems with hydrazine constitutes a convenient method for synthesising triazolones and triazolethiones with a mercapto-substituent in the side chain[51], which are difficult to obtain in other ways and which are of interest for pharmaceutical chemistry[52].

The conversion of benzylidenemercaptothiazolidine into mercaptobenzylidenetriazilone on refluxing with hydrazine, accompanied by ring expansion, has been described[53]:

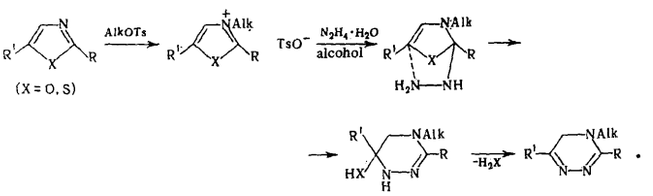


Condensed oxa- and thia-zole rings with a bridging nitrogen atom are converted in high yields into condensed cyclazine systems[54]. The reaction has a wide scope and in the pyrimidine series is of interest for the preparation of biologically active compounds:



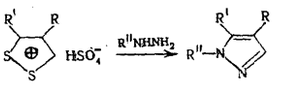
(X = S, O)

An effective method of increasing the reactivity of nitrogen-containing heterocycles in recyclisation reactions involves their conversion into a cationic state by the quaternisation of the ring nitrogen atom, as a result of which the electrophilic properties of the ring carbon atoms become much more pronounced. Even systems as stable as diaryloxazoles and diarylthiazoles are readily converted in this way into triazines[55,56]. Apart from this mechanism, which postulates a preliminary ring opening, yet another possibility of the rearrangement of cyclic cations via a quasi-1,2-addition of hydrazine to the ring has been considered[56]. In this case, after the initial attack by hydrazine on the azolium cation, the β-nitrogen atom interacts very rapidly with another electrophilic centre, which entails the dissociation of the C—X bridge bond:



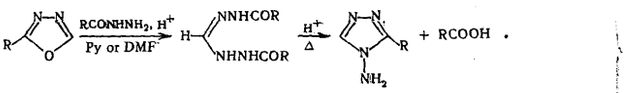
(X = O, S)

Dithiolium salts are very readily recyclised with replacement of the disulphide fragment in the ring by the hydrazine fragment[57,58]:

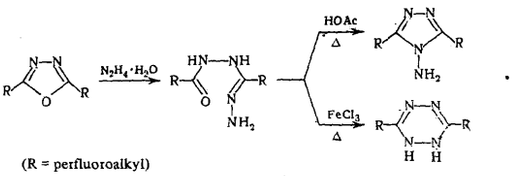


Five-Membered Heterocycles with Three Heteroatoms

Triazoles, particularly symmetrical triazoles such as pyrazoles, are extremely resistant to the action of hydrazine. Among five-membered heterocyclic compounds with three heteroatoms in the ring, derivatives of 1,3,4-oxadiazole have been most thoroughly investigated in recyclisation reactions under the influence of hydrazine. Despite their formal aromaticity, they are capable of exhibiting iminoether properties[59,60]. Alkyl- and monoaryl-substituted oxadiazoles are very sensitive to nucleophilic attack[61]. According to Eggert et al.,[62] they can be converted into aminotriazoles when acted upon by hydrazines:



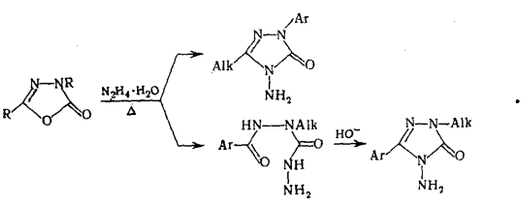
The recyclisation of perfluoroalkyl derivatives of oxadiazole under the influence of hydrazine hydrate has been described[63]. It takes place in two stages: ring hydrazinolysis (under mild conditions) and recyclisation into tetrazine or aminotriazole derivatives:



(R = perfluoroalkyl)

The substitution of both hydrogen atoms by aryl residues in the oxadiazole ring lowers its reactivity in recyclisation reactions with nucleophilic agents[61], probably in consequence of an increase of the overall aromaticity of the system[60]. Such oxadiazole derivatives do not react with hydrazines under the usual conditions. However, in the cationic state they are capable of recyclisation into *N*-aminotriazoles or tetrazines depending on the conditions[56]. In contrast to other azolium salts, the reaction is very sensitive to the nature of the anion.

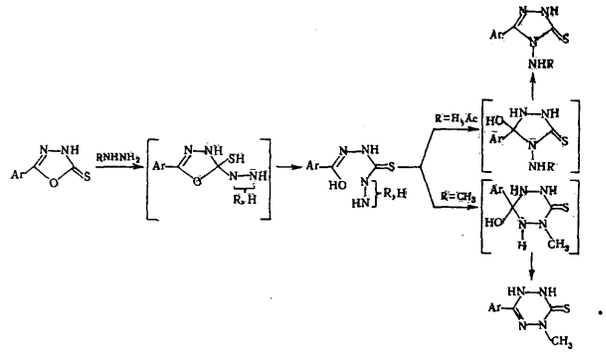
The presence in oxadiazoles of exocyclic oxo-, thio-, or amino-groups promotes the recyclisation reaction with hydrazine. On heating with stoichiometric amounts of hydrazine hydrate, oxadiazolones are converted into aminotriazolones[64]:



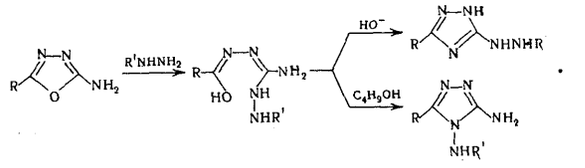
The reaction is very sensitive to the nature of the substituents and to the reactant ratio. On heating in an excess of hydrazine, oxadiazalones merely decompose into hydrazides[64-66].

On heating with hydrazines, oxadiazolethiones are capable of rearrangement via two pathways: into *N*-aminotriazolethiones (with unsubstituted hydrazines and acid

hydrazides) or into tetrazinethiones (with methylhydrazine)[67,68]. The reaction mechanism can be interpreted as follows:



The interaction of amino-oxadiazole derivatives with hydrazines has been widely investigated. It has been shown that, on heating with hydrazine, amino-oxadiazoles are capable of recyclising into *N*-aminotriazoles or hydrazinotriazoles[69]:



It has been stated[70,71] that the hydrazinolysis of the oxadiazole ring can involve both the $C_{(2)}-O$ and the $C_{(5)}-O$ bonds, depending on the nature of the substituent in the ring and in the amino-group. The reaction can lead directly to the triazole system[72-74] or, as usually happens when substituted hydrazines are employed, stops at the stage of the acyclic ring hydrazinolysis product. The subsequent mode of ring closure depends on the medium and the substituent[75-78].

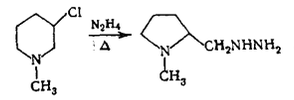
In the series of thiadiazoles, conversions into tetrazines under the influence of hydrazine are known[56]. Diarylthiadiazoles are inactive in relation to nucleophilic agents, but, like other azole systems, in a cationic state they are very vigorously recyclised into tetrazines under the influence of hydrazine.

2. SIX-MEMBERED HETEROCYCLES

The recyclisation reactions of six-membered heterocyclic compounds with two-centre nucleophilic agents take place not only with expansion or retention of the size of the initial ring, as in five-membered heterocycles, but can also involve ring contraction, although in the latter case hydrazine is involved via both its nitrogen atoms in the ring rearrangement. The outcome of the recyclisation is not determined solely by the positions of the centres of nucleophilic attack and the reactivity of the nitrogen atoms in the hydrazines. Energy factors can assume significant importance, for example in recyclisation reactions in the series of aromatic six-membered heterocycles with a single heteroatom, when there is a choice between the formation of a non-aromatic strained diazepine structure and an aromatic azole or pyridine system.

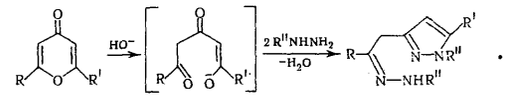
Six-Membered Heterocycles with a Single Heteroatom

Hydrogenated heterocycles—tetrahydro-γ-pyrone and tetrahydro-γ-thiapyrone and its sulphone as well as the thione analogues of both types of compound—do not react with amines but readily react with hydrazine, apparently owing to the α-effect[2], via the exocyclic heteroatom to form the corresponding hydrazones or azines[79], but there is no recyclisation. β-Chloro-*N*-methylpiperidine is known to undergo ring contraction when the halogen is replaced by hydrazine[80]:



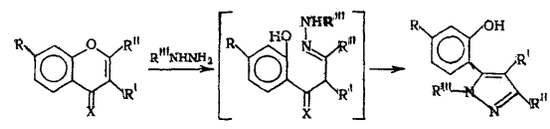
Unsaturated systems—pyrones, thiapyrones, and pyridones as well as their condensed analogues (chromones and coumarins)—readily enter into recyclisation reactions with two-centre nucleophilic agents. Although these compounds are represented in a non-ionic form, according to Schweizer[8] they can also assume the betaine-like structure of pyrylium, thiapyrylium, and pyridinium cations respectively, which show a very high tendency towards ring rearrangement, particularly on reaction with hydrazine. Although, depending on the nature of the heteroatom in the six-membered ring, the recyclisation reactions exhibit certain characteristic features, their outcome in the above series of compounds depends mainly on the position of the exocyclic heteroatoms, which determine the sites of nucleophilic attack in the ring. Therefore, fairly significant differences are observed between the recyclisation reactions of γ- and α-pyrones and their thio-analogues.

γ-Pyrone and its derivatives are readily converted under the influence of hydrazine or its substituted derivatives (on heating with the latter) into pyrazole derivatives[82-84]:



It is appropriate to mention here that the rearrangement of γ-pyrones under the influence of another two-centre nucleophilic agent (hydroxylamine) does not lead to isoxazoles, as might have been expected by analogy with the reaction quoted above, but to pyridone *N*-oxides[85]. Probably in this case the energy factors prevail over kinetic factors, since the isoxazole ring is less aromatic than the pyridine ring, while the pyrazole ring shows a high degree of aromaticity[81].

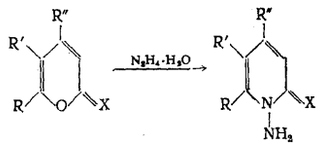
The condensed system—chromones and thiochromones—behave in recyclisation reactions with hydrazine analogously to γ-pyrones, being readily converted in the presence of catalytic amounts of alkali into *o*-hydroxyphenyl derivatives of pyrazoles in high yields[86-89]:



The authors believe[86,87] that the hydrazine molecule attacks primarily the C — O bond of chromone, since under analogous conditions the reactivity of both the carbonyl

and the thione group in these compounds in relation to nucleophilic agents is very low. When chromones and thiochromones react with arylhydrazines in a neutral or acid medium, only the corresponding hydrazones are formed; the latter are no longer capable of rearrangement under the influence of alkali[87].

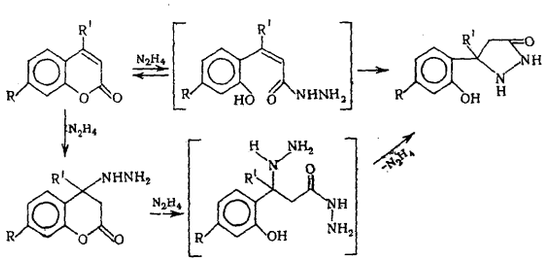
In contrast to γ-pyrones, α-pyrones and α-thiopyrones react with nucleophilic agents with much more difficulty. With hydrazine, they are converted fairly slowly into aminopyridones or aminopyridinethiones[90-92]:



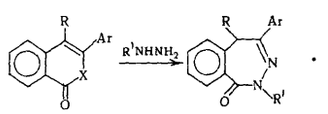
The rate of recyclisation of pyrones is appreciably influenced by the ring substituents. Aryl substituents in the hydrazine molecule hinder recyclisation. When α-thiopyrones react with phenylhydrazine, there is only a replacement of the sulphur atom by the hydrazine group[91,93]. It is noteworthy that the analogous reactions involving amines takes place with difficulty.

As stated above, condensed systems of the γ-pyrone type (chromones) are recyclised similarly to non-condensed analogues on reaction with hydrazine. In the series of α-pyrones, two condensed isomers are known—coumarins and isocoumarins—which differ very appreciably in the recyclisation reactions both from one another and from their monocyclic analogues. This is due to a different distribution of centres of nucleophilic attack which is greatly altered on condensation.

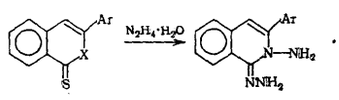
On heating with hydrazine hydrate, coumarins give low yields of pyrazoline derivatives[94]. The authors consider two alternative pathways for this reaction:



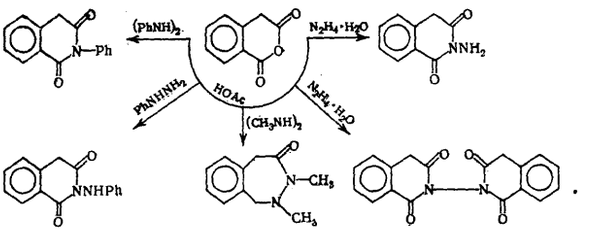
Under the influence of hydrazines, isocoumarins and isothiacoumarins recyclise into diazepinones[95-98], which are obtained in high yields:



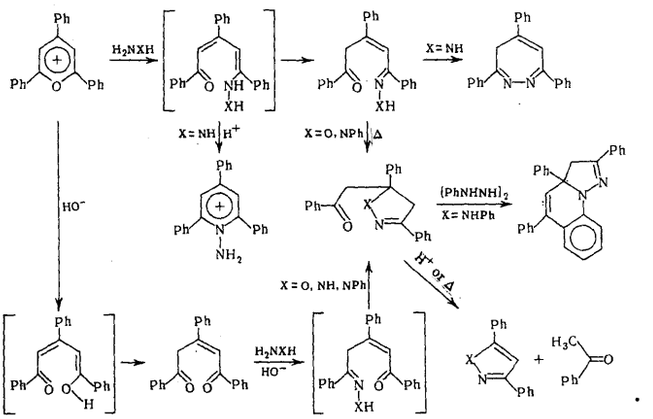
On the other hand, in the presence of an excess of hydrazine, thioisocoumarins and thioisothiacoumarins yield *N*-amino-1-hydrazonoisoquinolinones. In the case where equimolar amounts of the reactants are employed, there is merely a replacement of the thione sulphur atoms by the hydrazine group[99,100]:



In certain studies[101,102] the diazepine structure was attributed to the products of the recyclisation of homophthalic anhydride and its derivatives in the reaction with hydrazine. Subsequently these views were revised[103] and it was shown that, depending on the substituents in the hydrazine molecule, the reaction yields products with an imide structure and not azepines, which could not be detected either when the reaction was carried out in neutral solvents or in acetic acid. However, the formation of diazepine was noted when homophthalic anhydride reacted with *sym*-dimethylhydrazine:



The recyclisation reactions of pyrylium and pyridinium salts with hydrazines take place with exceptional ease. Their outcome is influenced significantly by the nature of the ring heteroatom and the substituents in both components, the nature of the anion, and also the medium. Depending on these factors, the cyclic cation can be transformed via three pathways: with ring expansion to the diazepine system, with ring contraction to the pyrazoline system and subsequent aromatisation by conversion into the pyrazole ring, and with replacement of the terminal heteroatom by the nitrogen atom and formation of *N*-aminopyridinium salts. The different types of recyclisation reactions in the series of pyrylium salts with two-centre nucleophilic agents (hydrazines and hydroxylamine) are most completely accounted for by Balaban's scheme[104-106] illustrated here for triphenylpyrylium perchlorate as an example:



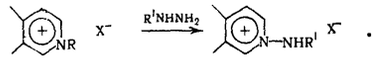
Triarylpyrylium salts are very readily converted into diazepines when acted upon by an excess of hydrazine hydrate[107]. However, pyrylium cations containing even only one methyl group in the α-position, for example 2-methyl-4,6-diphenyl- and 2,4,6-trimethyl-pyrylium perchlorates, are rapidly converted into pyrazoles in an excess of hydrazine hydrate in alcohol even at room temperature[108]. It has been shown[105,109,110] that the conversion into pyrazoles is more characteristic of pyrylium pseudobases. It is the main recyclisation pathway for pyrylium salts reacting with methylhydrazine[109] and benzenesulphonylhydrazine[110] and also for condensed pyrylium systems containing an activated γ-position and reacting with hydrazine hydrate (even in acetic acid)[111], but such

rearrangement takes place more slowly, usually on heating.

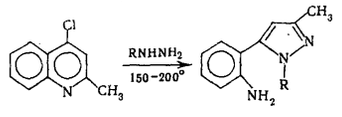
The interaction of hydrazine and its derivatives (phenylhydrazine and acid hydrazides) with pyrylium salts on heating in acetic acid leads to their recyclisation into *N*-aminopyridinium salts[105,112-116]. It has been shown[108,114] that 2,4,6-trimethylpyrylium perchlorate reacts with equimolar amounts of hydrazine hydrate even in an alcoholic medium with conversion into *N*-aminocollidinium perchlorate at a temperature as low as 0 – 5°C. Various substituted derivatives[117-119], including condensed pyrylium salts[108], were investigated in this reaction. The formation of two aromatic systems, pyrazole or pyridine, is probably due to competing processes which depend not only on the reactant ratio and the medium but also on the nature of the anion in the pyrylium salt[109], which affects the distribution of the electron density in the cyclic cation[120].

Balaban's scheme illustrated above includes also an interesting variant of the "pyrazole" recyclisation of arylpyrylium salts on heating in alcohol with an excess of phenylhydrazine, which involves a catalytic effect of the latter on the formation of the condensed pyrazoloquinoline system[121]. Under these conditions, neither hydrazine itself, nor hydroxylamine, nor various amines catalyse this reaction.

Recyclisation with hydrazines into *N*-aminopyridinium salts is characteristic of pyridinium salts[122-125]. It is also typical for their condensed analogues (isoquinolinium salts) and takes place under mild conditions in an alcohol – dioxan medium both with hydrazine and with its derivatives—phenylhydrazine, acid hydrazides, and thiosemicarbazide[125]:

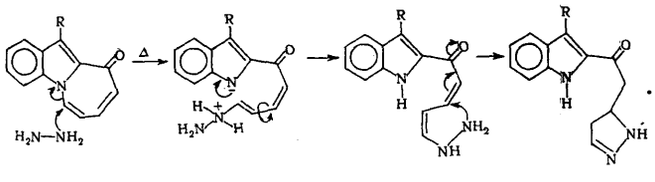


If the pyridinium ring contains an electronegative substituent in the 4-position, as in 4-chloroquinaldine, it is capable of recyclising into the pyrazole ring under the influence of hydrazine or phenylhydrazine[89]:



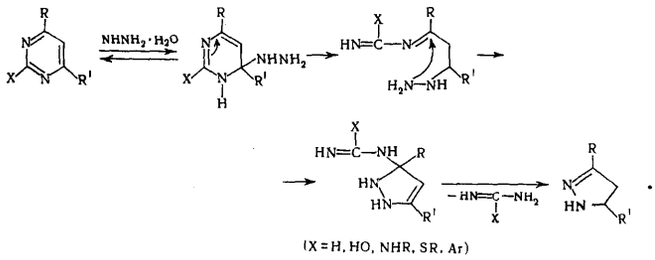
(R = H, Ph)

With increase of ring size, geometrical factors can assume a significant importance in recyclisation. For example, when indolinoazepinones react with hydrazine, the azepine ring is not converted into a six-membered derivative but into a five-membered derivative (pyrazoline)[126]:



Six-Membered Heterocycles with Two Heteroatoms in the Ring

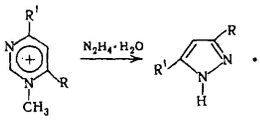
With increase of the number of heteroatoms in the ring, its electrophilic reactivity becomes enhanced and recyclisation reactions with hydrazine take place even without additional activating factors in the molecule. While unsubstituted or alkyl(aryl)-substituted pyridine bases do not undergo recyclisation under the usual conditions when acted upon by nucleophilic agents, pyrimidines are converted into the corresponding azole systems depending on the positions of the centres of nucleophilic attack. With sodium hydrazide[127], pyrimidines give high yields of pyrazole even at room temperature. With hydrazine hydrate and methylhydrazine, the conversion of pyrimidines into pyrazoles takes place under more severe conditions (130 – 200°C, 5 h).[128] It has been suggested that this process involves attack by the hydrazine molecule on the 4- or 6-position in the pyrimidine ring with its subsequent recyclisation, which is completed by aromatisation as a result of the elimination of a urea moiety[129]:



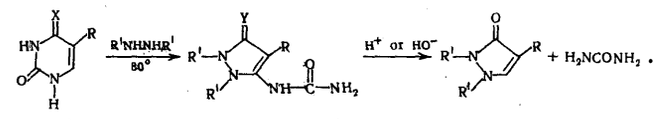
(X = H, HO, NHR, SR, Ar)

The recyclisation reactions of pyrimidines are extremely sensitive to the nature and position of the ring substituents. Electron-donating substituents (alkyl, aryl, OH, NH_2, SCH_3) in the 2- and 4-positions of the pyrimidine ring do not alter the above mode of reaction but polar groups appreciably accelerate it[130-134]. The electron-donating properties and the steric effect of the methyl group in the 4- or 6-position inhibit the reaction, which requires higher temperatures[129]. Depending on the substituents in the heterocyclic nucleus[131], in certain cases the interaction can lead only to hydrazinolysis products.

The quartenisation of one of the nitrogen atoms in the pyrimidine ring greatly facilitates the above recyclisation reaction without altering its outcome[129]:



In the series of certain biologically important pyrimidine derivatives, the following sequence of their reactivities in relation to hydrazine has been noted[133,134]: uracil, cytosine, thymine. In the reaction with methylhydrazines it is possible to isolate intermediates containing the ureide group, which is subsequently split off under the influence of alkali or acid[133]:

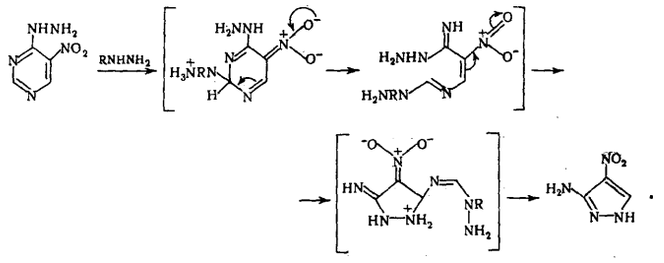


(R' = H, CH_3; X = O, NH; Y = O, NH, NNHR')

The hydrazinolysis of purines, pyrimidines, and the related nucleosides and nucleotides, which is completed by the formation of pyrazole systems, has been widely investigated in order to identify the pyrimidine bases[135-140].

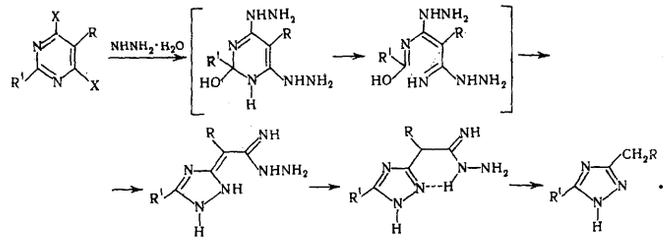
The introduction of powerful electron-accepting substituents into the pyrimidine ring has a significant influence on the distribution of electron density in the latter[130], with a corresponding alteration of the centres of nucleophilic attack, which influences the mode of the

recyclisation reaction. The effect of the nitro-group is particularly pronounced; when it is present in the 5-position, the recyclisation mechanism is significantly modified[141,142]. The reaction occurs even at room temperature in the presence of an excess of hydrazine (or methylhydrazine) and leads to aminopyrazoles. In contrast to the mechanism quoted above[129], nucleophilic attack by the hydrazine molecule on the 2- or 6-position in the heterocycle, its opening at the 2 — 3 bond, and recyclisation are suggested[142]. Under these conditions, the $N_{(3)}$ atom is converted into an exocyclic amino-group and the residue comprising the $N_{(1)} - C_{(2)}$ fragment of the pyrimidine ring is split off:



The above mechanism is confirmed by the reaction of methylhydrazine with 6-hydrazino-5-nitropyrimidine[142] which resulted in the isolation of the same pyrazole and not its methyl analogue.

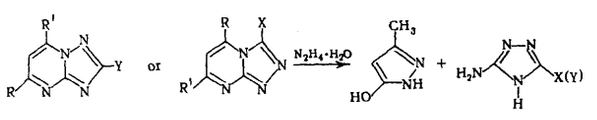
Pyrimidines containing polar substituents (OCH_3, $NHNH_2$) in the 4- and 6-positions are capable of transformation via a different pathway (with rearrangement of the ring to triazole)[128,143]. The reaction takes place with a 30 — 90% yield but under fairly severe conditions (210°C, 5 h):



According to van der Plas and Jongejan[143], the elimination of the carbazide residue is promoted by the formation of a hydrogen bond.

Special cases of the recyclisation of pyrimidines, occurring under severe conditions probably by ring fragmentation, are also known. Thus, on refluxing with hydrazine for 24 h, 4-hydroxy-6-methyl-2-phenylpyrimidine gives a 75% yield of 4-amino-3,5-diphenyl-1,2,4-triazole together with 3-methyl-5-pyrazolone.

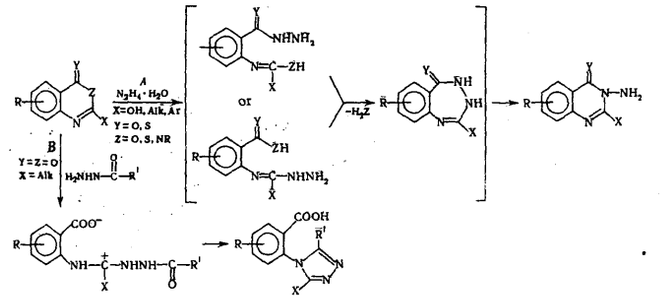
The recyclisation of condensed derivatives of pyrimidine containing the triazole ring, which is very resistant to the action of hydrazine, involves only the pyrimidine ring. It results in the formation of the corresponding pyrazoles and triazoles[144]:



(R = CH_3; R' = OH; X = SH, SAlk; Y = SAlk, NH_2, H)

The mode of reaction is not altered as the substituents (X, Y) in triazaindolizine are varied, but it is sensitive to substituents in the hydrazine molecule and the reaction does not occur when phenylhydrazine is employed.

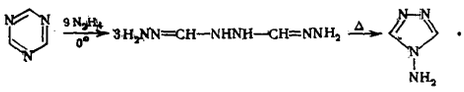
The recyclisation of the heterocyclic nucleus when hydrazine adds to quinazolones[145,146], benzoxazolones[147], and their thioanalogues[148], where a six-membered heterocyclic nucleus containing two different heteroatoms is condensed with the benzene ring, yields either *N*-aminoquinazolones (pathway *A*) or pyrazole derivatives (pathway *B*):



The rearrangement of benzoxazinones on reaction with benzoyl hydrazide, semicarbazide, and carbohydrazide leads to the formation of quinazolones. In the reaction with dicarboxylic acid dihydrazides, quinazolones are formed together with triazoles. In the reaction with formyl-, acetyl-, cyano-, nitro-, phenoxy-, and diaminoacetyl-hydrazines, triazoles are the main reaction products[147,149]. Owing to the higher nucleophilicity of the unsubstituted β-nitrogen atom compared with the α-nitrogen atom in the hydrazine fragment, the transformation of such systems via pathway *A* should occur, as suggested for benzothiazinethiones[148], via a diazepine structure with its subsequent rearrangement (of the type described below) to quinazoline, which is favoured by energy factors. If there is an acyl substituent at the β-nitrogen atom, the α-nitrogen atom, which has a steric advantage in this case, is probably involved directly in ring closure. However, such recyclisation is much slower. On the other hand, in the formation of triazoles by pathway *B*, the reactivity of the second competing carbonyl centre in the substituted hydrazine is decisive.

Six-Membered Heterocycles with Three and More Heteroatoms

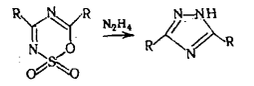
In the series of triazines, the mode of reaction with hydrazines is determined to a considerable degree by the nature of the substituents in both the ring and in the hydrazine derivatives employed. Unsubstituted *sym*-triazine in anhydrous hydrazine undergoes complex hydrazinolysis at a temperature as low as 0°C with subsequent recyclisation into *N*-aminotriazole:



Sym-disubstituted hydrazines do not react under these conditions, but semi- and thiosemi-carbazides and aminoguanidine yield respectively 3-hydroxy-, 3-mercapto-, and 3-amino-1,2,4-triazoles[150-153].

Among the recyclisation reactions of heterocycles containing several different heteroatoms in the ring, the

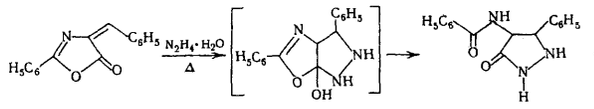
conversion of 4,6-diaryl-1,2,3,5-oxathiadiazine-2,2-dioxides into 3,5-diaryl-1,2,4-triazoles is known[154,155]:



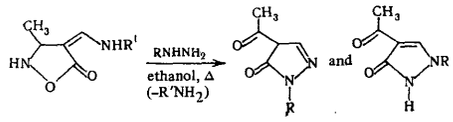
III. RECYCLISATION REACTIONS OF HETEROCYCLES WITH ONE CENTRE IN THE RING SUSCEPTIBLE TO NUCLEOPHILIC ATTACK

The recyclisation reactions of heterocyclic compounds containing one centre of nucleophilic attack in the ring and another in the side chain are nucleophilic addition or addition — elimination reactions involving polar multiple bonds. They can take place via two main mechanisms: with the intermediate formation of a bicyclic system and subsequent rupture of the initial ring or with preliminary ring opening after the initial addition of hydrazine and subsequent ring closure. The recyclisation pathway should be influenced mainly by steric factors and by the reactivity of the reaction centres. If the reaction centre in the ring adjoins the side chain but its reactivity is lower (or almost the same) than that of the electrophilic centre in the side chain, one may expect the reaction to proceed via an intermediate bicyclic compound. If, however, owing to the higher reactivity of the centre of nucleophilic attack, the primary addition of hydrazine begins at the heterocyclic nucleus, ring opening can take place initially†.

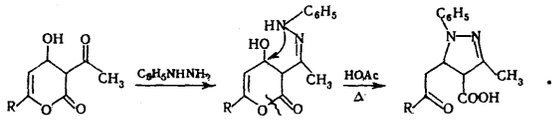
In the series of five-membered heterocyclic compounds, azlactones are probably recyclised[156] via the first pathway into the corresponding pyrazolidinones on heating with hydrazine:



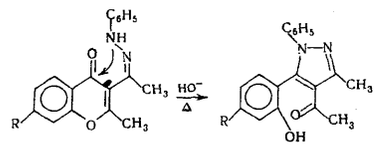
A similar reaction has been described also for isomeric isoxazolidinones[157]:



In the series of six-membered heterocycles such reactions are known for pyrone derivatives[158] on heating with substituted hydrazines in acetic acid:

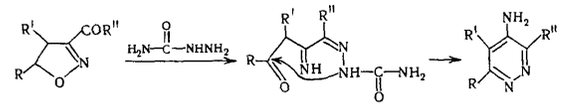


With condensed pyrone analogues (chromones), a similar conversion into pyrazole derivatives takes place under the influence of alkali[86]:



† See also Wamhoff and Korte[255].

The recyclisation of diacylfuroxans into dihydroxyiminopyrazolines[159] and of *N*-chloroethyl-2-oxazolidinone into N-aminoimidazolinone[160] under the influence of hydrazines has been described in the literature; the authors believe that it proceeds via the intermediate opening of the initial ring, which is a general characteristic of such systems[161]. The conversion of heterocycles in which the reaction centre in the ring does not adjoin the side chain with another electrophilic atom may proceed similarly and therefore the formation of a bicyclic system is hindered by steric factors. Under the influence of semicarbazide, acyl derivatives of isoxozole are converted into pyrazines[19,162]:



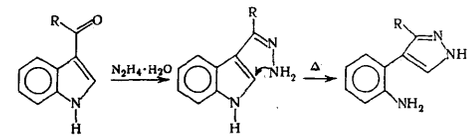
IV. RECYCLISATION REACTIONS DUE TO HETEROCYCLIC REARRANGEMENTS INVOLVING THE HYDRAZINE MOIETY IN THE MOLECULE

1. THE ALBERTI — BOULTON — KATRITZKY REARRANGEMENT OF HETERYLHYDRAZINES

The Alberti — Boulton — Katritzky rearrangement is a special case of recyclisation reactions involving one centre of nucleophilic attach in the ring. Heterocycles containing an electrophilic centre adjoining the ring heteroatom with a substituent containing the hydrazine group in the α-position relative to the electrophilic centre are capable of undergoing such rearrangement. The rearrangement consists in the formation of a new ring via an intramolecular interaction of the hydrazine nitrogen atom in the side chain with the electrophilic centre of the initial heterocycle.

Both a carbon atom and heteroatoms such as nitrogen (usually in the sp^2-hybridised state) can behave as an electrophilic centre in the heterocycle. The rearrangement takes place under the action of heat or bases.

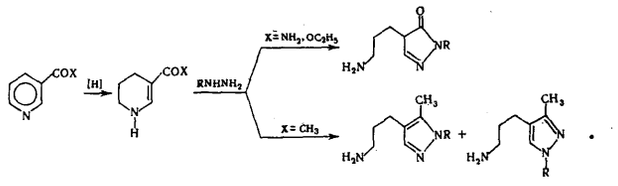
The rearrangement of heterocycles with a carbon atom as the electrophilic centre was discovered by the Italian chemist Alberti[163], who showed that, when 3-acetylindoles are heated in an alcoholic medium with hydrazine hydrate, a hydrazone is formed initially and then isomerises further to a pyrazole derivative[163,164]:



Alberti suggested that heterocyclic compounds containing the group $-X-C=C-CO-R$, where X is the heteroatom, undergo a similar recyclisation when acted upon by hydrazine[165]. The reaction was extended to other classes of heterocycles containing an acyl substituent in the β-position relative to the ring heteroatom—the thionaphthene, pyrrole, quinoline, and γ-pyrone series, from which pyrazole derivatives were obtained. However, whereas in the indole, γ-pyrone, and γ-chromone series the rearrangement takes place when the initial components are refluxed in alcohol, in the pyrrole and quinoline series heating to 160 — 165°C in an autoclave is required[166-168].

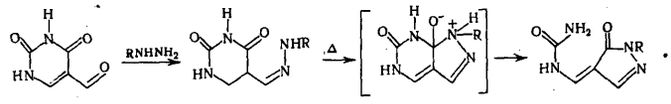
The conditions governing the rearrangement were examined in a series of studies by Alberti[169-174].

Recyclisation reactions of various heterocycles with an electrophilic centre in the α-position relative to the acyl group were described later. These reactions evidently proceed via the same rearrangement. They usually occur when the heterocycle is heated briefly with hydrazine but the intermediate hydrazone was not always identified. Thus pyrazole derivatives were obtained in high yields from acyltetrahydropyridines[175,176]:

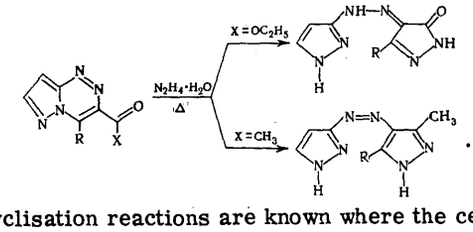


The reaction can serve as a convenient method of synthesising aminoalkylpyrazolones or pyrazoles from acylpyridines, which are readily reduced to tetrahydroderivatives.

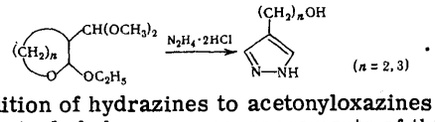
In the above examples, an olefinic carbon atom served as a centre of nucleophilic attack in the ring. In pyrimidine derivatives [177] the carbon atom of a carbonyl group functions as a centre of this type:



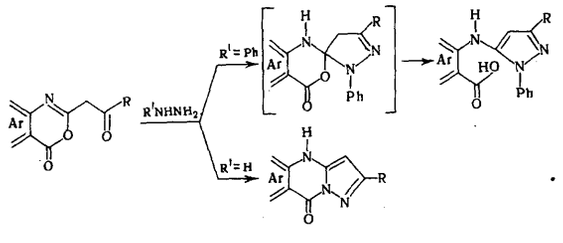
The rearrangement can occur also in systems such as pyrazolotriazines[178], where the electrophilic centre adjoins a bridging heteroatom:



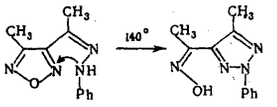
Recyclisation reactions are known where the centre of nucleophilic attack in the ring is a saturated carbon atom subjected to the influence of two electronegative heteroatoms—endocyclic and exocyclic. Here the rearrangement is based on a substitution reaction. Such rearrangements occur readily in both five-membered and six-membered heterocycles[82]:



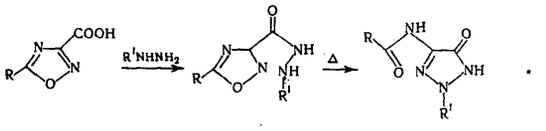
The addition of hydrazines to acetonyloxazines can probably be included among rearrangements of this kind [179,180]; the outcome of the reaction depends in this case on the presence of substituents in the hydrazine. Here isomerisation proceeds via an intermediate spirocompound:



Boulton and Katritsky[181-183], who studied heterocyclic isomerisations, greatly extended the scope of this rearrangement and established that a nitrogen atom can also serve as a centre of nucleophilic attack in the ring. For example, acetylfurazan phenylhydrazone can be converted into a 1,2,3-triazole system on heating in dimethyl sulphoxide in the presence of alkali[181]:



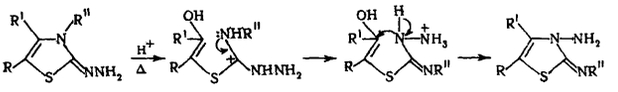
Hydrazine derivatives of 1,2,4-oxadiazoles[184] and isoxazoles[185,186] isomerise similarly into triazole. The rearrangement can proceed not only with participation of a base but also under the influence of heat. 1,2,4-Oxadiazole-3-carboxylic acid hydrazides isomerise almost quantitatively into a triazole system[187] not only under the influence of a base but also on heating above the melting point:



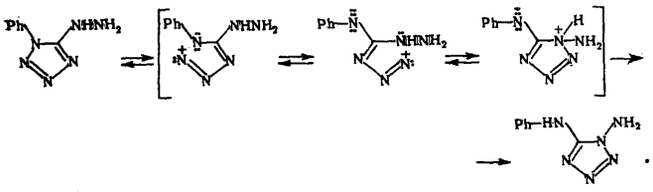
It is noteworthy that in almost all the cases considered a similar rearrangement occurs also in the presence of another two-centre nucleophilic agent—hydroxylamine.

2. THE DIMROTH REARRANGEMENT OF HYDRAZINE CONTAINING HETEROCYCLES

The Dimroth rearrangement consists in the interchange of endocyclic and exocyclic heteroatoms (together with their substituents) adjoining the same carbon atom in the ring and proceeds via ring opening in the presence of acids and bases or under the influence of heat. For example[188,189]:



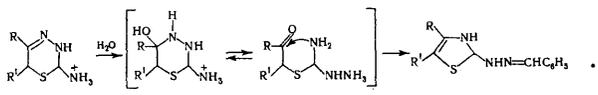
Dimroth observed the rearrangement in the series of 5-amino-1,2,3,4-tetrazoles[190,191]. Nirenburg and Postovskii described a similar thermal isomerisation and its mechanism for 5-hydrazino-1,2,3,4-tetrazoles[192]:



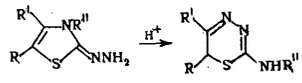
Hydroxylic solvents are the most suitable media for such isomerisations.

A number of general relations noted by Wahren[193] for the Dimroth rearrangement are also typical for heterocyclic hydrazines, although the latter have their own characteristic features. Here the rate of isomerisation should depend on the electron density at the α-carbon atom[194-197]. An important characteristic of the rearrangements of hydrazine-containing heterocycles is that the hydrazine group can participate in the isomerisation via the α- or β-nitrogen atom. Frequently the α-nitrogen atom is more reactive regardless of whether the β-atom is substituted or free. This may be due to the marked

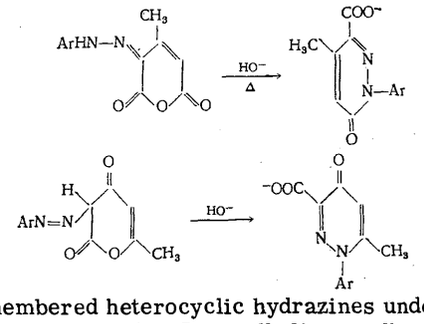
polarisation of the α-nitrogen atom of the hydrazine group in the acyclic intermediate owing to the influence of electronegative substituents. As a result, it can give up a proton to the polar medium, becoming more nucleophilic in the ring closure reaction. This variant corresponds to the Dimroth rearrangement where the ring sizes before and after isomerisation remain unchanged[193]. From the standpoint of the process mechanism, this limitation is hardly obligatory for hydrazine-containing compounds. When 3-amino-5,6-dimethyl-1,3,4-thiadiazine hydrochloride is heated with benzaldehyde in alcohol, ring contraction takes place with formation of the corresponding thiazolehydrazone[198]. Such recyclisation fits quite satisfactorily within the framework of the Dimroth rearrangement, which follows from the following mechanism:



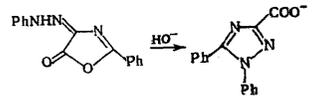
The example considered constitutes, as it were, a retrorearrangement in relation to the isomerisation of heterocyclic hydrazines accompanied by ring expansion where the hydrazine residue is involved via the β-nitrogen atom. Thus the conversion of thiazolehydrazones into thiadiazines is known[199]:



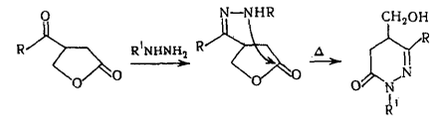
The isomerisation reactions of hydrazine-containing heterocycles accompanied by the exchange of complete fragments of the ring are probably related to the Dimroth rearrangement. For example, the isomerisation of hydrazinopyrones to pyridazones, which occurs on heating in an alkaline medium[200-202], constitutes an exchange of the exocyclic hydrazine group in the β-position in the ring with the endocyclic —CO—O fragment. Here the hydrazine group does not adjoin the ring heteroatom and it enters the ring via the β-nitrogen atom and not the α-atom:



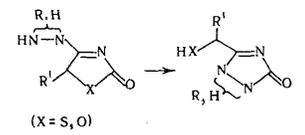
Five-membered heterocyclic hydrazines undergo a similar rearrangement. In an alkaline medium, 4-phenylhydrazono-2-phenyloxazolin-5-one undergoes a very rapid quantitative conversion even at room temperature into 3-carboxy-1,5-diphenyl-1*H*-1,2,4-triazole[203]:



Rearrangements involving the β-nitrogen atom of the hydrazine group are regarded in the literature also as transannular addition of hydrazine[126] which does not proceed via a preliminary hydrazinolysis of the initial ring. An attack on the ring electrophilic centre by the hydrazine β-nitrogen atom has been suggested; it takes place via a transannular mechanism and leads to an intermediate bicyclic system in a manner similar to the formation of bicyclic acetals and lactones in the pyran series. For this purpose, the hydrazine group or the substituents containing it should be located at a tetrahedral carbon atom in a ring in which there is a sterically accessible electrophilic centre. According to Wamhoff and Korte[204], the hydrazones of β-acyl-γ-lactones isomerise on heating to pyridazines via a transannular mechanism:



In heterocyclic compounds where the hydrazine group is attached to an unsaturated carbon atom, transannular rotation is difficult owing to the rigidity of the bond. However, it becomes possible under the influence of alkalis or other nucleophilic agents, which results in a tetrahedral configuration of the carbon atom linked to the hydrazine group. The isomerisation of hydrazinoazolidinones[41,205-207], occurring in alkaline media or on heating, has been interpreted in this way. Here a second molecule of the hydrazinoazolidinone behaves as the nucleophilic agent:



(X = S, O)

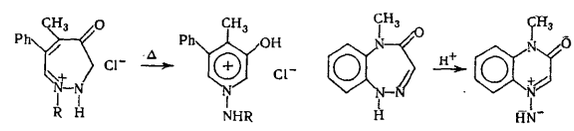
Various substituted hydrazinoazolidinones (derivatives acylated at the hydrazine group, hydrazones, and azines) undergo similar rearrangements.

The Dimroth rearrangement can occur in complex reactions and is accompanied by the cleavage of unstable components of the molecule. For example, the recyclisation of uloses into pyrazole derivatives in an acid medium, via the corresponding hydrazone, is known[208,209]. Alkaline cleavage of imidazophthalazine[5], the recyclisation of 2-hydrazino-4-hydrazono-3-phenylquinazoline into 2-anilino-4-hydrazinoquinazoline[210], etc.[113,211] also involve the Dimroth rearrangement.

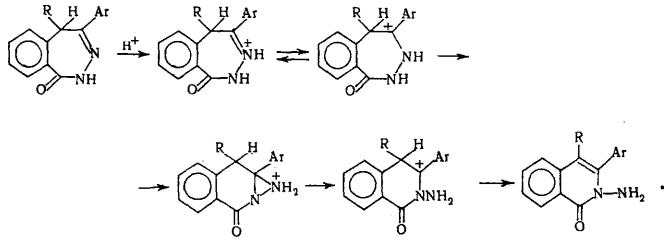
3. REARRANGEMENT OF CYCLAZINES

Heterocyclic compounds containing an endocyclic hydrazine group and multiple bonds are capable of a rearrangement involving the contraction of the ring by one nitrogen atom, which passes to an exocyclic *N*-imino- or *N*-amino-group. The rearrangement, which takes place under the influence of heat or an acid, is characteristic of various six-membered and seven-membered azine systems: diazines, triazines, tetrazines, and diazepines.

Depending on the structure of the initial cyclazine, the final isomerisation products may be betaines or cyclic *N*-amines. 4-Oxo-2,3-dihydro-1,2-diazepines[212] or 4-oxo-1*H*-4,5-dihydro-1,2,5-benzotriazepines rearrange to betaines:

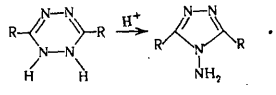


If there is a possibility that the charge in the betaine structure may be compensated by the β-elimination of a proton, the final product is a cyclic *N*-amine[98]:

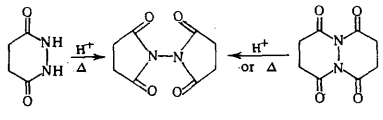


The isomerisation of cyclazines may be regarded as an endocyclic sextet rearrangement. The above scheme shows that its mechanism involves[98-100,141,212,213] an endocyclic interaction between the nitrogen atom of the hydrazine moiety and an activated unsaturated carbon atom or a carbonium centre with formation of an intermediate three-membered condensed ring, the opening of which results in the liberation of the amino group. The role of the acid as a catalyst reduces to the protonation of the heteroatom adjoining the sp^2-hybridised carbon atom. However, one should note that, under certain conditions, one cannot rule out the possibility that such a rearrangement can also proceed via a preliminary hydrolytic ring opening at the azomethine linkage with subsequent ring closure under acid conditions, as rule via the α-nitrogen atom of the hydrazine group.

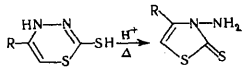
The cyclic *N*-amine rearrangement is very characteristic of tetrazines, which are readily converted in an acid medium into *N*-aminotriazoles[214,215]:



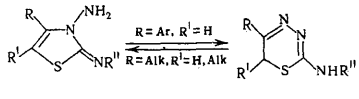
The isomerisation of cyclic hydrazides[216,217], including hydrazides condensed with ring systems[216,218] and their thioanalogues[219], allows a ready synthesis of *NN'*-bis-succinimides, *N*-aminothiazolethiones, and *N*-aminohydantoins:



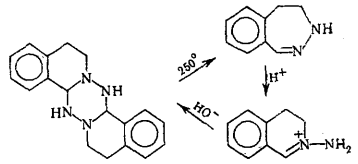
Cyclic thiohydrazides and thiadiazinethiols[219], for which a Dimroth rearrangement might have been expected in an acid medium, undergo preferentially the cyclic *N*-amine isomerisation:



Depending on the structure of the compound, it is possible to achieve the reverse transition from cyclic *N*-amines to cyclazines. Such interconversion has been described for the thiadiazine — *N*-aminothiazole series[199] and others[22,23]:

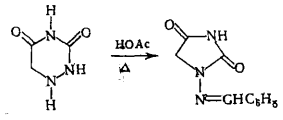


The cyclic *N*-amine rearrangement and its retrovariant were observed by Schmitz and Ohme[220].

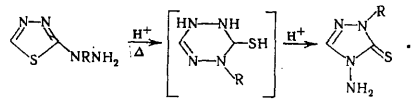


One may suppose that the retrorearrangement also proceeds via the intermediate formation of a three-membered condensed ring.

The cyclic *N*-amine rearrangement can occur in combination with other reactions. On heating with aldehydes, usually in the presence of acetic acid, cyclic hydrazides are converted directly into the corresponding cyclic *N*-arylideneamines[217]:



Complex recyclisation reactions may be also accompanied by the above type of isomerisation, as happens, for example, in the conversion of hydrazinothiadiazoles into *N*-aminotriazolethiones[221]:

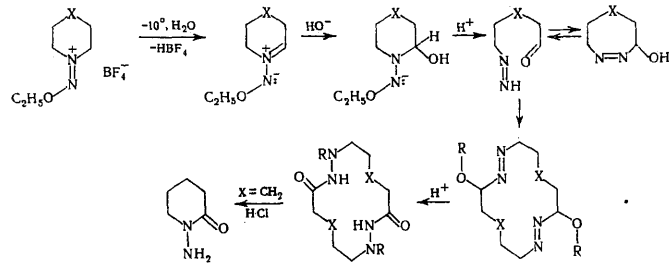


On reaction with hydrazines, certain isochromones recyclise directly into isoquinolinones[98].

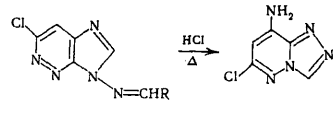
V. OTHER REARRANGEMENTS AND RECYCLISATIONS OF HYDRAZINE-CONTAINING HETEROCYCLES

The reactions of heterocycles involving hydrazines which are described in the literature can be usefully examined separately owing to their characteristic features. Here we shall be concerned also with the recyclisation reactions of small rings under the influence of hydrazines.

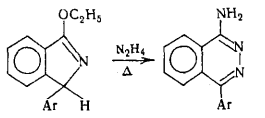
In an alkaline medium under very mild conditions, substituted iminopiperidinium and iminomorpholinium salts undergo a dimerisation recyclisation with formation of a macroring, which in the case of piperidinium recontracts under the influence of acids into the aminopiperidine system[222,223]:



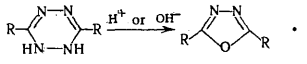
The recyclisation of imidazopyridazine derivatives into triazolopyridazines, which occurs on heating in an acid medium, was described recently[224]:



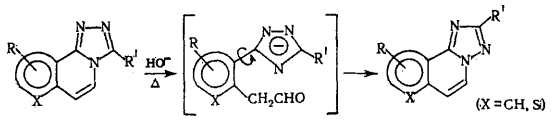
The reaction of 1*H*,1-aryl-3-ethoxyisoindolinenes with hydrazine, with recyclisation into benzopyridazines, is somewhat unusual:



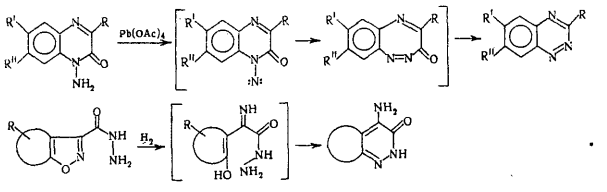
Certain substituted tetrazines are converted in acid or alcoholic alkaline media into oxadiazoles and not into *N*-aminotriazoles. The reaction is greatly influenced by the nature of the ring substituent[56,226-228]:



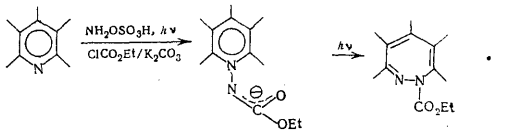
Thermal recyclisation of tetrazines into pyrazoles is also known[229]. On heating in alkaline media, triazoloisoquinolines and triazolothienopyridines undergo an isomerisation involving the hydrazine moiety of the triazole ring[230]:



In many cases recyclisation reactions involving the hydrazine group in the molecule can occur as a result of oxidation — reduction processes[231-233]:

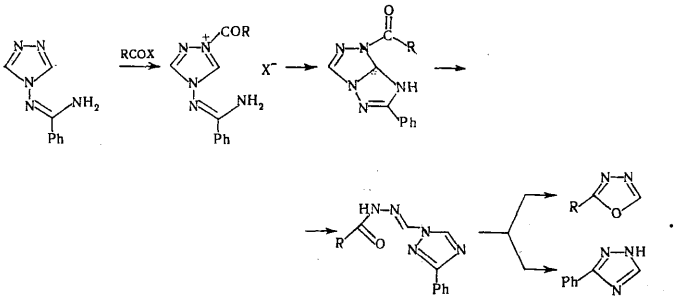


Photochemical recyclisation reactions of heterocycles involving the hydrazine moiety are known for a series of five-membered[234] and six-membered heterocycles, in particular the conversion of *N*-aminopyridines into diazepines[235,236]:

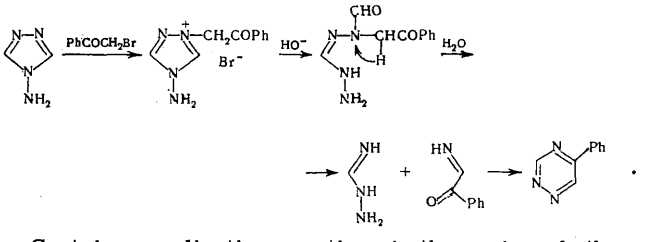


Relay Syntheses

In a series of studies by Becker and coworkers[237-244], recyclisation reactions of hydrazine-containing heterocycles, called relay syntheses, are described. They consist of ring opening and closure, for example the formation of triazole rings, accompanied by fragmentation. Despite their complex mechanism, these syntheses usually take place smoothly and they are of preparative value. As an example, one may quote the coupled recyclisation reaction of triazole derivatives[239]. It can be divided into stages or can be carried out successfully in one stage:



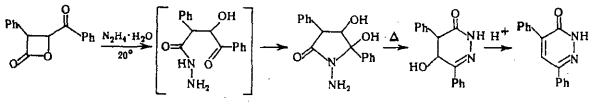
The authors believe[240] that relay syntheses can be achieved via complete fragmentation of the ring with its subsequent reassembly into a new ring, as shown in the following scheme:



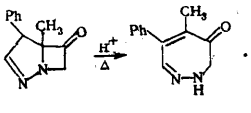
Certain recyclisation reactions in the series of other heterocycles (oxadiazolopyrimidines[245] and amino-oxadiazolium salts[246]), which permit a conversion into triazole and imidazole derivatives, can also be included among the relay syntheses.

Recyclisation Reactions of Small Rings

The recyclisation reactions of small rings under the influence of hydrazines are accompanied by ring expansion. Cyclic β-ketoesters form bicyclic pyrazole derivatives. According to Jacobs[247], the synthesis of 3-methyl-1-phenylpyrazol-5-one from diketen and phenylhydrazine is of industrial interest. In the series of β-lactones, the rearrangement of a four-membered ring to a six-membered ring takes place by successive recyclisation; under certain conditions, the intermediate heterocycles were isolated and identified[248]:



The bicyclic pyrazoline system condensed with a four-membered ring via a C — N bond isomerises to a diazepine structure on heating in a weakly acid medium[249,250]:



Three-membered rings usually rearrange to five-membered rings and more rarely to six-membered rings, mainly depending on the nature and positions of the substituents in the small ring. Reaction involving the recyclisation of aziridines into pyrazoles[247], pyrrolines[251], and imidazoles[252], of azirines into a six-membered triazine system[253], and of oxirans into pyrazoles[247,254], are known.

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Non-standard Phosphorus-containing Derivatives of Carbohydrates

E.E.Nifant'ev and I.P.Gudkova

The review deals with the analogues of natural carbohydrate phosphates modified in the phosphorus-containing fragment. Synthetic pathways leading to compounds which are of greatest interest owing to their chemical properties and their behaviour in certain enzymatic reactions have been examined.
The bibliography includes 110 references.

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I. INTRODUCTION

Numerous studies on the synthesis and chemical properties of phosphorus-containing carbohydrate derivatives and their applications in biochemical studies have been published. As a rule sugar mono-, di-, and tri-phosphates or phosphoramidates were investigated. Such substances are either natural products or their close analogues, differing in detailed features of the ester groups.

However, there exists another group of phosphorus-containing carbohydrate derivatives consisting of derivatives of phosphorus-containing acids which have not been detected hitherto in animal and plant organism. The importance of these substances (we shall call them "non-standard phosphorus-containing derivatives of carbohydrates")† is evident, since they can be widely used to investigate many questions of sugar metabolism at a molecular level and to elucidate the structure of the active centres in the corresponding enzymes. Moreover, some of the above types of compounds are of interest for the synthetic chemistry of carbohydrates.

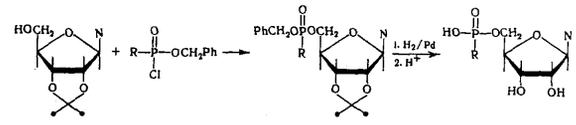
The non-standard phosphorus-containing carbohydrate derivatives were begun to be investigated mainly recently and in the literature there are no reviews dealing with their chemistry. Bearing this in mind, we undertook the writing of the present review, which covers the literature mainly up to the end of 1970: the first section deals with problems of the chemistry of phosphorus(V) acid derivatives and the second with phosphorus(III) acid derivatives. Each section begins with a description of phosphorylated pentoses.

II. DERIVATIVES OF PHOSPHORUS(V) ACIDS AND CARBOHYDRATES

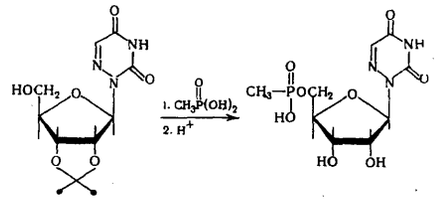
Among other non-standard phosphorus-containing carbohydrate derivatives, the phosphonic analogues of natural phosphates have been most widely investigated both chemically and biochemically and therefore the first subsection of the first section will be devoted to them. Alkylphosphoric, phosphoramidic, and phosphorothioic acid esters of carbohydrates and some of their derivatives containing quinquevalent phosphorus will be considered next.

1. Carbohydrate Phosphonates‡

The phosphonates of natural sugars were obtained for the first time in 1951 by Todd[3], who described analogues of adenosine 5'-phosphate, and uridine 5'-phosphate containing phenyl- and ethyl-phosphonic acid residues instead of the orthophosphoric acid residue. These esters were synthesised by phosphorylating 2',3'-*O*-isopropylidene-adenosine and 2',3'-*O*-isopropylideneuridine by the corresponding phosphonochloridic acid with subsequent elimination of the protecting groups:



Subsequently the synthesis of nucleoside phosphonates was investigated by Holý[4]. By allowing 2',3'-*O*-isopropylidene-6-azauridine to react with pyridinium methylphosphonate in the presence of dicyclohexylcarbodi-imide, he obtained 6-aza-uridine 5'-methylphosphonate:

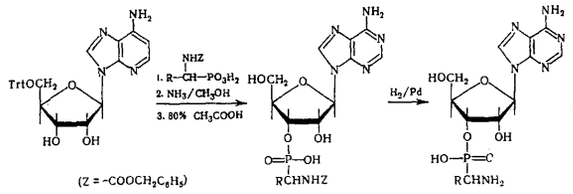


When 5'-*O*-acetylazauridine is used as the starting material, 6-azauridine 2'(3')-methyl-phosphonates are formed.

† One should bear in mind that the term "non-standard phosphorus-containing carbohydrate derivatives" is to some extent arbitrary. Recently phospholipids[1] and an antibiotic[2] belonging to the class of phosphonic acids have been found in natural products and therefore it now appears quite likely that phosphonates and other unusual sugar derivatives will be detected among products of plant and animal origins.

‡ This subsection will also deal with the esters of other acids with C–P bonds containing two or three phosphorus atoms. Such acids, which do not have generally accepted names as yet, will be combined under the term "phosphonic" just as orthophosphoric, pyrophosphoric, and triphosphoric acids are frequently referred to as "phosphoric" acids.

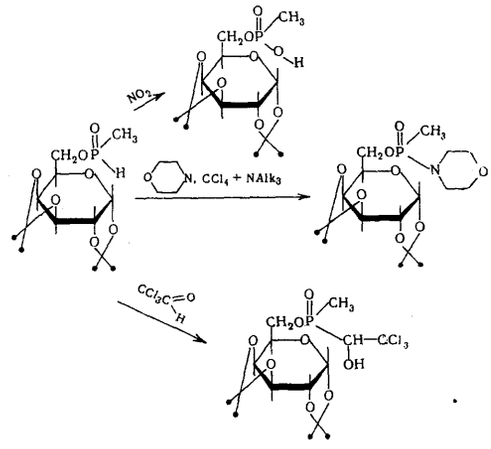
Žemlička and Chladek[5] obtained by this procedure the phosphonic analogues of 2′(3′)-*O*-alanyl- and 2′(3′)-*O*-phenylalanyl-adenosines in which the carboxy-group of the aminoacyl residue was replaced by the H–O–P=O group:



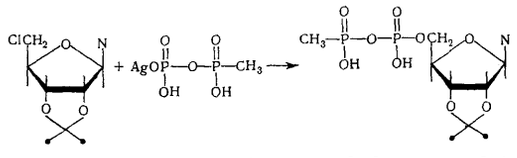
According to preliminary data, α-aminophosphonates of nucleosides inhibit the biosynthesis of certain peptides; in this respect they behave similarly to the antiobiotic chloramphenicol.

Comparison of the above two methods of synthesis of nucleoside phosphonates shows that the latter is preferable, since it is simpler, gives better yields of the desired compounds, and requires much more readily available phosphorylating compounds.

Carbohydrate phosphonates may be also obtained from the corresponding phosphonites. Thus 1,2;3,4-di-*O*-isopropylidenegalactose-6-methylphosphonite was oxidised to the corresponding methylphosphonate[6]. The same phosphonite was made to react successfully with morpholine and carbon tetrachloride to form a phosphonamidate, and with chloral to form 1,2;3,4-di-*O*-isopropylidenegalactose-6-ββ-trichloro-α-hydroxyethylmethylphosphinate:

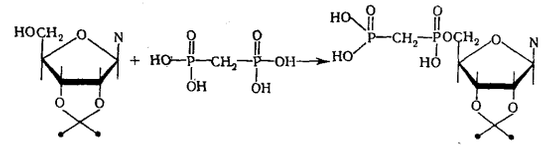


In the first half of the 1960's, the analogues of nucleoside pyrophosphates, in which one of the acid hydroxy-groups was replaced by a carbohydrate substituent, were investigated. Two methods were proposed for the synthesis of these compounds. The first consists of the interaction of a 5′-deoxy-5′-halogenonucleoside, the hydroxy-groups of which are protected, with a metal salt of the corresponding acid[7], for example:

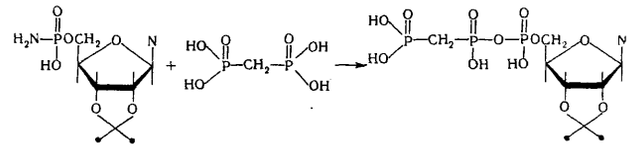


This investigation cannot be regarded as complete. The point is that the structures of the compounds obtained have not been proved. Indeed one can imagine the formation of two pyrophosphonate isomers in one of which the sugar is linked to the phosphate fragment of the acid residue and in the other to the phosphonate fragment. On the basis of general concepts concerning the electronic effects in the series of phosphorus-containing acids, one can postulate a greater probability of the formation of the second structure, while the authors chose the alternative structure without any explanation. The second method, which was investigated in greater detail, is based on the reaction of nucleotides with alkylphosphonic acids in the presence of dicyclohexylcarbodi-imide[8] or another condensing agent[9,10].

Analogues of nucleoside di- and tri-phosphates in which one of the oxygen bridges between the phosphorus atoms has been replaced by a methylene unit have also been described in the literature. It has been suggested that these nucleoside diphosphonates be obtained by the condensation of partly protected nucleosides with methylenediphosphonic acid in the presence of condensing agents[10], for example:



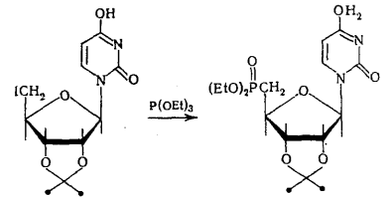
Myers et al. proposed two methods for the preparation of phosphonic analogues of adenosine triphosphate[10]. In the first, adenosine 5′-phosphoramidic acid is allowed to interact with methylenediphosphonic acid:



In the second method adenosine 5′-monophosphate is condensed with methylenediphosphonic acid under the influence of dicyclohexylcarbodi-imide. The first method gives a higher yield of the final product, while the second is simpler.

The compounds described above are of definite interest from the standpoint of biochemical studies of those reactions in which the dissociation of phosphoanhydride linkages is postulated[11,12].

Compounds in which there is a direct covalent bond between the phosphorus atom and the carbon atom of the main sugar chain are extremely interesting phosphonic analogues of natural phosphates. Such structures were obtained for the first time by the Arbuzov reaction. Bannister and Kagan synthesised in this way diethyl 5′-deoxyuridine 5′-phosphonate[13]:

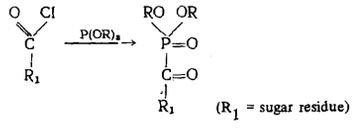


In the hydrolysis of the diethyl phosphonate under severe conditions, undertaken to eliminate the *O*-ethyl groups, the sugar molecule decomposed and the free phosphonic acid could not be isolated. Griffin and Burger reported[14] that this difficulty may be overcome by using specially

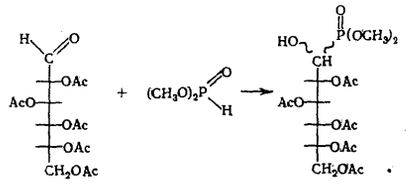
selected esters with a high chemical lability, for example benzyl phosphonates. However, it is difficult to achieve this reaction, since the required phosphonates are obtained from phosphites which enter into the Arbuzov reaction with difficulty. Thus, according to Holy's data, phosphites with 2-cyanoethyl, 2-chloroethyl, 2,2,2-trichloroethyl, and benzyl groups are not alkylated satisfactorily by halogenodeoxynucleosides. Therefore Holy suggests the use of tri-(2-benzoyloxyethyl) phosphite which gives a satisfactory result; however, in this case one has to employ a multistage procedure for the removal of protecting groups[15]. On the basis of the results of Maruszewska-Wieczorkowska et al.[17], Rammler et al.[16] suggest that the phosphite group be protected with allyl groups, which can be subsequently removed by catalytic hydrogenolysis.

Apart from riboside derivatives, derivatives of 6-halogeno-6-deoxyhexoses have been introduced into the Arbuzov reaction: 6-bromo-6-deoxytetra-acetylglucopyranose[14], 7-(2,3,4-tri-*O*-acetyl-6-bromo-6-deoxy-β-D-glucopyranosyl)theophylline[18], and 6-benzamido-9-(2,3,4-tri-*O*-acetyl-6-bromo-6-deoxy-β-D-glupyranosyl)purine[19]. In all these cases, substances differing sharply in hydrolytic stability from the corresponding phosphates were synthesised. It is significant that the phosphonic acids obtained are structurally very similar to the related hexose-ω-phosphates, but they possess a skeletal system of covalently linked atoms which is shorter by one unit.

Recently Zhdanov and coworkers[20] extended the Arbuzov reaction to aldonic acid chlorides and obtained a new type of sugar derivative in which the phosphorus atom is linked directly to the first carbon atom of the carbohydrate chain:

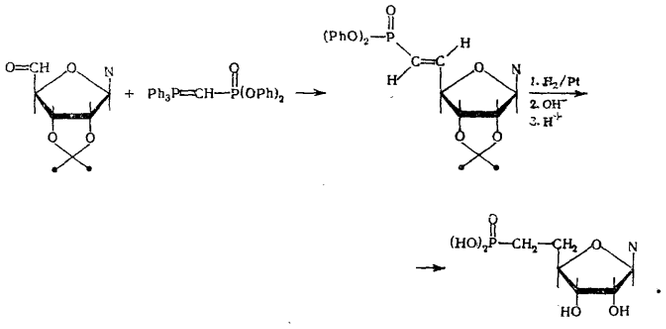


Apart from the Arbuzov reaction, other fundamental methods of the chemistry of organophosphorus compounds, in particular the Abramov and Wittig reactions, may be employed for the synthesis of the phosphonic analogues of sugar phosphates under discussion. Certain esters of phosphonic acids containing a hydroxy-group at the α-carbon atom (in relation to phosphorus) have been obtained by the Abramov reaction[21,22], for example:



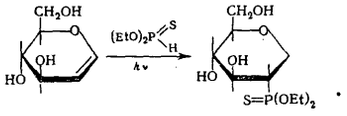
The authors suggest that the products be employed as insecticides.

The Wittig reaction makes available compounds in which the phosphorus atom is joined to the polyol fragment of the carbohydrate residue by an ethylene link. Thus, when modified adenine- or uridine-nucleosides with an aldehyde group at the 5′-carbon atom react with the corresponding Wittig reagent, the following products are obtained after hydrogenation[23]:

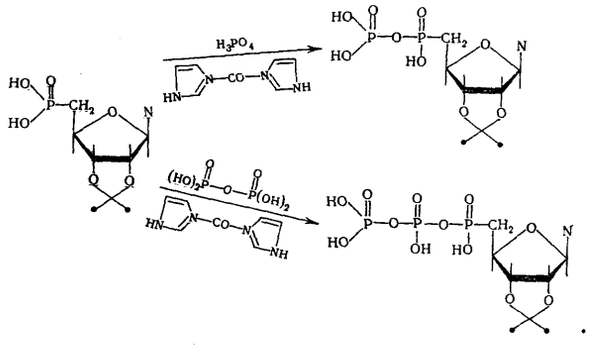


Phosphonic acid derivatives of carbohydrates containing a direct linkage between the phosphorus atom and a carbon atom in the sugar residue can also be synthesised by oxidising the corresponding phosphonous acids which have become available recently (see p. 858–859).[24]

There are literature data on the synthesis of a number of esters of the thioanalogues of the phosphonic acids under consideration. For this purpose, diethyl phosphorothioite was linked to unsaturated sugars[25], for example:



A method based on phosphonic acid derivatives of carbohydrates has been developed for the synthesis of phosphonate analogues of sugar diphosphates and triphosphates differing structurally from the esters with two and three phosphorus atoms already mentioned. The synthesis is carried out according to the following simple scheme[16] using inorganic phosphates and pyrophosphates in the presence of the usual condensing agents:



2. Carbohydrate Alkyl Phosphates

This subsection deals with compounds having the general formula nucl–O–P(=O)(OR)–OR and nucl–O–P(=O)(OH)–OR which are of direct interest for biochemical research. We shall not

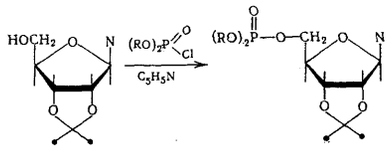
consider the numerous esters of this type which are used solely as intermediates in syntheses, for example, of benzyl, phenyl, and 2-cyanoethyl phosphate derivatives of sugars. The literature data on this problem have already been discussed[26].

Nucleoside dialkyl phosphates were obtained by the usual methods developed in the chemistry of organophosphorus compounds. The main problem, always arising in the extension of the phosphorylation procedures to carbohydrates, was the choice of suitable protecting groups.

Todd and coworkers[27] described the synthesis of the dimethyl ester of uridine 3′-phosphate by treating the corresponding acid with diazomethane. Szer and Shugar[28] extended their method to the synthesis of the dimethyl esters of uridine 5′-phosphate and cytidine 5′-phosphate. Later the reaction with diazomethane was investigated in detail for several mononucleotides[29] and *N*-aminoacid derivatives of nucleotides[30]. It was shown that not only the phosphate fragment but also the heterocyclic ring is methylated, the latter pathway being preferred.

Probably this side reaction also occurred in the earlier investigations[27,28].

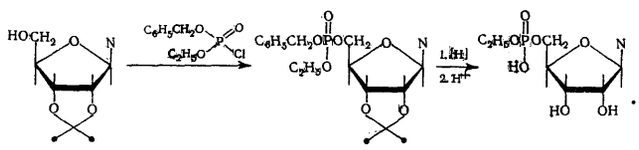
Montgomery et al.,[31] Libman and Heidelberger[32], and later Šorm[33] investigated another method of synthesising alkyl nucleoside 5′-phosphates. It consists of the interaction of 2′,3′-isopropylidenenucleosides with dialkyl phosphorochloridates in the presence of pyridine:



We shall now consider the monoalkyl esters of nucleotides. In a number of studies it has been stated that the desired compounds are formed on partial hydrolysis of the corresponding neutral esters[27,28,31-33]. Probably this procedure is of no preparative value, since under the conditions of such treatment the bond linking the phosphorus atom to the sugar residue is the first to dissociate.

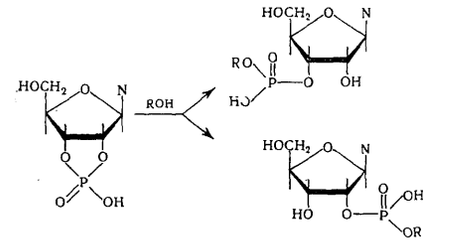
An unsuccessful attempt to obtain the methyl ester of uridine 5′-phosphate by treating the nucleoside with methyl phosphorodichloridate in the presence of pyridine has been described. In this case the main reaction product was the nucleotide. When ethyl phosphorodichloridate is employed, a mixture of products is obtained[34].

The monoethyl esters of adenosine and uridine 5′-phosphates were obtained by the reaction of 2′,3′-*O*-isopropylidenenucleosides with benzyl ethyl phosphorochloridate and subsequent elimination of the isopropylidene and benzyl protecting groups[35]:

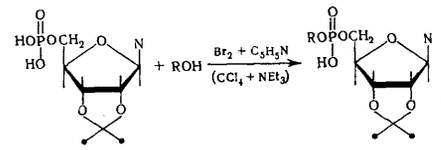


Another method of synthesising alkyl nucleoside 5′-phosphates consists of the treatment of a mixture of the alcohol and the nucleotide with carbodi-imide[33,36]. Despite the weak nucleophilic properties of alcohols compared with those of the phosphate anion, a large excess of the alcohol ensures that the reaction takes place in the required direction.

Alcoholysis of nucleoside 2′:3′-cyclicphosphates by primary alcohols, catalysed by both bases[37] and acids[38] (the latter is preferable), leads to a mixture of alkylnucleoside 2′- and 3′-phosphates:



An interesting method for the preparation of nucleoside esters with monoalkylphosphoric acids is the oxidative phosphorylation proposed by Todd[39]. The synthesis is carried out according to one of two variants—using bromine in pyridine as the oxidising system or carbon tetrachloride and triethylamine:

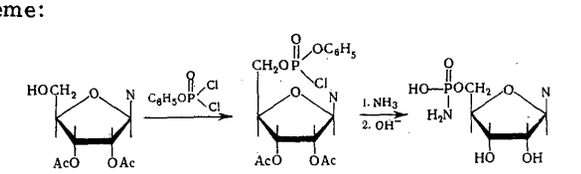


The alkyl esters of nucleotides are of interest in the study of certain problems in molecular biology. Thus it has been shown that they increase the permeability of cell membranes to nucleotide analogues[32]. Moreover alkyl esters of nucleotides have been used in the synthesis of highly specific chemical modifying agents for nucleic acids[40].

3. Carbohydrate Phosphoramidates

Numerous studies have been devoted to the phosphoramidates of various sugars. In the present review we have excluded from consideration those compounds with a P–N bond which are of purely synthetic importance. Data concerning the very interesting aminoacid derivatives of nucleotides have also been omitted, since the latter were considered recently in detail in a review by Shabarova and Prokof'eva[41].

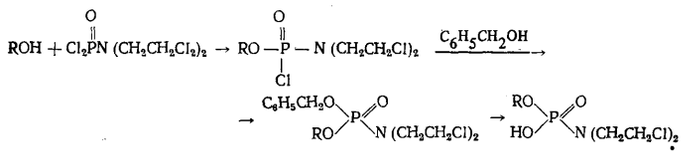
The first study on the synthesis of the relevant compounds[42] was carried out according to the following scheme:



A more effective single-stage method of synthesis of the required amides, based on the condensation of nucleotides with ammonia in the presence of dicyclohexylcarbodiimide, was developed somewhat later[43]. Adenosine, uridine, cytidine, and guanidine phosphoramidates were obtained in high yields by this general method[43,44]. The piperidide and morpholide derivatives of nucleotides were synthesised similarly[45].

Several examples of the synthesis of phosphoramidate derivatives of monoses[46] with the general formula sugar–O$\overset{\displaystyle O}{\overset{\|}{P}}$(OH)–N$(CH_2CH_2Cl)_2$ are also known. The following

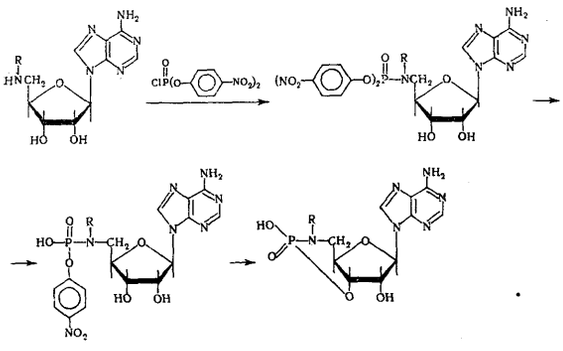
scheme is employed. Partly protected sugars are phosphorylated with an excess of an acid dichloride—*NN*-bis-(dichloroethyl)phosphoramidic dichloride; next the phosphoramidochloridate, which is the primary product, is converted by treatment with benzyl alcohol into an asymmetric diesteramide which yields the required compound after the removal of the protecting groups:



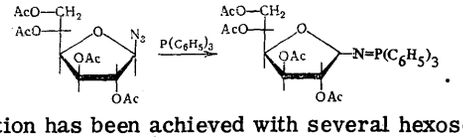
Derivatives of ribose, fructose, and glucose were used as the carbohydrate components. It is suggested that, owing to the presence of the carbohydrate residue, these compounds can readily penetrate the cell, where, under the influence of phosphatase and phosphoamidase, they split off bis-β-chloroethylamine, which suppresses the growth of malignant cells.

In addition to the methods for the preparation of sugar phosphoramidates described above, yet another procedure for their synthesis, based on the corresponding amides of acids containing phosphorus(III), may be mentioned. Thus 1,2;3,5-di-*O*-isopropylidineglucofuranose-6-(*NNN'N'*-tetramethyl)phosphorodiamidite is readily oxidised by oxygen, nitric oxide, and nitrogen dioxide[47]. 2,3,4,6-Tetra-*O*-acetylglucopyranose 1-(*NNNN'*-tetramethyl)phosphorodiamidite was oxidised under similar conditions[48].

Several compounds in which the nitrogen of the amide group in the phosphoramidates is linked directly to a carbon atom in the sugar ring have been described. Starting with 5'-amino-5'-deoxynucleosides and di-*p*-nitrophenyl phosphorochloridate, Jastorff and Hettler[49] obtained 50–85% yields of nucleoside phosphoramidate diesters[49]. Later the 5'-amide analogue of adenosine, converted subsequently into 3':5'-cyclicphosphoramidate, was obtained by a similar procedure[50]:



In conclusion of this subsection, mention should be made of compounds which are only indirectly related to the phosphoramidates discussed above as regards their structures. These are sugar derivatives of phosphine imide, for which a synthesis involving the treatment of the sugar azide with triphenylphosphine has been proposed[51]:

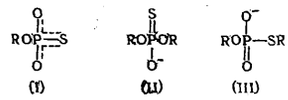


The reaction has been achieved with several hexoses. The final products are obtained in high yields.

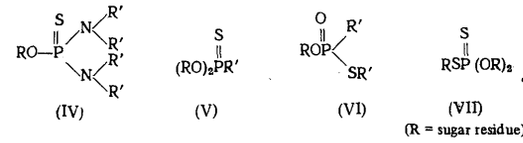
4. Sugar Phosphorothioates

In studies of enzymatic reactions at a molecular level using analogues of natural sugar phosphates, the phosphorothioates should be investigated first, since they involve minimal structural changes but differ significantly in one feature. Unfortunately, certain difficulties arise in their synthesis and this is why they have been comparatively little investigated hitherto.

The nucleoside phosphorothioates described in the literature can be represented by three types of general formulae:

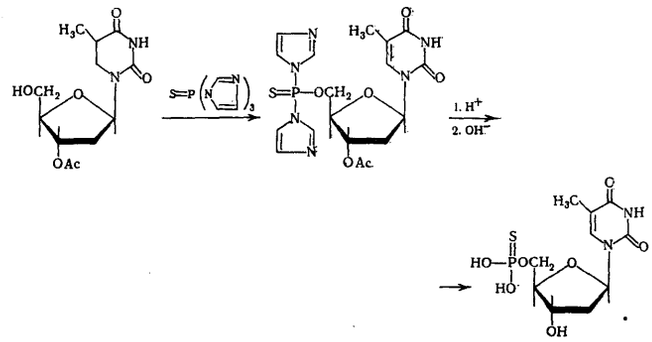


In addition, compounds with the following structures have been obtained from hexoses:



The methods of synthesising sugar phosphotothioates in the sequence (I)–(VII) specified above will be discussed below.

Nucleoside phosphorothioates were first obtained by Eckstein in 1966.[52] He phosphorylated 3'-*O*-acetyl-2'-deoxythymidine with tri-imidazolylphosphine sulphide:



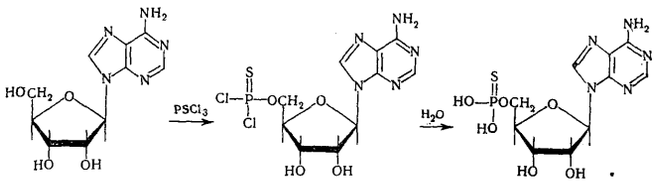
Somewhat later other investigators synthesised a series of nucleoside 5'-phosphorothioates using the same phosphorylating agent[53].

Eckstein employed tri-imidazolylphosphine sulphide to synthesise 2':3'-cyclic phosphorothioates from 5'-*O*-acetyluridine[54]. However, the desired product was isolated in a yield of 12% only. Moreover, the reaction was complicated by a side process involving the formation of 5'-*O*-acetyluridine 2':3'-cyclicphosphate.

Uridine 2':3'-cyclicphosphorothioate is interesting as a substrate for pancreatic ribonuclease[55].

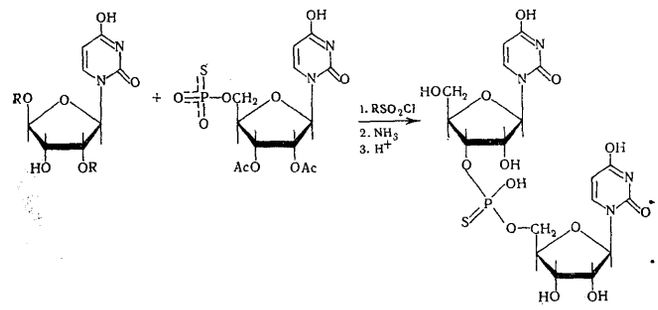
It is stated in the literature that tri-imidazolylphosphine sulphide employed as a phosphorylating agent gives satisfactory results only in the synthesis of the 5'-analogues of nucleotides. The attempts to synthesise the 3'-isomers were unsuccessful[56].

Phosphorus thiochloride was also used for the synthesis of nucleoside phosphorothioates. Thus adenosine 6′-phosphorothioate was obtained in a high yield by this procedure[57]:



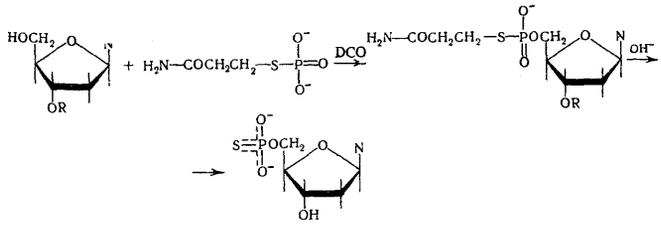
However, when phosphorus thiochloride was used in the phosphorylation of 2′,3′-*O*-isopropylideneinosine, the desired product was isolated in a relatively low yield after the removal of the isopropylidine protecting group[58].

It has been reported that nucleoside 5′-phosphorothioates are themselves effective phosphorylating agents. By treating 2′,5′-di-*O*-ethoxyethyluridine with 2′,3′-di-*O*-acetyluridine 5′-phosphorothioate, Eckstein achieved the synthesis of diuridine-3′,5′-phosphorothioate[59]:



In this reaction tri-isopropylbenzenesulphonyl chloride was employed as an activator.

Unfortunately the carbodi-imide method, which has been developed satisfactorily in the chemistry of nucleotides, could not be extended for a long time to the synthesis of phosphorothioates because the intermediate complex of the phosphorothioate and dicyclohexylcarbodi-imide decomposes with formation of dicyclohexylthiourea[60]. Cook et al. found a way of obviating this difficulty by employing in the carbodi-imide synthesis an inorganic phosphorothioate with a protected thio-group. Initially ethyl phosphorothioate was employed in the synthesis of sugar phosphorothioates[61]. However, subsequently it was suggested that the 2-carbamoylethyl protecting group, which is labile in an alkaline medium and can be readily removed at the end of the synthesis, be employed[62].

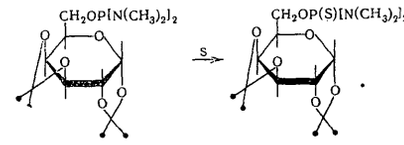


Nucleoside 3′ as well as 5′-phosphorothioates were obtained in this way in high yields.

The use of the 2-carbamoylethyl protecting group in this synthesis is analogous to the employment of the commoner 2-cyanoethyl protecting group in nucleotide synthesis. The reason for the above modification is that the authors were unable to synthesise 2-cyanoethyl phosphorothioates.

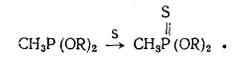
Carbohydrate phosphorothioates as well as phosphoramidates can be synthesised from the corresponding phosphorus(III) compounds.

Compounds with trico-ordinate phosphorus are known to combine readily with sulphur. This reaction has been carried out with 2,3;5,6-di-isopropylidinemannofuranose 1-(*NNN′N′*-tetramethyl)phosphorodiamidite[48], 1,2;3,5-di-isopropylideneglucofuranose 6-(*NNN′N′*-tetramethyl)phosphorodiamidite, and 1,2;3,4-di-isopropylidenegalactopyranose 6-(*NNN′N′*-tetramethyl)phosphoramidite[47], for example:



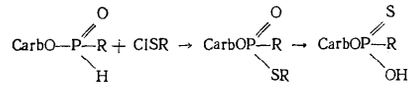
Glycosyl phosphoramidites react with sulphur on fusion of the starting materials and non-glycosidic sugar phosphoramidites react with spontaneous heating simply on mixing the components. In both cases the reaction gives high yields. Thus it is easy to obtain from readily available phosphorodiamidites the closest analogues of natural products—phosphoramidothioates. The biochemical properties of glucose 6-(*NNN′N′*-tetramethyl)phosphorodiamidothioate were investigated in a number of enzymatic reactions and it was shown that the compounds behave like the natural glucose-6-phosphate when acted upon by a number of glycolytic enzymes. However, the rates of its reactions are lower[63].

The addition of sulphur to disugar methylphosphonites has also been achieved[64]:



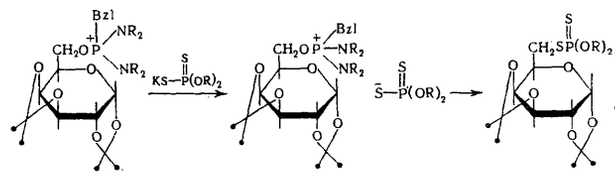
It has been shown that on heating the phosphonothioates [phosphonothionates?] thus synthesised partly isomerise to phosphonothiolates.

It has been suggested that phosphonothiolates, in which sulphur is present as a thiol group, be synthesised by treating partial sugar phosphonite esters with sulphenyl chlorides; the esters can be converted also into the corresponding phosphonothionates[6]:



The synthesis of acid phosphonamidothioates from phosphonamidites has also been described[65]. In this case the thione–thiol isomerisation does not take place.

Dialkyl sugar phosphorodithioates were obtained very recently by replacing the halogen anion by a phosphorodithioate anion in quasiamidophosphonium compounds with subsequent decomposition via the mechanism of the Arbuzov reaction[66]:



A characteristic feature of these compounds is the position of the sulphur atom between the phosphorus atom and the carbohydrate skeleton of the molecule.

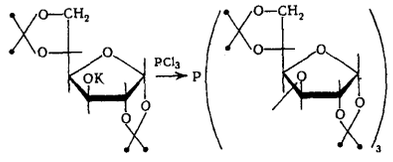
III. DERIVATIVES OF PHOSPHORUS(III) ACIDS AND CARBOHYDRATES

In recent years studies were begun in a number of laboratories on the synthesis and chemical properties of derivatives of phosphorus(III) acids and carbohydrates. These substances appear to be very promising as intermediates for the preparation of a wide variety of non-standard phosphorus-containing derivatives of carbohydrates, natural phosphates, and numerous dephosphorylation products. This assessment is due primarily to the high chemical reactivity of derivatives of tervalent phosphorus acids and sugars and also the fact that they are obtained under milder conditions and usually in higher yield than the corresponding phosphorus(V) acids. There is no doubt that the analogues of natural carbohydrate phosphates containing phosphorus(III) acid residues are of independent interest for biochemical research. Studies on those lines have already begun [63,67-69]. Certain facts now suggest that phosphites and other phosphorus(III) acid derivatives are formed in organisms as metabolic intermediates from a number of sugar phosphates and phosphoramidates.

In this review we shall consider the derivatives of phosphorus(III) acids and carbohydrates in the following order: neutral and acid phosphites and phosphoramidites and neutral and acid phosphonites, phosphonamidites, and phosphinites.

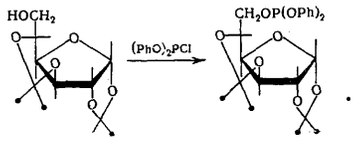
1. Neutral Phosphites

In the first studies on the synthesis of neutral sugar phosphites, acid chlorides were employed as phosphorylating agents. The phosphorylation of the potassium alkoxide derivatives of diacetoneglucose with phosphorus trichloride was reported in 1934. For a 3:1 reactant ratio, the formation of a neutral phosphite was postulated [70]:

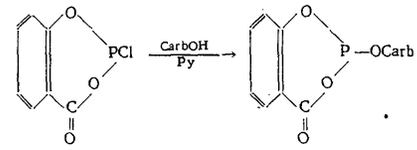


Unfortunately the yield of the reaction product, the methods of its purification, and necessary evidence for the individuality and structure of the trisugar phosphites are not included in the above report.

Later attempts were made to employ phosphorochloridite esters for the phosphorylation of carbohydrates. Thus the reaction between 1,2;3,5-di-isopropylideneglucofuranose and diphenyl phosphorochloridite has been described [71]:

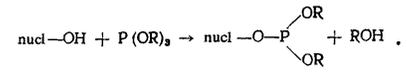


Later Tanaka published data on the preparation of diacetoneglucose-6-phosphite and diacetone galactose-6-phosphite using bis-(2,4-dichlorophenyl)phosphorochloridite as a phosphorylating agent [72]. The same investigator drew attention to the desirability of choosing cyclic phosphorochloridites, for example salicyl phosphorochloridite [73]:



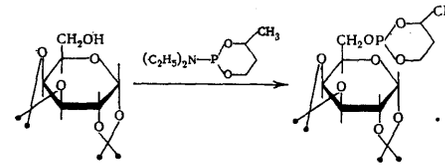
One may suppose that the phosphorochloridite method described has not found wide application because it suffers from disadvantages such as the instability of the initial reactants and the occurrence of side reactions. It is significant that phosphorochloridites cannot be used in the synthesis of glycosyl phosphites. Like other glycoside esters, they should be decomposed by amine hydrochlorides, which are formed as side products in the phosphorylation reactions [74], with formation of glycosyl halides.

Neutral phosphite esters have been proposed as phosphorylating agents for carbohydrates. In a series of studies by Czech chemists, a transesterification reaction for the synthesis of nucleoside phosphites has been described [75-81]. They employed triethyl and triphenyl phosphites as the transesterifying components:

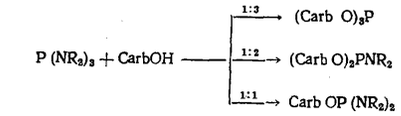


On treatment with triphenyl and triethyl phosphites, ribonucleosides yield nucleoside mono-, di-, and triphosphites and possibly also cyclicphosphites and dinucleoside phosphites. On subsequent hydrolysis, all these substances decompose to dihydrogen phosphite esters. Ribonucleosides with protected 2′- and 3′-hydroxy groups yield 5′-phosphites on transesterification with neutral phosphites [75-79].

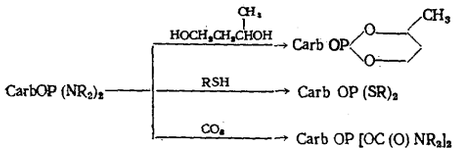
The transesterification method appears to be promising for the chemistry of sugars and nucleosides. However, recently the range of its applications has been restricted owing to the appearance of a new method—the alcoholysis of phosphoramidites [82,83]. This reaction has important advantages in syntheses: it is achieved under mild conditions, it does not involve the liberation of corrosive side products, and the starting materials are readily available. The method can be illustrated by the following example [84]:



An interesting variant of this reaction is phosphorylation of sugar derivatives with phosphorous hexa-alkyltriamides. In this case, depending on the reactant ratio, it is possible to obtain one of three types of compounds [65,84]:



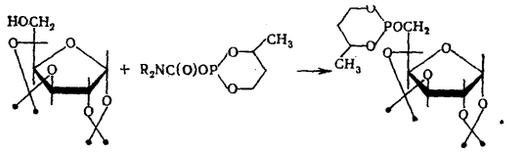
Phosphorodiamidites are valuable intermediates for the preparation of new phosphite derivatives. Thus, they readily react with alcohols[85], aminoalcohols[86], mercaptans[87], and carbon dioxide[88] and are converted into new phosphoramidite esters, phosphorothioite esters, phosphite esters, and carbamoyl phosphites. In particular, the following reactions have been achieved:



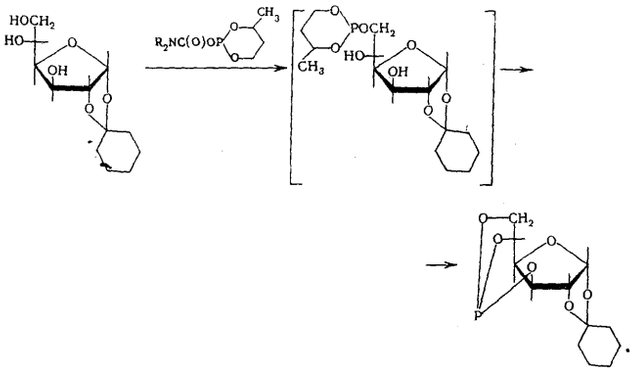
The phosphoramidites can be converted into monosugar phosphites by hydrolysis and acidolysis[89].

The synthesis of phosphites and phosphoramidites involving the alcoholic sugar hydroxyls was described above. The synthesis of glycosyl phosphites was achieved using phosphoramidous acids and their esters[48].

Sugar acyl phosphites[90], particularly carbamoyl phosphites[90], react under even milder conditions than the phosphoramidites, for example:

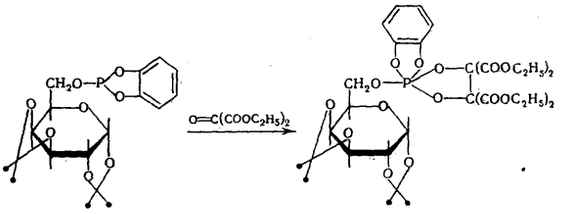


1,3-Butylene *NN*-dimethylphosphoramidite and 1,3-butylene dimethylcarbamoyl phosphite were investigated in a reaction with 1,2-cyclohexylideneglucofuranose[92]. In the phosphorylation with the carbamoyl phosphite, the reaction takes place at room temperature with formation of a bicyclic phosphite. Probably the first stage involves the formation of the sugar 1,3-butylene phosphite, which undergoes spontaneous transesterification to 1,2-cyclohexylideneglucofuranose 2,5,6-phosphite as a result of the specific properties of the carbohydrate phosphite system:



The structure of the bicyclic phosphite was demonstrated by synthesis involving the phosphorylation of 1,2-cyclohexylideneglucose with phosphorous hexaethyltriamide[92].

In the preview section of the review it was already mentioned that neutral sugar phosphites and phosphoramidites serve as starting materials for the synthesis of the corresponding phosphorus(V) derivatives. In addition, other reactions involving them have been achieved. Thus, alkylation, leading to a wide variety of deoxysugar derivatives[66,93], and the reaction with mesoxalic esters[94] deserve mention:

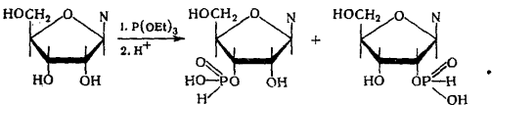


2. Acid Phosphites

It has been suggested that sugar dihydrogen phosphite esters be synthesised by the reaction of the sugar with phosphorous acid in the presence of dicyclohexylcarbodiimide as the condensing agent. This method was employed for the first time in 1961 by Todd[95]. Subsequently Holý et al.[96] developed on this basis a preparative synthesis for certain nucleoside phosphites.

A second method for the preparation of mononucleoside phosphites involves the hydrolysis of Menshutkin acid chlorides of the type $ROPCl_2$, formed when specially protected nucleosides are treated with phosphorus trichloride[97,98]. The problem of whether the phosphorodichloridite esters enter into various side reactions before treatment with water still remains uninvestigated. Therefore it is difficult to assess the preparative value of the method.

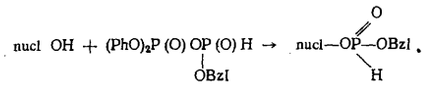
It has been suggested that mononucleoside phosphites be obtained by the hydrolysis of the corresponding neutral phosphites[76-78]. Initially 2′(3′)-phosphites were obtained from nucleosides with a protected 5′-hydroxy-group[76]. However, subsequently it was reported that nucleoside 2′(3′)-phosphites can be synthesised by the reaction of unprotected ribonucleosides with triethyl phosphite[78]:



The authors suggest that such selectivity of the secondary hydroxyl in the presence of a free primary hydroxyl is due to the formation of the thermodynamically more favourable 2′:3′-cyclic phosphite structure the hydrolysis of which leads to the acid phosphite. However, the formation of such cyclic esters is possible only when *cis*-hydroxy-groups are present. Thus all the acid phosphites which may be expected on hydrolysis of the cyclic phosphites, presumed to be formed via the transesterification of the alkyl phosphites with the *cis*-hydroxy-groups of the sugar, were obtained from lyxose, xylose, and arabinose[79]. Moreover, it is asserted that ribonucleosides with protected 2′,3′-hydroxy-groups as well as 2′-deoxyribonucleosides altogether fail to be phosphorylated by triethyl phosphite under the chosen conditions.

A synthesis of monosugar phosphites by the acidolysis and hydrolysis of the corresponding phosphorodiamidites has been proposed[85,89].

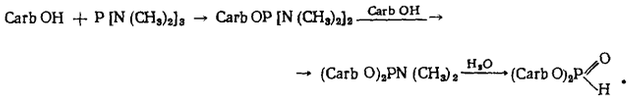
For the synthesis of monohydrogen phosphite esters, Todd proposed the method of mixed anhydrides requiring the use of the *O*-benzylphosphorous-*OO*-diphenylphosphoric anhydride:



Ribonucleosides containing blocking groups at the 2',3'- and 3',5'-hydroxyls and also 5'-protected 2'-deoxyribonucleosides are usually introduced into this reaction.

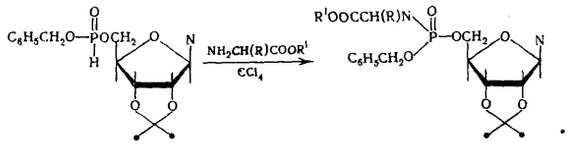
Nucleoside benzyl phosphites are synthesised in connection with the solution of a wide variety of chemical problems and such synthesis has become fairly common[26]. However, its further applications are restricted by the low availability of phosphorylating agents which can only be obtained by a fairly complex procedure.

Monohydrogen phosphite esters containing one or two sugar residues are formed on hydrolysis or acidolysis of the corresponding phosphoramidites, which are in turn obtained via a two-stage phosphorylation procedure[85], for example:



Acid phosphites of carbohydrates are very interesting synthetically. Dihydrogen phosphite esters have been suggested as intermediates in the synthesis of phosphates. Nitrogen dioxide[85], hexachloroacetone[76], and mercury(II) chloride[98] have been used as oxidising agents. Monohydrogen esters are readily converted into the corresponding phosphorochloridates by treatment with *N*-chlorosuccinimide and similar reagents[100]. Such phosphorochloridates are highly reactive and are readily converted into a wide variety of carbohydrate derivatives.

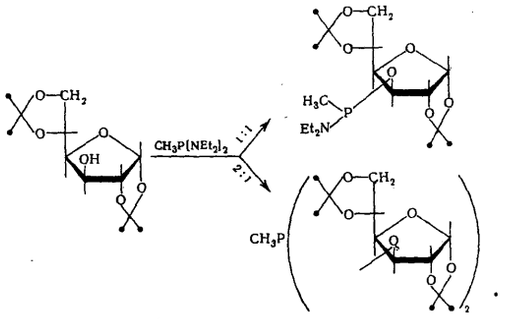
Benzyl nucleoside phosphites react with amines in the presence of carbon tetrachloride to form phosphoramidates[101]. This reaction was employed by Prokof'ev, Shabarova, and coworkers to synthesise compounds containing the phosphoramidate linkage between a nucleotide and an aminoacid[102-104], for example:



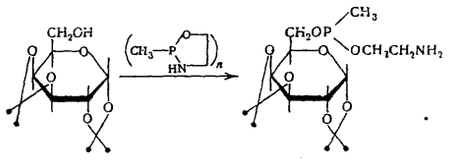
3. Neutral Phosphonites and Phosphonamidites

The alcoholysis of methylphosphonite esters and methylphosphonamidous acids has been suggested as a method of phosphorylating carbohydrates. Thus isopropylidineadenosine can be converted into an asymmetric phosphonite by treating it with diphenyl methylphosphonite[105] and diacetonehexoses can be converted into the corresponding methylphosphonamidites by reaction with methylphosphonous tetraethyldiamide[65].

With a 2 : 1 reactant ratio, disugar methyl phosphonites are formed[65], for example:



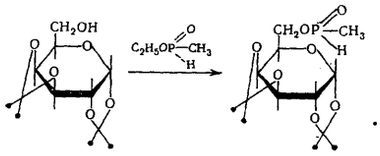
The following synthesis has been suggested for asymmetric phosphonites containing the ethanolamine residue:



Carbohydrate phosphonites and phosphonamidites are highly reactive. They are readily oxidised, combine with sulphur to form the corresponding phosphorus(V) derivatives[65,85], and enter into the Arbuzov reaction with formation of deoxysugars[93]. Phosphonamidites also react with a wide variety of reagents containing a mobile hydrogen, becoming converted into other sugar phosphonites[6,65].

4. Acid Phosphonites

Acid phosphonites of protected monoses have been obtained by the transesterification of phosphonites and by the alcoholysis of amides. The transesterification method has been used to prepare 1,2;3,4-di-isopropylidenegalactose 6-methylphosphonite by treating the sugar with ethyl methylphosphonite[6]:

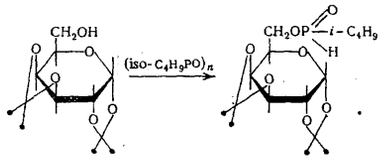


The reaction takes place under severe conditions (170°C, 7h). In the alcoholysis of amides, the phosphorylation takes place under milder conditions. The reaction temperature is reduced (110°C) and the yield of the final product increases.

Acid phosphonites can also be obtained by the acidolysis and hydrolysis of the corresponding phosphonamidite esters[89].

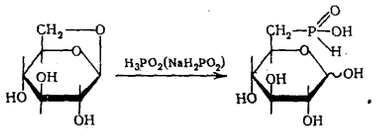
Acid carbohydrate phosphonites can be obtained under the mildest conditions by the interaction of protected sugars with anhydrides of the type $(R-PO)_n$.[106] The

reaction is not accompanied by the formation of side products and takes place at room temperature on simple mixing of the reactants:



Both alcoholic and glycosidic hydroxyls can be phosphorylated in this way. However, the anhydrides themselves are extremely labile. They polymerise rapidly with formation of unreactive products.

Among phosphorus(III) acid derivatives, analogues of natural phosphates with a direct covalent bond between the phosphorus atom and the carbon atom of the main sugar chain have also been obtained. Such phosphonous acids have been synthesised by the opening of the ring in 1,6-anhydrohexoses with hypophosphorous acid or its mixture with sodium hypophosphite[24]:



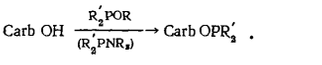
This reaction has been achieved with 1,6-anhydroglucose and 1,6-anhydrogalactose.

The above method of synthesis of phosphonous acids is particularly valuable because it makes it possible to avoid the laborious procedures involving the introduction and removal of protecting groups.

Phosphorous acid has also been investigated in the reaction with laevoglucosan, but in this case a product with a phosphorus-carbon bond was not isolated.

5. Carbohydrate Phosphinites

Two methods have been proposed for the synthesis of carbohydrate phosphinites: using phosphinite esters[107] and phosphinous amides[84,107] as phosphorylating agents:



These substances have been less thoroughly investigated than the phosphites and phosphonites owing to the experimental difficulties in their synthesis. Nevertheless, it has been shown that sugar phosphinites enter into a wide variety of substitutive phosphorylations leading to halogenodeoxy-[84,107-109] and mercaptodeoxy-derivatives[110] of sugars.

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Some Applications of the Optical Activity of Coordination Compounds

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The review covers the principal directions in which electronic absorption spectra, rotational dispersion curves, and circular dichroism are at present used in determining the absolute configurations of complex compounds and their structure. A list of 225 references is included.

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I. INTRODUCTION

During recent years the study of the dispersion of optical rotation and the circular dichroism of dissymmetric coordination compounds has become widely recognised as a method for solving spectroscopic and stereochemical problems. The discovery of definite relations between optical activity and various structural features of complex compounds, a more discriminating approach to the observed spectral characteristics (optical rotatory curves and circular dichroism spectra [1,2]), the enhanced sensitivity and extended spectral range of modern spectropolarimeters and dichrographs—all this has created a basis for the successful application of the optical rotatory dispersion and the circular dichroism of coordination compounds in solving various problems both in the chemistry of complex compounds and in organic chemistry.

The present review surveys some of the main directions in which the use of optical rotatory dispersion and circular dichroism has proved especially fruitful—the interpretation of electronic absorption spectra because of the better resolution of bands into individual transitions and further opportunities for their assignment, the determination of the absolute configurations of complex compounds from configurational effects (information which can be obtained by no other method except X-ray diffraction), determination of the absolute configurations of organic compounds from the sign of the rotatory power of $d-d$ transitions of metals in their complexes with the test substances, and the study of complicated natural macromolecules containing a coordinated metal ion.

The abbreviated symbols for ligands, often used in the text, are listed here for the convenience of the reader.

aaH	amino-acid
aba	*o*-aminobenzaldehyde
acacH	pentane-2,4-dione (acetylacetone)
ala	alanine
ala_2en	*NN'*-dialanylethylenediamine
alaglygly	alanylglycylglycine
allothr	allothreonine
asp	aspartic acid
atcH	acetylcamphor
big	biguanidine
bipy	2,2'-bipyridyl
bn	butane-2,3-diamine
2,3-bnpic	*NN'*-bis-(2-methylpyridyl)butane-2,3-diamine
chxn	cyclohexane-*trans*-1,2-diamine
cptn	cyclopentane-1,2-diamine
diam	diamine
dien	diethylenetriamine
1,10-diMetrien	2,5,8,11-tetra-azadodecane
2,9-diMetrien	2,9-dimethyl-1,4,7,10-tetra-azadecane
3,8-diMetrien	3,8-dimethyl-1,4,7,10-tetra-azadecane
5,6-diMetrien	5,6-dimethyl-1,4,7,10-tetra-azadecane
ece	*trans-NN'*-bis-(2-aminoethyl)butane-2,3-diamine [see 5,6-diMetrien]
edda	ethylenediaminediacetic acid
edta	ethylenediaminetetra-acetic acid
edts	ethylenediaminedisuccinic acid
eee	3,6-dithiaoctane-1,8-diamine
$ee(salH)_2$	1,8-bis-salicylideneamino-3,6-dithiaoctane
en	ethylenediamine
epe	4-methyl-3,6-dithiaoctane-1,8-diamine
$epe(salH)_2$	4-methyl-1,8-bis-salicylideneamino-3,6-dithiaoctane
glut	glutamic acid
gly	glycine
glyalagly	glycylalanylglycine
gly_2chxn	*NN'*-diglycylcyclohexane-*trans*-1,2-diamine
glyglyala	glycylglycylalanine
gly_2pn	*NN'*-diglycylpropylenediamine
hmcar	hydroxymethylenecarvone
hmch	hydroxymethylenecamphor
ibn	isobutane-1,2-diamine
leu	leucine
$\alpha\alpha$-Me_2gly	$\alpha\alpha$-dimethylglycine
N-Mepn	*N*-methylpropylenediamine
7-MesalH	*o*-hydroxyacetophenone
meth	methionine
5-Metrien	5-methyl-1,4,7,10-tetra-azadecane
mpkH	2-acetylpyrrole
ox	oxalic acid
pcaH	pyrrole-2-carboxaldehyde
pdta	propylenediaminetetra-acetic acid
penten	pentaethylenehexamine
pep	1,8-dimethyl-3,6-dithiaoctane-1,8-diamine
$pep(salH)_2$	1,8-dimethyl-1,8-bis-salicylideneamino-3,6-dithiaoctane
o-phen	1,10-phenanthroline
phenen	phenylethylenediamine
pn	propylenediamine
prol	proline
ptnta	pentane-2,4-diaminetetra-acetic acid
sal_2pn	*NN'*-disalicylidenepropylenediamine
ser	serine
stien	stilbenediamine
tart	tartaric acid
tdta	trimethylenediaminetetra-acetic acid
2,3,2-tet	1,4,8,11-tetra-azaundecane
$tet(salH)_2$	[1,11-disalicylidene-1,4,8,11-tetra-azaundecane (?)]
threo	threonine
tn	trimethylenediamine
trien	triethylenetetramine
val	valine

II. ELECTRONIC SPECTROSCOPY AND SPECTROPOLARIMETRY

Spectropolarimetry and ordinary electronic spectroscopy are complementary and undoubtedly mutually useful methods of solving structural and spectroscopic problems. Both consist essentially in recording electron transitions occurring in a symmetrical or an unsymmetrical environment. Their main advantage is the appearance of a new parameter—the sign of the optical rotation—in addition to the usual characteristics of an absorption band (extinction coefficient ϵ, frequency ν of maximum, and band half-width $\delta_{1/2}$). The complicated sigmoid character of individual inverse curves of optical rotatory dispersion corresponding to an individual transition often complicates interpretation of the curves observed when several such inverse curves are superposed.

Two bands of opposite sign can be distinguished in the circular dichroism spectra even if their separation does not exceed 100 cm^{-1}. In such a situation the absorption spectrum will give only a single overall band, which the usual methods—graphical and mathematical—are generally almost completely unable to resolve [3]. The use of circular dichroism spectra should be especially helpful in such cases, since the sum of the rotatory powers of bands obtained from almost degenerate transitions in related complexes of higher symmetry is zero [4].

Furthermore, certain differences in the selection rules for optically active and inactive absorption bands provide extremely valuable information for the assignment of bands in the absorption spectrum on the basis of an analysis of the intensities of the corresponding dichroic components. The rotatory power of an electronic transition is defined as the real part of the pseudoscalar product of the electrical and magnetic moments of the transition. The presence of the former is due to the transfer of charge (dipole moment), and of the latter to its rotation (magnetic dipole moment). And since by definition the transition is optically active only when the two moments act collinearly, this corresponds to a helical displacement of charge. Movement along a right-hand helix is associated with positive circular dichroism, and along a left-hand helix with negative circular dichroism [5].

As a consequence of this, transitions whose electrical and magnetic moments are mutually perpendicular cannot be optically active. Transitions that are magnetic-dipole-forbidden give a Cotton effect of insignificant amplitude [6]. On the other hand, d–d transitions of slight or moderate intensity (in the absorption spectrum) in dissymmetric metal complexes show strong dichroism, provided that these electronic transitions are magnetic-dipole-allowed in the given microsymmetry group [7]. Hence the character of the transition in an optically active molecule can be deduced from the value of the g-factor†, which usually exceeds 0.01 for magnetic-dipole-allowed transitions, and is smaller than this value for electric-dipole-allowed transitions [8]. For example, the anisotropy factors for the two transitions of Cr^{3+} in O_h symmetry, $^4T_{2g} \leftarrow {}^4A_{2g}$ and $^4T_{1g} \leftarrow {}^4A_{2g}$, are respectively 0.013 and 0.0008, in conformity with their magnetic-dipole-allowed and -forbidden character [9].

Another criterion which may be useful for assigning bands in the absorption spectrum to definite electron transitions is the specific effect of polarisable anions (phosphate, selenite, and certain others) on the circular dichroism spectra of complex cations. In the case of trisdiamine complexes (symmetry D_3), for example, the effect is evident in an increase in intensity of the A_2 dichroic component at the expense of a decrease in the E_g component, while the absorption spectrum in the region of the $^1T_{1g}$ band remains almost unchanged [10].

Thus important information on the number and nature of the components of an absorption band covering several closely located transitions can be obtained by determining and analysing the optical rotatory dispersion curves and especially the circular dichroism spectra.

On the other hand, progress in the electronic spectroscopy of certain metals, especially those free from d^3 spin (Cr^{3+}) and those with d^6 spin pairing (Co^{3+}, Rh^{3+}, Pt^{4+}), has enabled several empirical relations to be derived between the type of a transition and the sign of its rotatory power. These have subsequently been widely used for investigating the configuration of complexes, the conformation of the chelate ring in them, the configuration of asymmetric carbon atoms in a ligand, and several other stereochemical features of coordination compounds.

It has been established, for example, that all trichelate complexes of Co^{3+} having the absolute configuration $S(C_3)R(C_2)$ are characterised by a $^1E_a \leftarrow {}^1A_1$ transition of positive rotatory power [11]. This relation has since proved useful both for determining the absolute configuration of related complexes from the sign of the circular dichroism of this transition and for assigning a band to a definite transition on the basis of the sign of its circular dichroism with a known absolute configuration [12]. Qualitative similarity of the circular dichroism spectra in a certain spectral region for two complexes having the same absolute configuration can often be a basis for accepting that the energy levels of the d-orbitals of the complexing metals are arranged in the same sequence. Such comparison has been made [13] for the tri-α-alaninates of Co^{3+} and Rh^{3+}.

This type of interrelationship between electronic spectroscopy and spectropolarimetry makes a parallel study of all three types of spectra—absorption spectra, rotatory dispersion, and circular dichroism—especially fruitful. We shall examine several examples of spectroscopic results obtained by the use of optical rotatory dispersion and circular dichroism for various types of complexes of several transition metals.

1. Metals with d^3 and d^6 Electronic Configurations

Trisbidentate complexes $[M(AA)_3]^{n+}$

When six ammonia molecules in the coordination sphere of Co^{3+} are replaced by three ethylenediamine molecules, the d-levels of the metal are split in D_3 symmetry with the appearance of two dichroic components of opposite signs in the region of absorption band I of Co^{3+} ($^1A_{1g} \rightarrow {}^1T_{1g}$, a magnetic-dipole-allowed transition), corresponding to ^1E and $^1A_2$ transitions. Of the two components into which band II is split ($^1A_{1g} \rightarrow {}^1T_{2g}$), corresponding to ^1E and $^1A_1$ states, only the first transition is optically active. This resolution is insufficiently large to affect the absorption spectrum, which consists of two bands as before [14].

† The g-factor—or anisotropy factor—is defined as follows:

$$g = \frac{\epsilon_l - \epsilon_r}{\varepsilon},$$

where ϵ_l and ϵ_r represent absorption of the left-hand and the right-hand circularly polarised rays.

The corresponding trichelate complexes of Co^{3+} and Cr^{3+} with biguanidine (an optically inactive ligand, which on coordination forms planar rings containing the metal) are distinguished from the diamine chelates by a considerably greater intensity of the $d-d$ bands in the absorption and circular dichroism spectra, but the qualitative pattern of splitting is preserved in the latter spectrum. The chromium(III) complexes exhibit ^4E and $^4A_2$ components in the long-wavelength range, and only a ^4E component in the short-wavelength range [15].

The unsymmetrical character of amino-acids leads, on their coordination with metals, to the formation of two geometrical isomers of complexes of type $[M(AB)_3]$—1,2,3 (β) and 1,2,6 (α)—which differ in symmetry and can be identified spectroscopically. In fact the β-isomer is characterised by one Cotton effect in the region of absorption band II of Co^{3+}, whereas the less symmetrical α-isomer has three Cotton effects in the same region [11].

trans-Bisbidentate complexes $[MX_2(AA)_2]$

In these complexes the octahedral triplet states $^1T_{1g}$ and $^1T_{2g}$ are split into $^1A_{2g} + {}^1E_a$ and $^1B_2 + {}^1E_b$ components respectively [16]. The fact that band I is magnetic-dipole-allowed is responsible for the high rotatory power (of opposite signs) of the first two transitions in the complexes with diamines, in contrast to band II, where smaller circular dichroism is observed only for the E_b component [8]. Splitting of this type is exhibited also by the spectra of such complexes in polarised light [17].

The circular dichroism spectra of optically active bis- and tris-β-diketone complexes also consist of two components of opposite sign [18] in the region of band I (the dominant peak at a higher energy) and a broad maximum within the octahedral absorption band II of Co^{3+}.

Splitting of band I of Co^{3+} in the circular dichroism spectrum into two components is observed, also with *trans*-(*N*)-bis-amino-acid complexes having a *trans*-$[MO_4N_2]$ chelate unit, in conformity with the same microsymmetry (D_{4h}). However, splitting of this band into three components, corresponding to the true C_{2v} symmetry of such complexes, could be observed only in the circular dichroism curves of the vicinal effect for the ions $[MX_2(AB)_2]$, e.g. with AB = *L*-ala. [19]

cis-Bisbidentate complexes *cis*-$[MX_2(AA)_2]$

When AA = diam, four dichroic components are now observed in the region of the two $d-d$ bands in the absorption spectrum. Each absorption band corresponds to two dichroic maxima if X_2 represents unidentate ligands; when the latter are replaced by a single bidentate [and conjugated] ligand, one and three maxima in the circular dichroism spectrum are associated respectively with the long-wavelength and with the short-wavelength unpolarised absorption bands [20].

Similar complexes having configurational asymmetry with AA = acac [$X_2 = (NH_3)_2$ or en] exhibit a smaller separation in the circular dichroism spectrum—two components of opposite sign $A_1 \rightarrow B_1$ and $A_1 \rightarrow B_2 + A_2$ (dominant at higher energies) near absorption band I of CO^{3+} and a third component in the region of absorption band II. We note for comparison that $d-d$ transitions are represented in the absorption spectrum by one maximum in band I, while band II is represented by a shoulder on a neighbouring, more intense charge-transfer band [18].

Monobidentate complexes

The microsymmetry of these complexes, e.g. $[Co(L\text{-aa})(NH_3)_4]$, is D_{4h}. Resolution of the experimental optical rotatory dispersion curves into inverse curves corresponding to individual optically active transitions [8] showed the presence of two Cotton effects for band I and one in the region of band II. The g-factor of 0.002 for this last transition is consistent with an electric-dipole-forbidden transition [21]. Splitting of the octahedral $^1T_{1g}$ level into three singlet ^1A levels, corresponding to the actual symmetry C_1, could be observed in the circular dichroism spectrum of the monochelate complex with aa = leu (all components magnetic-dipole-allowed and therefore optically active). [22]

[Complexes with unidentate amino-acids]

In conformity with theory the circular dichroism spectra of such complexes as $[Co(L\text{-aaH})_2en_2]^{3+}$ and $[Co(L\text{-aa})(NH_3)_5]^{2+}$, which have D_{4h} and C_{2v} symmetry, show the resolution of Co^{3+} absorption band I into two components of opposite sign [22]. Under certain conditions the degeneracy of the E_g transition is also removed when the circular dichroism spectra of complexes of the latter type are determined, the two resolved components having opposite signs [23].

[Multidentate complexes]

It has never proved possible to observe splitting of the octahedral $^1T_{1g}$ level in the absorption spectra of the Co^{3+} complex with the multidentate ligand propylenediaminetetra-acetic acid, although theory predicts three components in the region of band I for the symmetry C_{2v} characteristic of this complex. The circular dichroism spectra exhibit two resolved components in conformity with the formal symmetry D_{4h} of this chelate unit $[MX_4Y_2]$. [3]

2. Metals with a d^7 Electronic Configuration

Interesting results have been obtained in the study of the absorption spectra and circular dichroism in the visible and near infrared of several square planar complexes of cobalt(II) with quadridentate Schiff bases of general formula (7-X-sal)$_2$(−)-pn, having the chelate unit $[MN_2O_2]$ and symmetry C_{2v}. Three of the ten spin-allowed $d-d$ bands of the metal should occur in the infrared, but they are represented by a single band in the absorption spectrum owing to the nearness of the $d_{xz,yz}$ and d_{z^2} orbitals. Determination of the circular dichroism spectra in the near infrared enabled all three components associated with the $(d_{xz} \pm d_{yz}), d_{z^2} \rightarrow d_{xy}$ transition to be observed [24]. In the visible range $d_{xy} \rightarrow d_{x^2-y^2}$ and $d_{z^2} \rightarrow d_{x^2-y^2}$ transitions could be identified only from the circular dichroism spectra, since interpretation of the absorption spectrum in this range is greatly impeded by the superposition of intense charge-transfer bands. The assignment of the bands led to the following proposed [24] scheme for the arrangement of d-orbitals in the cobalt(II) complexes investigated

$$d_{z^2} < \frac{1}{\sqrt{2}}(d_{xz} - d_{yz}) < \frac{1}{\sqrt{2}}(d_{xz} + d_{yz}) < d_{xy} < d_{x^2-y^2}.$$

3. Metals with a d^8 Electronic Configuration

(*a*) Octahedral coordination

In an octahedral field Ni^{2+} has three spin-allowed $d-d$ transitions. Measurement of the circular dichroism spectrum of the $[Ni(l\text{-chxn})_3]^{2+}$ ion in the range 300–1200 nm showed optical activity in all three bands, which, in view of their strong, moderate, and weak rotatory power, were assigned to $^3A_{2g} \rightarrow {}^3T_{2g}$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)$, and $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ transitions [25]. The first transition in the similar complex ion $[Ni(l\text{-pn})_3]^{2+}$ has $g = 0.23$, whereas for the other two transitions $g < 0.01$.[26] The complete absence of optical activity in the $d-d$ transitions in the nickel(II) complex of tribenzo[*bfj*]-1,5,9-triazacycloduodecine—a macrocyclic Schiff base—with appreciable rotatory power of the charge-transfer bands is rather unexpected [27].

(*b*) Square planar coordination

The nearness of the three possible $d-d$ transitions of square planar complexes of d^8 metals and their strong overlapping with charge-transfer bands create considerable difficulties in the interpretation of their absorption spectra. A further complication is the dependence of the energy levels of the d-orbital on the degree of tetragonal distortion of the chelate unit and on the strength of π-bonding of the metal with the ligand. This has resulted in several different arrangements of d-levels for square planar complexes of D_{4h} symmetry (Fig. 1).[28] Of the four possible $d-d$ transitions in scheme (III) (Fig. 1)—$d_{xy} \rightarrow d_{x^2-y^2}(A_{2g})$, $d_{xz}, d_{yz} \rightarrow d_{x^2-y^2}(Eg)$, and $d_{z^2} \rightarrow d_{x^2-y^2}(B_{1g})$—only the first two have magnetic moments, and in the A_{2g} transition the electrical and magnetic moments are mutually perpendicular. Hence only the transition to the Eg state should be optically active.

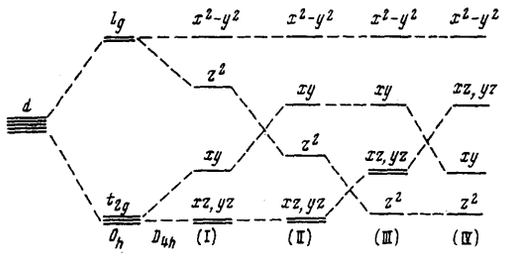


Figure 1. Possible types of splitting of the α-levels in square planar complexes of symmetry D_{4h}.

Scheme (III) is evidently supported [6,28] by the presence of two positive dichroic components in the $d-d$ region with several complexes of types $[M(diam)_2]^{2+}$ and $[MCl_2diam]$, where diam = *l*-pn, *l*-chxn and M = Pd^{2+}, Pt^{2+}, Au^{3+}. However, a study of the circular dichroism of the $[Ni(l\text{-pn})_3]^{2+}$ ion, which exists in certain solvents as a yellow (planar, diamagnetic) form, showed the existence of three dichroic $d-d$ bands, two of which had $g \geqslant 0.01$, which was interpreted as supporting scheme (IV).[26] A similar result was obtained from a study of the optical rotatory dispersion and the circular dichroism of dichelate complexes of Ni^{2+} and Pd^{2+} with amides of amino-acids, which also exhibited considerably greater splitting of the band in the circular dichroism spectra than in the absorption spectra [29]. The 1 : 1 and 1 : 2 complexes of Ni^{2+} with the amino-acids themselves have also been examined spectropolarimetrically [30].

The circular dichroism spectra of square planar complexes of Ni^{2+} and Pd^{2+} [31,32] with deprotonated tri- and tetra-peptides each contain two maxima in the $d-d$ range, which have been assigned, on the basis of their position and intensity, to $A_{1g} \rightarrow A_{2g}$ and $A_{1g} \rightarrow Eg$ transitions, in conformity with scheme (II) (Fig.1).

The pattern changes substantially on passing to complexes of nickel(II) with cysteine and its ester. The latter complex has three components in the absorption and circular dichroism spectra, the middle one of which is split into peaks of opposite sign in the complex of the cysteinate ion. Since only Eg among the three possible $d-d$ transitions is degenerate, this type of splitting of the bands indicates the sequence $A_{2g} < Eg < B_{1g}$ for the three transitions: i.e. the order of the a levels in complexes having the chelate unit $[MN_2S_2]$ differs significantly from their sequence in systems with an $[MN_4]$ chelate unit [31].

Complexes of nickel(II) with quadridentate Schiff bases [33,34], such as $(sal)_2(-)$-pn and its analogues produced by varying both the diamine component [RR(−)-chxn] and the aldehyde component (7-Mesal, acac, aba, pca, mpk), [35] exhibit an especially marked contrast between the circular dichroism and absorption spectra. The former displays up to three components in a range where the absorption spectrum contains only a shoulder on an intense charge-transfer band. As was to be expected, the increase in symmetry on passing to complexes with an $[MN_4]$ chelate unit, e.g. with $(aba)_2(-)$-pn as ligand, leaves only one transition in the circular dichroism spectrum, which does not appear at all in the absorption spectrum [35].

A new method of interpreting the absorption spectra of optically inactive complex compounds, based on a study of the circular dichroism induced in the $d-d$ transitions of the metal by optically active solvents, should prove extremely useful. Thus measurement of the circular dichroism spectra of the ions $[PtCl_4]^{2-}$ and $[Ni(CN)_4]^{2-}$ in $d(-)$-butane-2,3-diol and $d(-)$-propane-1,2-diol respectively has confirmed scheme (I) for the arrangement of the d-levels of these metals [7,36].

4. Metals with d^1 and d^9 Electronic Configurations

Depending on the symmetry of the environment, Cu^{2+} ions may give up to four transitions in the $d-d$ range, whereas the absorption spectrum usually contains one or at best two individual bands. Even in the spectra of single crystals of $[Cu(L\text{-aa})_2]$ in polarised light only two transitions could be observed—$^2A \rightarrow {}^2A$ and $^2A \rightarrow {}^2B$.[37]

The circular dichroism spectra of 1 : 2 complexes of Cu^{2+} with amino-acids revealed all four components of magnetic-dipole-allowed $d-d$ transitions, in conformity with the predictions of theory for C_{2h} symmetry (*trans*-$[MN_2O_2]$ chelate unit). The signs of these dichroic bands for amino-acids of the *L*-configuration are +, +, −, − in the hypsochromic direction [38]. Complexes with *D*- and *L*-alanine, *L*-serine, *L*-valine, *L*-threonine, *L*-allothreonine, *L*-proline, etc. have been investigated [39]. The circular dichroism spectra of 1 : 2 complexes of Cu^{2+} with

(+)-pseudoephedrine and (+)-2-aminopropanol each contain two dichroic components of opposite sign in each of the two bands in the absorption spectrum [40].

The circular dichroism spectra of complexes containing a *cis*-$[MN_2O_2]$ chelate unit—including chelates of Cu^{2+} with quadridentate Schiff bases from optically active diamines, e.g. R(−)-pn and RR(−)-chxn—contain three bands (symmetry of complexes C_2) all representing electric and magnetic-dipole-allowed transitions, and hence quite intense. These bands were assigned to $d_{z^2} \rightarrow d_{xy}$, $d_{x^2-y^2} \rightarrow d_{xy}$, and $d_{xz} \rightarrow d_{xy}$ transitions on the basis of a study of the effect of solvents coordinated along the z-axis of the complex on the circular dichroism spectra (the effect is largest with the $d_{z^2} \rightarrow d_{xy}$ transition) and an analysis of the relative sensitivity of these bands to the increasing degree of tetragonal distortion of the chelate unit when the azomethine hydrogen of the ligand is replaced by alkyl (the effect is greatest for the $d_{x^2-y^2} \rightarrow d_{xy}$ transition owing to the breakdown of π-bonding). The assignment of the bands led to the following proposed [41] sequence of the Cu^{2+} orbitals

$$d_{xy} \gg d_{x^2-y^2} > d_{z^2} > d_{xz}.$$

Observation of the individual components in the $d-d$ region has also permitted a more definite arrangement of all the ligands investigated [Schiff bases of various aldehydes with (−)-pn] with increase in the field that they produce [41].

Thus in these cases the circular dichroism spectra have proved extraordinarily useful not only as a method of observing individual $d-d$ transitions but also for studying the slightest distortions of planar complexes, information on which cannot be obtained in any other way [41].

The molecular orbital model predicts for oxovanadium-(IV) complexes the scheme of levels $^2B_2 < {}^2E < {}^2B_1 < {}^2A_1$, where the ^2E state may be resolved if the symmetry diminishes. The circular dichroism spectra of vanadyl-(IV) *d*-tartrato- and *l*-lactato-complexes show that this splitting into two components of opposite sign is sufficiently large only in the 1 : 2 complexes. In the region of one broad band in the absorption spectrum the circular dichroism spectrum reveals three electronic transitions, two of which ($^2B_2 \rightarrow {}^2E$ and $^2B_2 \rightarrow {}^2B_1$) are magnetic-dipole-allowed, while $^2B_2 \rightarrow {}^2A_1$ is not so allowed [42].

5. Metals with d^0 and d^{10} Electronic Configurations

The optical activity of complexes of zinc and isoelectronic metals is concentrated in the ultraviolet and is due only to internal transitions in the ligand and perhaps to a charge-transfer band. In zinc complexes of amino-acids, for example, an $n \rightarrow \pi^*$ transition of the acyl portion of the ligand is the first at long wavelengths [43]. However, valuable information on the structure of a complex can be extracted from the optical activity even of intraligand transitions. Thus the splitting of the $\pi \rightarrow \pi^*$ transition of the azomethine chromophore in the complex $[Zn(sal)_2(-)$-pn] into two components of opposite sign in the circular dichroism spectrum has been attributed, in conformity with the postulates of exciton theory, to a tetrahedral structure of the complex compound [33,34].

6. Metals with an f^n Electronic Configuration

The spectral behaviour of rare-earth metal complexes is especially complicated. The absorption spectra of lanthanide(III) ions in the visible and ultraviolet ranges are due to transitions of electrons from the ground j-level to the following j-levels in the f^n configuration ($n = 2-12$). Splitting of the j-levels of the free ion into the Stark components, which is usually too small to appear in the absorption spectra, is observed excellently in the circular dichroism spectra. The contrast between the resolving power of these two types of spectra is especially marked here. For example, the absorption spectrum of the 1 : 1 praseodymium(III)–tartrate complex contains three bands in the range 430–510 nm, whereas 21 components are observed in the same wavelength range of the circular dichroism spectrum [45]. Spectra of the latter type contain several sharp extrema near each band in the former with all the spectropolarimetrically investigated complexes of amino-acids with neodymium(III) [46] and praseodymium-(III), [47] hydroxy-acids with praseodymium(III), [45] and *l*-propylenediaminetetra-acetic acid with praseodymium-(III), neodymium(III), samarium(III), dysprosium(III), and erbium(III). [4]

The absorption spectra of rare-earth metal ions usually vary little with the chemical environment, in comparison with 3*d*-transition metal complexes. The only exceptions are a few transitions, which have been termed hypersensitive [48]. Study of the circular dichroism spectra of optically active rare-earth metal complexes has significantly expanded the number of such hypersensitive bands, which have been called c.d.-sensitive, in contrast to most other components of the circular dichroism spectrum, whose intensity is proportional to that of the corresponding band in the absorption spectrum. These latter dichroic maxima usually have g-factors of $10^{-5}-10^{-6}$, whereas this quantity increases tenfold for the c.d.-hypersensitive bands, to the order of $10^{-4}-10^{-3}$. [49]

The increase in the number of bands responsive to a change in the structure of the complex, on passing from the absorption to the circular dichroism spectrum, undoubtedly enhances the value of applying spectropolarimetry to structural investigations. For example, the conversion of unidentate ligands (amino-acids, gluconic and galactonic acids) in the coordination sphere of the europium(III) ion into chelated ligands, with increase in the pH, produces a considerable increase in intensity and reversal of sign in the dichroic band corresponding to the $^5D_1$ transition, while the absorption spectrum remains almost unchanged. The substantial differences both in intensity and in the character of the splitting of circular dichroism spectra may be due to finer structural differences in related ligands, such as e.g. alanine and serine, gluconic and galactonic acids [48].

The above values for anisotropy factors demonstrate the far smaller rotatory power of $f-f$ than of $d-d$ transitions. The weakening of the asymmetrising effect is probably due to the effective screening of f-electrons in the deeper atomic orbitals. The superposition of such weak Cotton effects due to $f-f$ transitions on the more intense Cotton effects centred in the short-wavelength region leads merely to a smooth resultant curve when the dispersion of optical rotation is measured, as has been observed e.g. with the lanthanide complexes of (−)-propylenediaminetetra-acetic acid. Because of such sharply diminished resolution of individual bands in the dispersion of optical rotation, this method is evidently far less useful for spectroscopic purposes. An interesting regularity in this case is the smooth increase in the molecular rotation at any point on such smoothed curves as a function of the ionic radius of the metal—from −275° to +210° for $[M]_D^{20}$ on passing from Yb^{3+} to La^{3+}. [50]

Thus the application of circular dichroism spectra to the investigation of rare-earth metal complexes is especially useful because of their higher resolving power compared with the absorption spectra and the presence of c.d.-hypersensitive (to fine structural features) bands.

III. DETERMINATION OF THE ABSOLUTE CONFIGURATION OF COORDINATION COMPOUNDS

It is important to determine the absolute configuration of optically active complex compounds not only for the sake of pure knowledge but also for spectroscopic purposes. As already remarked, bands observed in the absorption spectrum can be assigned to definite transitions on the basis of the sign and magnitude of the rotatory power of the latter, provided that the chirality of the environment of the metal ion is known.

Existing indirect methods for determining the absolute configuration of dissymmetric metal complexes usually involve measuring the circular dichroism and the optical rotatory dispersion and are of three types—(*a*) non-empirical methods based on the postulates of exciton theory, (*b*) semi-empirical methods, which include all kinds of octant rules, and (*c*) empirical methods, in which certain properties of the test substance (mostly the character of the dispersion of optical rotation or the circular dichroism in a certain range) are compared with those of a standard compound whose absolute configuration is known from X-ray examination.

As in organic chemistry, X-ray examination is undoubtedly the most direct and convincing. The sharp increase in the number of X-ray structural studies on optically active coordination compounds during recent years provides a firm foundation for further correlations among related compounds by means of the dispersion of optical rotation and circular dichroism [51].

1. Nomenclature

A quite varied notation has been used for absolute configurations in the literature. Opposite (left and right) chiralities in tri- and *cis*-di-chelate compounds are denoted as *D* and *L*, *M* and *P*,[52] Λ and Δ, $S(C_3)R(C_2)$ and $R(C_3)S(C_2)$, and are represented by the stereochemistry respectively of a left-handed and right-handed three-bladed propeller on clockwise rotation about the C_3 axis, and of right-handed and left-handed on rotation about the C_2 axis. The symbols Δ and Λ are used also to denote the absolute configurations of tetrahedral complexes of bivalent metals [34].

Preliminary proposals have recently been published for the nomenclature of conformations and configurations of octahedral six-coordinate complexes of various types, based on the representation of helical systems by two non-orthogonal skew lines [53].

2. Non-empirical Methods

The absolute configuration of a complex compound can be determined by quantum-mechanical calculation of the signs of the circular dichroism to be expected in the region of internal transitions of the ligands [54], especially those having their own system of π-bonds, such as 1,10-phenanthroline and 2,2′-bipyridyl [54]. This line of attack is especially important for complexes of metals having a d^0- or d^{10}-electron shell, to which the usual correlations based on the signs of the rotatory powers of *d*–*d* transitions are inapplicable [55].

The first successes in this field [56,57] have since been greatly extended by Bosnich [58,59] and several other workers [60–62]. The use of the exciton theory of optical activity to determine the absolute configuration of a complex ultimately requires knowledge merely of the direction of polarisation of a certain electron transition in the ligand and the approximate geometry of the complex. The method is based on analysis of the type of exciton splitting of one of the ligand transitions (most frequently $\pi \rightarrow \pi^*$) in the circular dichroism spectrum into two equal and opposite components. With a Λ absolute configuration about the central metal atom in tetragonal complexes, for example, the negative component of such a doublet should occur at a higher energy, but conversely with the Δ configuration [33]. In fact, with copper(II) complexes of quadridentate Schiff bases from RR(−)-chxn, which preserves stereospecifically the Δ configuration at the central metal ion, positive and negative resolved components of the azomethine $\pi \rightarrow \pi^*$ transition are observed at higher and lower energies respectively [41].

There are certain indispensable conditions for the exciton splitting of a transition: firstly, two or more chelate rings having π-electron systems must be present; secondly, the two chromophores of two ligand molecules in the complex must be non-coplanar (thus analysis of the optical activity of complex compounds in the ultraviolet yields the most valuable information on the smallest departures from planarity in the chelate unit); and thirdly, the transition should have approximately the same energy and intensity whether the ligand is free or coordinated [18]. A further condition for the successful application of this method is absence of overlapping between the components of the exciton splitting and adjacent bands, e.g. a charge-transfer band.

The predictions of the exciton theory have been confirmed by chemical methods [63] in a series of complexes related to $[Co\,phen_3]^{3+}$ and $[Co\,bipy_3]^{3+}$. Determination of the absolute configurations of complexes by means of the criteria of the exciton theory is undoubtedly a promising method [64,65].

3. Octant Rules

Various octant rules are widely applied in organic chemistry to determine the absolute configurations of cyclic carbonyl compounds from the sign of the Cotton effect for the $n \rightarrow \pi^*$ transition in the carbonyl group [66].

In coordination chemistry the situation is greatly complicated by the practical impossibility of finding any isolated non-degenerate transition common to all complexes of various metals with different types of ligands. Nevertheless, such regular relations between the signs of the Cotton effect and of the octant (and hence the configuration) have been established for *d*–*d* transitions chosen in a certain fashion.

The sign of each octant is given by the product of its coordinates; the octant sign of the complex is obtained by adding those of its component chelate rings, where the sign of each atom should correspond to that of the octant in which it is situated. The main rules for arranging complexes in a right-hand coordinate system were worked out by Hawkins and Larsen [67], who showed their applicability not only to diamine chelates but also to other complexes containing bi- and multi-dentate ligands [68,69]. This

last is especially important, because establishing the absolute configurations of complexes containing multidentate ligands by comparing their circular dichroism and optical rotatory dispersion with those of complexes of bidentate ligands does not always yield the correct results[70].

The following general empirical octant rule has been suggested for cobalt(III) complexes from an analysis of well known published data: if a cobalt(III) complex of symmetry D_3, D_2, C_2^a, and C_2^b‡ has a ^1E, $^1B_1$, ^1A, or ^1B transition respectively with a negative Cotton effect, it possesses an absolute configuration corresponding to a negative octant sign[71]. Similar rules can probably be deduced for complexes of other metals.

This general octant rule was found to apply also to several square planar complexes of copper(II) with such ligands as gly$_2$(−)-pn, gly$_2$(−)-chxn, and (+)-ala$_2$en.[72] On passing to complexes of copper(II), nickel(II), and palladium(II) with deprotonated tri- and tetra-peptides, however, their optical activity can no longer be explained in terms of a simple octant rule, since substituents attached to an α-carbon atom are situated in octants of opposite sign with the same absolute configurations of the amino-acid residues. A so called double octant or hexadecadic rule was therefore suggested, according to which the complex is placed in a coordinate system with sixteen sectors alternating in sign. The example in Fig. 2 shows that all methyl groups of the three L-alanine fragments are located in negative octants, which correlates well with the negative total Cotton effect of the $d-d$ transitions of this complex[73].

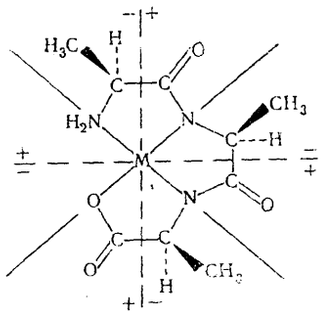


Figure 2. Distribution of charges in square planar complexes according to the octant rule.

Both the identity of sign of the dichroic bands for a series of tripeptides in which the position of an optically active amino-acid residue varies (e.g. alaglygly, glyalagly, glyglyala) and the additivity of the contributions made by asymmetric carbon atoms in different positions in an oligopeptide ligand in its 1 : 1 complex with nickel(II)[31] and palladium(II)[32] are excellently explained on the basis of the hexadecadic rule. Certain departures from additivity in the presence of an amino-acid residue with a bulky side-chain in the N-terminal position are explained by the appearance of a conformational contribution, opposite in sign to the vicinal contribution[31].

The octant rules for the $n \rightarrow \pi^*$ transition of the carbonyl chromophore, worked out by Moffitt for organic compounds, have been used equally successfully in coordination chemistry[74]. Thus a study of copper(II) complexes with L-cysteine and L-histidine showed that the Cotton effect of the $n \rightarrow \pi^*$ transition (~220 nm), which is positive in the copper(II) complex with the methyl ester of cysteine, becomes strongly negative in the complex with the free amino-acid. The opposite octant signs of the two complexes result from a change in conformation: chelation involving the carboxyl stabilises a conformation which is impossible for the ester[75,76].

Thus the employment of octant rules in interpreting optical rotatory dispersion and circular dichroism yields valuable information both on the absolute configuration of a complex and on its conformational features.

4. Empirical Methods

Several empirical methods can be distinguished depending on the way in which the relatedness of configurations of two complexes is established.

(*a*) Spectroscopic methods

The absolute configurations of two related dissymmetric molecules can be said to be identical if the Cotton effects have the same sign in the same spectral range. Thus the occurrence of a positive Cotton effect at 470 nm in the series of complexes—D(+)-[Co en$_3$]$^{3+}$, (+)-[Co(+)-pn$_3$]$^{3+}$, (−)-[Co(+)-chxn$_3$]$^{3+}$, (+)-[Co(−)-tn$_3$]$^{3+}$, (+)-[Co.(*meso*-2,3-bn)$_3$]$^{3+}$, (+)-[Co(−)-cptn$_3$]$^{3+}$, and (+)-[Co en$_2$.ibn]$^{3+}$—enabled the same, D-configuration to be assigned to all of them on the basis of the L-configuration established for the first member by X-ray diffraction[77].

However, such configurational correlations without preliminary assignment of the bands give sufficiently correct results only with closely related compounds. The possibilities of the method are considerably extended by using the rotatory powers of individual transitions to relate the configurations. An empirical rule for trigonal metal complexes (symmetry D_3) connects their configuration with the sign of the rotatory power of the E_a transition ($^4E \leftarrow {}^4A$ for Cr^{3+} and $^1E \leftarrow {}^1A$ for Co^{3+}): the rotatory power (R) of the E_a transition is positive for complexes having the $M(C_3)(D,\Lambda)$ configuration and negative for complexes having the enantiomeric $P(C_3)(L,\Delta)$ configuration[78]. The second component A_2 of band I has negative and positive Cotton effects for the $M(C_3)$ and $P(C_3)$ configurations respectively[79]. The range of application of this rule is probably quite wide: it covers the most diverse cationic, anionic, and inner-complex compounds with bi- and multi-dentate ligands, e.g. [Co diam$_3$]$^{3+}$,[9] [Co aa en$_2$]$^{2+}$,[80,81] [Co edda(L)] (where [(L) =] L-gly, L-ala, en, l-pn),[82] [Co ox$_n$acac$_{3-n}$]$^{m-}$ (where n = 1, 2, 3),[83] [Co(+)-pdta]$^{3-}$, and [Co aa$_3$].[52]

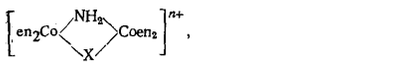
In the trisamino-acid complexes the $^1A \rightarrow {}^1E$ transition in the β-isomers and the dominant peak in the region of band I of Co^{3+} for the α-isomers have positive rotatory power if the complex has the D-configuration;[13,52,84] the latter has been confirmed by the determination by X-ray diffraction of the absolute configuration of α(+)-[CoL-ala$_3$].[85] This rule was used in assigning the D-configuration to the 1,2,3-isomer of (+)-[Co(+)-hmch$_3$], having a

‡ The notation C_2^a and C_2^b denotes complexes of symmetry C_2 with (*a*) configurational and (*b*) conformational asymmetry.

related geometry, on the basis of the positive rotatory power of the E-transition [34].

Similar regularities constituted the grounds on which the $\Lambda(C_3)$ configuration was ascribed to a series of rhodium(III) complexes, such as $(+)_D$-[Rh aa$_3$] [86] and the mixed $(-)_D$-[RhL-aa en$_2$]$^{2+}$, where aa = ala, val, leu, ser, threo, meth [87].

The absolute configurations of dinuclear complexes, e.g.



are established on the basis of the analogy of their circular dichroism spectra and optical rotatory dispersion curves with those of corresponding mononuclear complexes [88,89].

An exception to the general rule is $(-)_D$-[Cr big$_3$] with a $\Lambda(C_3)$ configuration according to X-ray diffraction [90] and a negative E_a component in the circular dichroism spectrum [15]. On the other hand, further investigations have shown that the above relations are entirely correct only when sufficiently analogous complexes are compared. Thus the absolute configuration $(-)_D$-[Co tn$_3$]$^{3+}$ determined by X-ray examination [91] was enantiomeric to that previously assigned on the basis of rules for complexes containing five-membered chelate rings [77]. Moreover, the two cations $(-)_D$-[Co tn$_3$]$^{3+}$ and $(-)_D$-*cis*-[Co(NCS)$_2$tn$_2$]$^+$, which have the same absolute configuration (Λ) according to X-ray results [91,92], have enantiomeric circular dichroism spectra, probably owing to a change in the sequence of the E_a and A_2 components into which the absorption band I of Co^{3+} is resolved [93].

Considerable risk is entailed [95] in the spectroscopic assignment of absolute configurations to complexes of multidentate ligands on the basis of the analogy of their optical rotatory dispersion and circular dichroism with those of analogous complexes of bidentate ligands of known configuration [94]. Thus X-ray determination showed the absolute configuration of the ion $(+)_D$-[Co penten]$^{3+}$ to be enantiomeric to that predicted earlier from the circular dichroism spectra [97].

Here we have the additional difficulties of bringing the chirality of the arrangement of the rings in a multidentate ligand into unambiguous correspondence with the simple Δ and Λ configurations. Thus even in the coordination of a terdentate ligand (2,3-diaminopropionic acid) into a 1 : 2 complex, for example, the helicity of the arrangement of the ethylenediamine chelate rings corresponds to a Λ configuration, while the α- and β-amino-acid chelate rings are arranged about the metal in a Δ-configuration [98].

In such cases the most unequivocal results are undoubtedly obtained by X-ray examination of typical representatives of the classes of complexes. Determination of the absolute configuration of the cobalt(III) complex of L-3,8-diMetrien suggested [69] the following empirical relation between the sign of the circular dichroism and the chirality of the complex for linear quadridentate ligands: a complex having a negative Cotton effect in the region of the band corresponding to the $^1A_{1g} \rightarrow {}^1T_{1g}$ transition in Co^{3+} has a Δ-configuration [69].

However, errors can be avoided even within the limits of spectral methods by "ring pairing", which consists essentially in constructing every possible combination of two non-bonded chelate rings, and determining for every pair the chirality with respect to the C_2 axis. The dominant chirality determines the designation of the configuration [99].

In some cases it is useful, in determining the absolute configuration of the complex, to examine the effect of outer-sphere coordination of readily polarisable anions—such as selenite, sulphate, phosphate—on the dispersion of optical rotation and the circular dichroism. If the complex has a D-configuration, the effect is to increase the intensity of the A_2 component in the circular dichroism spectrum with a parallel decrease in the height of the E peak, probably owing to formation of an ion-pair [97,100].

It is evidently possible to use not only spin-allowed but also certain spin-forbidden $d-d$ transitions to determine the absolute configuration of a complex. The absolute configurations of trichelate complexes of chromium(III) with the most diverse ligands—en, tn, *o*-phen, ox, tart, etc.—correlate well with the sign of the rotatory power of the low-frequency component in the circular dichroism spectrum that corresponds to a ^2E_a transition: if its rotatory power is positive, the absolute configuration of the complex ion is $\Delta(C_2)$. [101]

Nuclear magnetic resonance spectroscopy has recently found increasing use for confirming results obtained by analysing the dispersion of optical rotation and the circular dichroism of complexes of diastereomeric type, i.e. with two sources of asymmetry [102-104]. For example, comparison of the n.m.r. spectra of the two isomers (+)- and (−)-[Co ox$_2$(−)-pn]$^-$ revealed that the chemical shifts of methyl protons in (−)-pn were larger in the Δ- than in the Λ-configuration [105].

Study of the stereochemistry of substituted metallocenes [106-112] is also based on comparing the signs of the circular dichroism of certain $d-d$ transitions, but this class of sandwich compound constitutes too specialised a field of coordination chemistry to be discussed in greater detail here.

(*b*) Non-spectral methods

Chemical conversion of a complex compound into another of known absolute configuration is a quite rigorous method for correlating configurations provided that the reaction does not involve rupture of any M−L bond. Until recently the use of chemical correlations in coordination chemistry was only incidental, since in most reactions of complex compounds this condition—and hence the preservation of the configuration during the changes—cannot be guaranteed [113].

The oxidation of (+)-[Ru phen$_3$]$^{2+}$ with potassium permanganate followed by reduction of the resulting 3,3′-dicarboxy-2,2′-bipyridyl in the coordination sphere to (+)-[Ru bipy$_3$]$^{2+}$ served as basis for assigning optical configurations to a long series of complexes of general type [M bipy$_n$phen$_{3-n}$]$^{m+}$, where $n = 1-3$, and M = Ru^{2+}, Fe^{2+}, Ru^{3+}, Os^{2+}, Os^{3+}, Co^{3+}, and Ni^{2+}. [114] A similar attempt to convert [Co phen$_3$]$^{3+}$ into the bipyridyl complex halted at the stage of complexes of cobalt(III) with 5-nitro-1,10-phenanthroline and 1,10-phenanthroline-5,6-quinone, which is also of some value [63].

Reduction of the [Ru en$_3$]$^{3+}$ ion to [Ru en$_3$]$^{2+}$, during which the optical activity was maintained, enabled the rules for the assignment of configurations obtained with d^6 metals to be extended to dissymmetric trigonal complexes of d^5 metals [115].

Two further reactions in which the asymmetric centre is unaffected are the oxidation of the cysteine complex of cobalt(III) to the cysteinesulphinate complex [116] and the conversion of L-[Co gly en$_2$]$^{2+}$ into L-[Co ser en$_2$]$^{2+}$ by Knoevenagel's reaction [117].

The chemical assignment of configurations by oxidising a dinuclear tartrato-complex to a monomeric oxalato-complex is not only of intrinsic interest but also a basis for further correlations in a series of bridged dinuclear complexes by their spectroscopic comparison with mononuclear complexes [118,119].

The general configurations of a series of complexes of general type $[CoXYen_2]^{n+}$ [where XY = $(CN^-)_2$, $(NCS^-)_2$, $(NCS^-)(NH_3)$, and $(NH_3)_2$] has been established, on the basis of the known absolute configuration of the first member, from their interconversions under conditions that exclude racemisation [120].

The change from [Co edta]$^-$ to $[Co\,en_3]^{3+}$ involves the rupture of M–L bonds. Nevertheless, it occurs with partial retention of optical activity, the sign of which can be used in a certain range to establish the configuration of complexes of multidentate ligands [121].

Another useful criterion in determining absolute configurations is provided by the stereospecific requirements of an optically active ligand. In many cases only one isomer can be formed without special strain, and its configuration can be determined by constructing models based on the known absolute configuration of the ligand [5,122,123]. Sometimes the absolute configuration can be deduced from the preferential formation of one isomer rather than another [124]. The configuration of a complex with an optically inactive ligand can be established by comparing its optical rotatory dispersion and circular dichroism with those of an analogous complex of an optically active ligand, provided that the latter is formed stereoselectively. This is based on the insignificance of the vicinal contribution compared with the configurational contribution. An example is the establishment of identical configurations for the ions $(+)_D$-*trans*-$[CoCl_2trien]^+$ and $(+)_D$-*trans*-$[Co(SS)Cl_2(3,8\text{-diMetrien})]^+$, which have similar circular dichroism spectra [125]. However, such correlations, based on stereoselectivity, should evidently be confined to $d-d$ transitions, since in the region of a charge-transfer band the vicinal contribution becomes sufficient to affect not only the magnitude but also the sign of the rotatory power [124].

A solubility rule may also be useful in establishing the configuration of an optically active complex. It states that complexes of similar configurations have similar solubilities [126].

However, X-ray structural analysis undoubtedly provides the last word in solving the problem of the absolute configuration of a complex compound, as well as the soundest foundation for further correlations in a series of closely related compounds. The number of publications in this field has grown rapidly during recent years, the classic papers on trisethylenediamine [127–129] and tris-*l*-propylenediamine [130,131] complexes of cobalt(III) and of ethylenediamine with chromium(III) [132,133] having been supplemented by investigations on complexes of other metals, e.g. $[Cu\,l\text{-}pn_3]^{2+}$ [134] and $[PtCl_2en_2]^{2+}$, [135] and complexes with new ligands, e.g. *trans*-$[Cr\,atc_3]$. [136] Several reviews on this subject give a more detailed account of the state of the problem [51,85,137].

IV. NATURALLY OCCURRING OPTICALLY ACTIVE COMPLEX COMPOUNDS AND THEIR MODELS

This Section reviews the application of the optical rotatory dispersion and the circular dichroism of coordination compounds to structural studies on certain optically active natural macromolecular complexes and also complexes of metals with optically active natural macromolecules (polypeptides, nucleic acids).

Study of the optical rotatory dispersion of natural materials must take into account, besides the contributions from the asymmetric centres of amino-acids and from the helical secondary structure (where present), the role of the metal atom, which, on becoming an asymmetric centre, may make a large contribution to the total optical rotatory dispersion of the molecule. Establishment of the structure and the optical rotatory power of natural complexes of this type is made more important by the fact that metal atoms are usually biologically active portions of the molecule.

Complexes of metals with di- and tri-peptides can be regarded as model compounds. They are also of intrinsic interest as chelates with multidentate ligands.

Complexes of Di- and Tri-peptides

The optical rotatory dispersion curves for copper(II) complexes with dipeptides are in general similar to those of the corresponding amino-acid complexes, the shape of the curve being determined by several factors [138]. As was to be expected, the absolute configuration of the amino-acid residue contained in the dipeptide is the decisive factor in complexes without configurational asymmetry: the curves for mixtures of the Cu^{2+} ion with gly-*L*-ala and gly-*L*-ala are mirror images one of the other. Replacement of one amino-acid residue by another of the same configuration and without additional donor groups leads merely to an unimportant quantitative change in the optical rotatory dispersion. These two properties are undoubtedly of use for determining the configuration of an amino-acid involved in coordination.

Further, the form of the optical rotatory dispersion curve is strongly dependent on the type of complex present at a given pH. Addition of one, two, and three equivalents of alkali to a solution of a 1 : 1 mixture of the Cu^{2+} ion and a dipeptide (L)yields the complexes CuL^+, CuL, and $Cu(OH)L^-$, corresponding to successive stages of proton elimination from terminal amino-nitrogen, amide nitrogen, and a coordinated water molecule. The most marked changes in optical rotatory dispersion are observed on passing from the free ligand to the CuL^+ and CuL complexes, obviously owing to formation of the first and second chelate rings [138].

Similar titration with alkali with simultaneous determination of the circular dichroism spectra showed for amides of dipeptides the existence of two main types of complexes—CuL (protons dissociated from amide and peptide groups) and $CuOHL^-$ (third proton dissociates from coordinated water molecule). [139]

The position of the optically active amino-acid residue in the dipeptide molecule has a significant influence on the dispersion of optical rotatory dispersion. On passing from the Cu^{2+} complex with *L*-alagly to the complex with gly-*L*-ala, for example, the rotation increases sharply in absolute magnitude, and the curve passes into the negative region. Together with the close similarity in the dispersion of the gly-*L*-ala and *L*-ala-*L*-ala complexes, this presupposes that the carboxy-terminal amino-acid residue plays the dominant part, probably as a consequence of different degrees of non-planarity of the two types of chelate rings [138,140].

Investigations of the octahedral complexes of dipeptides with Co^{3+} are interesting because this ion activates certain

enzymes in reactions involving hydrolysis. Stereoselectivity in such systems is probably due to easier coordination of the metal with one of the enantiomorphs of the substrate, whose configuration is determined by the stereochemical requirements of the enzyme. Indeed it has been shown that, when dipeptides made up of amino-acids of *L*-configuration are coordinated with Co^{3+}, the preferred isomer of the complex also has always the *L*-configuration [141].

The optical rotation depends significantly on the position of the optically active amino-acid residue in the peptide chain also in complexes of copper(II) and nickel(II) with tripeptides. Thus we have the sequence

L-ala-*L*-ala-*L*-ala > gly-*L*-ala gly > gly gly-*L*-ala > *L*-ala gly gly

for the amplitude of the Cotton effect induced in $d-d$ transitions of the ions Cu^{2+} and Ni^{2+} (at 550 and 475 nm respectively) depending on the structure of the ligand in complexes of the type ML^-. Maximum rotatory power is thus obtained by introducing the optically active fragment into the middle chelate ring of the three. This is probably due to maximum departures from planarity in this metal ring, which contains two trigonal nitrogen atoms of deprotonated amide groups.

It is interesting that the contributions to the rotatory power of transitions made by asymmetric centres in each of the three chelate rings in tripeptide complexes are not only additive in magnitude but also identical in sign, which is readily explicable only within the framework of the hexadecadic (or double octant) rule [142]. Thus in a comparison of the integral circular dichroism areas in a definite region for the series of complexes of type NiL^- with the above four tripeptides containing the *L*-ala residue in different positions, for example, it was shown that the rotatory power of the complex with the first tripeptide constitutes 103% of the sum of those of the complexes with the other three tripeptides [141].

Tripeptides containing an *L*-histidine residue are already potentially quinquedentate ligands, and their complexes have considerably greater optical activity than those of simple tripeptides. This complicated ligand coordinates with metals through four nitrogen atoms—an imidazole, an amine, and two amide atoms. The circular dichroism data indicate that the optical rotatory dispersion curves represent the superposition of two Cotton effects (at 590 and 490 nm), the signs of which depend on the relative position of the histidine residue in the tripeptide molecule [143].

Detailed investigations of the coordination of model compounds—di- and tri-peptides—have permitted the study of more complicated systems. Thus the interaction of the polypeptide of apomyoglobin with Cu^{2+} and Ni^{2+} shows that it coordinates four metal ions—one at the terminal amino-portion and the other three at histidine portions inside the polypeptide chain [144]. Examination by means of circular dichroism of two copper-containing proteins—one of which acts as an electron-transmitting fragment in the cytochrome chain, while the other catalyses the oxidation of various aromatic structures by molecular oxygen—revealed a sharp increase in the rotatory power of $d-d$ transitions in these natural complexes compared with the models, perhaps as a consequence of a charge-transfer band between Cu^{2+} and Cu^+ located side by side [145].

Determination of the sites of coordination with a metal (Cu^{2+} and Ni^{2+}) in a series of proteins, such as lysin, vasopressin, conalbumin, α-chymotrypsin, etc., became possible as a result of preliminary investigation of the circular dichroism spectra characteristic of complexes of these metals with terminal amino-groups, histidine, and thiol-containing groups in model oligopeptides [146].

The circular dichroism spectra of rubredoxin (an iron-containing protein) have yielded evidence of the quasi-tetrahedral geometry of the environment of the metal (the chelate unit $[FeS_4]$, with the sulphur atoms from four cysteine residues) in this protein [147].

An interesting problem is the effect of metal ions on the secondary structure of polypeptides. Some metals stabilise a helical conformation of the macromolecules; others, on the other hand, break it down [148]. A model process—the interaction of copper ions with polyglutamic acid—has been examined by means of optical rotatory dispersion. Calculation of the spiral content from the rotation at 233 nm showed that the spiral structure is apparently preserved even at relatively high pH-values if a sufficient quantity of Cu^{2+} ions is added. The latter probably act as bridges stabilising the spirals [149]. A similar stabilising effect of metals on the structure of nucleic acids was suggested [150] from the dependence of the melting point and certain other properties of deoxyribonucleic acid on the content of metal ions. On the assumption that the sugars of DNA were involved in metal fixation, an investigation was made of equimolecular complexes of manganese, cobalt, nickel, and copper with adenosine triphosphate; their optical rotatory dispersion indicated that 2′,3′-hydroxy-groups of ribose were involved in coordinating the metal with the ATP molecule [151].

A further use of the optical activity of complex compounds is to establish the identity of natural and synthetic macromolecules from the optical rotatory dispersion of their metal complexes. For example, the optical rotatory dispersion curves of the natural antibiotic polymyxin B and its synthetic analogue, which are smooth up to 260 nm, carry too little information, in contrast to the complexes of these cyclic decapeptides, which exhibit clearly defined Cotton effects in the vicinal region. Analysis of the form of the curves for the complexes of the two substances showed their general qualitative similarity, with slight quantitative differences that disappear completely with time owing to denaturation of the natural macromolecule; this enabled the decapeptides to be regarded as identical [152].

Hitherto the discussion has been concerned mainly with complexes of metals with natural macromolecules. Such complexes are probably responsible for certain aspects of the functioning of enzymes containing a "labile metal". Another group of natural metal complexes contain various porphyrin systems, where the metal is firmly bound in a square planar complex with an $[MN_4]$ chelate unit, examples of which are haemoglobin, myoglobin [153], plastocyanin [154], cytochrome c [155,156], and other natural products, which have also been investigated by optical rotatory dispersion. The Fe^{2+} ion present in haem becomes asymmetric on coordination at the apical position with two different ligands (e.g. with two polypeptide chains, as in cytochrome c [155]). As a consequence both forms—oxidised and reduced—of this important respiratory pigment of blood have a sharp Cotton effect of great amplitude in the region of 530 nm. The optical rotatory dispersion results from the superposition of three effects—due to the asymmetric carbon atoms of the amino-acid residues, to the helical portions of the polypeptide chain, and to the asymmetric metal atom—and is quite complicated to interpret exhaustively. Nevertheless it was concluded, in view of the reversibility of the changes occurring in the dispersion on passing from the oxidised to the reduced

form of cytochrome c, that this process involved a change only in the electronic state of the metal, while the structure of the natural ligand remained unchanged [156]. Study of the concentration and temperature dependence of the circular dichroism spectra of ferrihaem octapeptide (a fragment of cytochrome c) has yielded information on the relative orientation of the haems; the results obtained on model systems are used to interpret certain structural features of haemoglobin and of cytochrome-c oxidase [157].

Several chlorophylls and protochlorophyll pigments have also been investigated by means of circular dichroism and magnetic circular dichroism [158]. A quite detailed study has been made of the effect of complex formation with several bivalent metals (zinc, copper, nickel) on the optical activity of bile pigments, which can also be included structurally among porphyrin ligands [159].

V. DETERMINATION OF THE ABSOLUTE CONFIGURATION OF ORGANIC COMPOUNDS

For many classes of organic compounds the transitions responsible for optical activity are at too high an energy level for direct observation of the Cotton effect to be possible without appropriate apparatus for the vacuum ultraviolet. This applies to alcohols, amines, carboxylic acids, hydroxy-acids, and most amino-acids [160]. The problem can be solved also by introducing into the molecule a chromophoric group, which absorbs in a spectral range convenient for measurement. Thus Djerassi and his coworkers achieved considerable success in using $n \rightarrow \pi^*$ transitions of C=S groups in so called "chromophoric derivatives" of hydroxy-acids, amino-acids, and steroids to establish their absolute configurations [66]. Yet complexes of transition metals are especially convenient as such "chromophoric derivatives", both spectroscopically (because of the position of their $d-d$ transitions in the visible range) and practically (thanks to the simplicity of preparation of the complexes and the possibility of working in solution without isolating them).

Since the first attempts at using the Cotton effects of metal complexes to study dissymmetric organic molecules [161-163] several papers have appeared on the use for these purposes of the vicinal effect in various types of complex compounds. The rational basis for such configurational comparisons is the hypothesis that similar ligands having the same configurations in related complexes should induce rotatory forces of the same sign in corresponding transitions of the metal ion. As the same ligand may form part of several types of complexes, e.g. trisbidentate and bisbidentate, this provides an opportunity for checking the accuracy of the assignment of a configuration. The absolute configuration can be postulated by comparison with complexes of a ligand of known absolute configuration. The identity of the configurations of a series of diamines—(−)-pn, (−)-bn, (−)-chxn, (−)-phenen, (+)-stien—has been established in this way [164].

Configurations have been assigned to a series of hydroxy-acids related to mandelic acid by use of the sign of the Cotton effect of the copper(II) complexes of the amidines of these acids, which is positive for complexes obtained from amidines of the $L(R)$ series and negative for those of the $L(S)$ series [165]. Since the amidines themselves also have a Cotton effect at 270 nm, it is recommended that the two optical rotatory dispersion curves of the ligand should be subtracted from the curve observed for the complex [166].

The absolute configurations of different asymmetric carbon atoms in polyhydroxy-carboxylic acids can probably be determined from the optical activity of complexes formed at definite pH-values. Thus the signs of the circular dichroism of praseodymium(III) complexes with hydroxy-acids obtained in acid and neutral medium correlate with the configurations of the α- and γ-carbon atoms respectively [45]. Europium(III) complexes of hydroxy-acids differing only in the configuration of the α-carbon atom have circular dichroism spectra of mirror-image type [48]. When hydroxy-acids coordinate with nickel(III) at low pH, the sign of the circular dichroism correlates with the absolute configuration of the α-carbon atom, whereas at higher pH the deprotonation of the β-hydroxyl and ring formation with the metal enable the sign for the neutral complex to be related to the configuration of the β-carbon of the ligand (aldonic acid) [167].

The sign of the Cotton effect in the visible range for biscomplexes of copper(II) and nickel(II) [30,168] with amino-acids also depends on the configuration of the ligand, rotatory powers of opposite sign being induced in transitions of these two metals [168]. Probably here too, on coordination of the metal with ter- and multi-dentate amino-acids under certain conditions, individual types of complex compounds can be distinguished by differences in the optical rotatory dispersion and circular dichroism. Thus L-asparagine on coordination with copper(II) induces in the region of 600 nm Cotton effects of opposite sign depending on the pH. [169] The circular dichroism spectra of 1 : 1 complexes of praseodymium(III) with potentially terdentate amino-acids have been used to study aspects of the chelation of these ligands in various media [47].

Torchinskii and Koreneva [170,171] proposed a method for determining the absolute configuration of α-amino-acids and their derivatives (including N-terminal amino-acid residues in peptides) by measuring the optical rotatory dispersion of chelate compounds of several metals—copper(II), nickel(II), zinc(II), cobalt(III), aluminium(III)—with Schiff bases of the amino-acids with certain aromatic o-hydroxy-aldehydes. The sign of the Cotton effect was shown to be determined by the absolute configuration of the α-amino-acid and to be independent of the sign of rotation of the free ligand: a negative Cotton effect corresponded to compounds of the L-series, and a positive effect to those of the L-series. The complexes do not need to be isolated in the free state.

We have been discussing the use for configurational correlations of the sign of the rotatory power of definite $a-a$ transitions in metal complexes. The use of charge-transfer bands has been proposed for the same purposes. In copper complexes of amino-acids this band is located at ~250–270 nm and is of the L→M type. The coordination of amino-acids of the L-configuration with copper(II) at pH 8–10 gives a charge-transfer band of negative rotatory power. It is supposed that correlations based on the rotatory power of these bands may be more generally applicable, since both possible conformations of five-membered chelate rings induce Cotton effects of the same sign in the charge-transfer bands for biscomplexes with copper [169].

A second possible way of eliminating additional effects due to conformational contributions is to use for the determination of configurations complexes in which the compound occurs as a unidentate ligand L, e.g. of the type $[CoL(NH_3)_5]^{2+}$, where L represents an amino-acid [160] or a hydroxy-acid [172]. Cobalt(III) complexes have the advantages of kinetic inertness and the fact that the spectroscopy of Co^{3+} has been well studied. There is no difficulty

in obtaining the above complexes under controlled conditions (pH ≃ 5, below 40°C), although in the case of potentially bidentate ligands raising the temperature may lead to loss of ammonia and chelation. The optical activity of complexes with unidentate ligands is due solely to the vicinal contribution by an asymmetric carbon atom: if the dominant Cotton effect of the long-wavelength spin-allowed transition in it is negative, the acid has the *L*-configuration, related to *L*(+)-lactic acid[160]. This method is obviously applicable only to carboxylic acids with an asymmetric centre in the α-position with respect to the carboxyl, since the increase in distance between this centre and the chromophore (here the metal) in β- and γ-substituted carboxylic acids produces a sharp decrease in the relatively small vicinal effect. Complexes of the same type $[CoLX_5]^{n+}$ but with more bulky optically inactive ligands X may be more useful in these cases. Even in a series of complexes $[CoLX(NH_3)_4]^{n+}$ increase in the volume of the optically inactive ligand X is accompanied by a significant increase in the vicinal effect of the *O*-coordinated unidentate α-amino-acid L, caused by the diminution in the conformational mobility of the optically active ligand L with growth in the steric requirements of the neighbouring group X.[173]

A further important advantage of using the non-chelate type of complexes consists in the possibility of making configurational comparisons between different classes of substituted carboxylic acids of general type R.CHX.COOH (X = Alk, OH, NH_2, etc.), since all $[CoL(NH_3)_5]^{n+}$ complexes have the same microsymmetry C_{4V} when the acids are coordinated through the carboxyl, so that the way in which the *d*-levels are split and the energetic sequence of the transitions should be the same independently of R and X. Such comparison of the configurations of amino- and hydroxy-acids cannot be based on the optical activity of chelate complexes of the type $[Co(R.CHX.COO)(NH_3)_4]^{2+}$, since their microsymmetry changes from C_{4V} when X = NH_2 to C_{2V} when X = OH. In conformity with this the splitting of the triply degenerate octahedral $^1T_{1g}$ level is different in the two cases: $^1T_{1g} \rightarrow {}^1A + {}^1E$ with C_{4V} microsymmetry, but $^1T_{1g} \rightarrow {}^1A + {}^1B + {}^1B$ with C_{2V}.

Nevertheless, monochelate complexes can be quite useful for comparing the configurations of a series of ligands of the same type. For example, an intense circular dichroism band in the region of the absorption band II of Co^{3+} at 342–335 nm may be useful for comparing amino-acids, its Cotton effect being negative for compounds of the *L*-configuration and positive for *D*-amino-acids in the complexes $[Co\,aa(NH_3)_4]^{2+}$.[8,22]

Complexes of other metals can also be employed for configurational comparisons. Thus the absolute configuration of the β-carbon atom of (+)-pseudoephedrine has been established[40] from the analogy of the circular dichroism and absorption spectra in the region of *d*–*a* transitions of copper biscomplexes of this ligand and of the related *L*-(+)-2-aminopropanol of known absolute configuration.

The effect of complex formation with copper (in the form of cuprammonium solutions) on optical rotatory dispersion is used widely for the stereochemical analysis of amino-sugars[174], cyclic diols and amino-alcohols[175], and their acyclic analogues[174]. The molecular rotation of sugars is significantly increased by complex formation with molybdate ions, and the anomaly in the dispersion at 345 nm has been proposed for the analysis of sugar isomers[176]. The conformation of the first three hydroxyls of the pyranose ring is significant for complex formation. Molybdate solutions of sugars show three or four Cotton effects in the range 220–350 nm if the hydroxyls are arranged in a *cis*–*cis* configuration, and two Cotton effects in the same wavelength range if they are in the *trans*–*trans* positions[177].

The configurations of alcohols and amines can be determined from the sign of the rotatory power of the bands at 480 and 420 nm due to dichelates of nickel with xanthate or dithiocarbamate ions obtained from these alcohols and amines respectively. Both the Cotton effects are negative when the alcohol or amine has the *l*-configuration, as has been shown for *l*-menthol, *l*-2-methylbutanol[178], and secondary amines obtained from *l*-phenylethylamine[179,180].

Another interesting application of the circular dichroism of metal complexes is to determine the configuration of alkenes, whose own π–π^* and n–σ^* absorption occurs in the fairly remote ultraviolet (190–200 nm). Existing methods for obtaining chromophoric derivatives—osmates and episulphides—disturb the geometry of the ethylenic bond and therefore are not always acceptable. The formation of π-complexes of platinum(II) with alkenes is free from this defect, so that chromophoric *d*–*a* transitions of Pt^{2+} have been successfully used for configurational comparisons.

When ethylenic compounds undergo π-type coordination with a metal, the substituted carbon atom of the double bond becomes asymmetric. Monosubstituted ethylenes acquire one asymmetric centre, and *trans*-disubstituted ethylenes acquire two such centres having the same configuration; *cis*-disubstituted ethylenes yield a *meso*-form on coordination, since the two asymmetric centres have opposite configurations[181]. In complexes of mixed type $[PtCl_2LL']$, containing an optically active amine L and an alkene L', the sign of the low-energy transition of Pt^{2+} is independent of the relative positions (*cis* or *trans*) of amine and alkene, and indicates only the configuration of the coordinated alkene. This conclusion is confirmed by applying the quadrant rule[182–189].

VI. DETERMINATION OF THE COMPOSITION AND THE STABILITY OF COMPLEX COMPOUNDS

As a consequence of the presence of an additional parameter—the sign of the optical rotation—optical rotatory dispersion and circular dichroism should be far more effective than ordinary spectrophotometry for determining the composition and the stability of complexes. Nevertheless, very little work has been done on these lines, and most investigators, even when working with optically active ligands, use only potentiometry or absorption spectra[190–192]. However, a few examples of the application of spectropolarimetry can be mentioned. A group of French workers have developed methods for determining the composition and the stability of complex compounds, in particular of copper(II), zinc(II), cobalt(II), nickel(II), and cobalt(III) with optically active amino-acids[193–196], and of iron(III) with tartaric acid[197]. The formation of complexes by molybdate, tungstate, and uranyl ions with hydroxy-acids[198], by zinc(II), cobalt(II), and nickel(II) with *L*-mandelic acid[199–201], and by arsenic acid with *d*(−)-mannitol[202] has been investigated by means of the optical rotatory dispersion or even simply by measuring the specific rotations at a single wavelength[203]. Similar results were obtained when the stability constants were determined by other methods, e.g. potentiometric pH measurement[200].

Circular dichroism can also be used to investigate complex formation [204], although the apparatus is less accurate [205]. However, determination of the stability constants of complexes of oxovanadium with lactic acid showed not only good agreement with those obtained by the independent method of absorption spectra over a wide range of values of $\bar{n}$ (the formation function) but also that circular dichroism is even more sensitive at low values of $\bar{n} \simeq 0.2$. [206]

The spectropolarimetry of complex compounds can be useful in determining not only their composition [207-209] and their stability [207,210] but also for the quantitative determination both of metals [211-214] and of organic compounds [212,215,216].

Measurement of the optical rotatory dispersion and the circular dichroism of coordination compounds will yield the most valuable information on the finest structural features of the environment of the metal. Thus a diminution in the rotatory power of $d-d$ transitions may indicate flattening of the chelate unit, e.g. by interaction with a donor solvent [217] or as a consequence of fewer steric interactions within the molecule of the complex [218-220].

Many other applications of spectropolarimetry—such as e.g. study of the reactions of coordination compounds by means of optical rotatory dispersion and circular dichroism [221-224], analysis of conformational equilibria in complex compounds [225], investigation of geometrical and optical stereoselectivity in the coordination of metals with optically active ligands, and certain other aspects—are not dealt with here, since they may form the subject of separate reviews.

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In conclusion it may be stated that the wide application of spectropolarimetry in the field of inorganic chemistry during recent years has in effect provided a new method for studying the structure of coordination compounds, the possibilities of which have been by no means fully revealed so far.

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Macromolecular and Oligomeric Compounds as Stabilisers for Polymers

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The preparation is described of various types of macromolecular and oligomeric compounds, together with their use as stabilisers for polymers (to heat and light as well as to oxidation). Possible mechanisms of their action are discussed. Carbon-chain polymers, macromolecular and oligomeric compounds containing elements in Groups IV–VI of the Periodic System (silicon, tin, nitrogen, phosphorus, oxygen, and sulphur), and polymers having a system of conjugated double bonds are considered as stabilisers. These products have the advantages over the usual stabilisers of being polyfunctional, non-volatile, long lived in the polymers, and in individual cases considerably more effective. A list of 221 references is included.

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I. INTRODUCTION

Polymeric materials, though possessing valuable physical and mechanical properties, have the important defect of undergoing various types of aging under the influence of heat, light, atmospheric oxygen, etc. One method for improving the operational durability of these materials is to introduce stabilisers into them. Various oligomeric and polymeric compounds have been proposed comparatively recently for this purpose, in addition to the usual stabilisers. As early as 1964 Kargin suggested that macromolecular additives to polymers were most effective for regulating almost any processes in them [1]. The chief advantages of macromolecular and oligomeric stabilisers can be summarised as follows.

1. By interacting with the polymer during its degradation such stabilisers may prevent a decrease in the molecular weight of the material [1] associated both with depolymerisation and with the chance rupture of macromolecular chains.

2. Macromolecular and oligomeric stabilisers possess valuable technical properties—non-volatility, prolonged retention in the polymer, and, when of similar chemical structure, good compatibility with the latter.

3. In several cases these stabilisers are more effective than analogous compounds of low molecular weight.

The chief obstacle to the widespread application of polymeric and oligomeric stabilisers is probably the difficulty of blending them with the stabilised polymer, and also the possible adverse influence of degradation products of these stabilisers.

Polymeric and oligomeric derivatives of elements in Groups IV–VI of the Periodic System—carbon, silicon, tin(IV), nitrogen, phosphorus(V), and oxygen, sulphur, selenium, tellurium(VI)—have now been suggested as stabilisers for plastics. A large number of novel heteroatomic polymers have been synthesised during recent years [2–4], many of which have still been little studied and have not found practical application. It must be expected that in the near future macromolecular derivatives of such elements as boron, germanium, lead, and antimony will considerably supplement the list of practically useful polymers in general and effective polymeric stabilisers in particular.

Mainly factual data on polymeric and oligomeric stabilisers have been published; very few investigations have been made on the mechanism of their action. The aim of the present Reviewers has been not only to assemble and systematise the available information but also to direct the attention of research workers to this new and interesting branch of the chemistry and technology of high polymers.

II. HETEROATOMIC MACROMOLECULAR AND OLIGOMERIC COMPOUNDS

1. Polyorganosiloxanes

Polyorganosiloxanes have been suggested comparatively recently for protecting polymeric materials from thermal and thermo-oxidative degradation and from the action of ultraviolet radiation. They possess great resistance to oxidation and high temperatures. Their own thermal stability is strongly influenced by the nature and number of the organic radicals attached to the silicon atom: methyl and ethyl groups lower the thermal stability of polyorganosiloxanes, whereas phenyl groups enhance it [5,6]. Chemical modification of polyalkenes by liquid polyorganosiloxanes [7–9] leads to an improvement in their stability towards aging by heat and light. Modification was effected by heat-treating either the crude polyalkene or manufactured articles in the liquid polyorganosiloxane. The first stage in the modification of (low-density) polyethylene is regarded as the production of free radicals by the oxidation of carbon–hydrogen bonds at tertiary carbon atoms. The resulting hydroperoxy-groups in turn oxidise the organic portion of the (stabiliser) molecules with the rupture of silicon–carbon bonds. Subsequent reactions yield Si–O–C groups, as is confirmed by the infrared spectra of the modified polyethylene (absorption in the region of 1077, 1044, and 936 cm^{-1}). Furthermore, polysiloxane units are grafted on also at double bonds, as evidenced by the diminished number of unsaturated groups in the modified polyethylene (disappearance of absorption in the region of 886 cm^{-1}). Thus the great stability of modified polyalkenes to all forms of aging is explained

by a decrease in the number of mobile hydrogen atoms at tertiary carbon atoms and by the formation of energetically stable siloxane bonds in the macrochains. Similar mechanisms are probably responsible for the action of liquid polyorganosiloxanes containing the units

$$[(CH_3)(OSnR_3)SiO]_n \qquad (I)$$

(where R is a C_1–C_{12} alkyl), [10,11] and also for those of polyphenyl(hydroxyphenylpropylphenoxy)silcane and polyphenylaluminosiloxane [12]. These compounds exert a strong stabilising effect at high temperatures and surpass industrial organotin stabilisers in effectiveness.

Poly(vinylidene chloride) preserves its colour well at 130°C in the presence of

$$R[-O-Si(CH_3)(C_6H_5)]_nOR \qquad (II)$$

where R = t-butyl or pentyl and $n = 1$–5. [13] Improving the stability of the liquid polyorganosiloxanes themselves to thermal oxidation may enhance their stabilising effect. Thus additions of 8-hydroxyquinoline–titanopolydimethylsiloxane increase the thermal stability of liquid polyorganosiloxanes by factors of 15–18. [14]

2. Tin-containing Polymers and Oligomers

Organotin compounds have become widely used for stabilising plastics based on poly(vinyl chloride). They improve the stability towards heat and light, and are antioxidants. An advantage of organotin stabilisers is that their decomposition products strengthen the stabilising effect; whereas the decomposition products of stabilisers not containing tin often accelerate the degradation of poly(vinyl chloride). [1,15] In fact, because of the presence of organic residues attached to the tin atom through an oxygen atom, a sulphur atom, or a carboxy-group, the double decomposition of organotin compounds with hydrogen chloride yields, depending on the nature of these residues, thiols, dienophilic reagents, epoxy-compounds, phenols, ethers, esters, and other products which themselves have a stabilising action. Effective organotin stabilisers of poly(vinyl chloride) combine the functions of an inhibitor of dehydrochlorination of the polymer, an acceptor of hydrogen chloride, and a dienophile [16,17]. Organotin stabilisers probably coordinate with segments of conjugated double bonds in the polymers, thereby ensuring that the polymer retains its original colour for a long time [18]. However, no convincing evidence has yet been found for this.

Increasing interest has recently been taken in polymeric organotin stabilisers, since they are usually more effective than the corresponding stabilisers of low molecular weight. They have the considerable advantages of almost complete non-toxicity and of insolubility in water. The mechanism of the stabilising action of polymeric organotin compounds has not been studied. It can only be assumed that their action is closely analogous to that of the corresponding simple compounds [1].

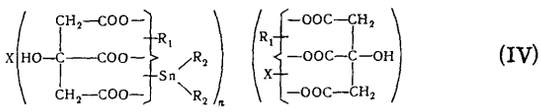
Poly(vinyl chloride) and copolymers of vinyl chloride are stabilised by polymeric alkyl(cycloalkyl)aryl-stannonic and -thiostannonic acids or their condensation products [19–22].

Polymeric organotin carboxylates and alkyl sulphides [23–26] are more effective than those of low molecular weight. Poly(vinyl chloride) resins are stabilised by the introduction of 0.1 -- 5.0 wt. % of the reaction product of a poly(alkyl(ene)tin oxide or dihalide) with an alkali-metal salt of lauric, thiobenzoic, β-mercaptopropionic, or octylthioglycollic acid or dodecanethiol [27,28]. Organotin compounds of formula [29]

$$R_1R_2R_3Sn[XSnR_4R_5]_mR_6 \qquad (III)$$

(where R_1–R_6 are hydrocarbon radicals (C_{1-30}) or OH groups, X = O or S, and $m = 0$–15) have also been used mixed with other stabilisers.

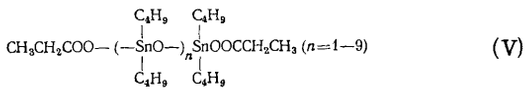
A polymeric organotin stabiliser, which improves the heat resistance of poly(vinyl chloride) and poly(vinylidene chloride), has been obtained by heating dibutyltin oxide with a polyester based on bicyclo[2,2,1]heptene-2,3-dicarboxylic acid (or its anhydride) and a glycol (ethylene, propylene, butylene, etc.). [30,31] The compounds



(IV)

(where X = H or an alkali metal, R_1 = Alk (C_{1-10}) or alkylene (C_{3-10}), R_2 = Alk (C_{1-20}), and $n = 1$–20), obtained from alkali-metal salts of citric monoesters and dialkyltin oxides or hydroxides, have been proposed as stabilisers against heat and light [32]. Poly(vinyl chloride) films stabilised with these compounds remain colourless after exposure to ultraviolet radiation for 500 h, whereas control films darkened after exposure for 20 h.

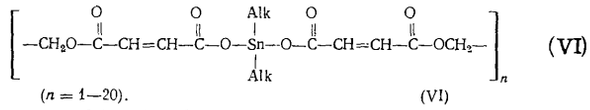
Polymeric dibutyltin dipropionate



(V)

was considerably more effective than its simple analogue ($n = 0$). [33–35]

Polymeric dialkyltin dicarboxylates



(VI)

have been used to stabilise halogen-containing polymers (0.5–5.0 wt. %). They possess diminished toxicity and blend well with the stabilised polymers [36,37]. Sulphur-containing organotin oligomers, e.g. polymeric tin dibutyl dithiodimaleate, have also been proposed as stabilisers [38,39].

3. Macromolecular and Oligomeric Compounds Containing Nitrogen

Among compounds containing nitrogen, aromatic amines have been most widely used as practical antioxidants. There is no generally accepted view on the mechanism of their action: formation of a charge-transfer complex between the aromatic ring of the inhibitor and the peroxy-radical responsible for the development of oxidative processes has been postulated [40]. Inactive products are formed when such a complex decomposes. A more soundly based hypothesis is that inhibition is accompanied by abstraction of hydrogen atoms from the amino-group [1,40,41]. This forms radicals stabilised by conjugation with the aromatic ring; their existence has been proved by means of electron spin resonance. The subsequent fate of these radicals depends both on their structure and on the reaction conditions. Several years' practical application of amines as antioxidants has shown that diamines in which the functional groups are close together are the most effective. The probable explanation [40] is that diamines are able to deactivate both active radicals

formed by the breakdown of a hydroperoxide, which prevents the development of degenerate branching processes. When a monofunctional inhibitor is used, only one of the radicals is deactivated, while the second escapes from the "cage" and continues the oxidation chain.

Products of the reaction of an epoxidised butadiene with *p*-aminodiphenylamine, 2-naphthylamine, aniline, *p*-aminophenol, and *p*-anisidine have been used to stabilise various classes of rubbers[42]. Considerably smaller quantities of the amine component are required when these compounds are employed than with the usual antioxidants. This is probably due to better compatibility of polymeric stabilisers with rubber. Low-temperature interfacial polycondensation of the bischloromethyl ether of ethylene glycol with hexamethylenediamine yields polyamine-ethers, whose use has been proposed[43,44] for stabilising synthetic rubber.

Polyalkenes have been stabilised by introducing polycarbodi-imides of molecular weight exceeding 500.[45,46]

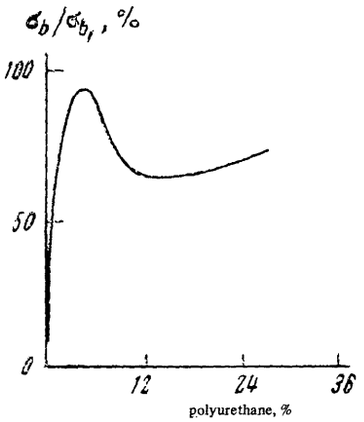


Figure 1. Dependence of tensile strength of acetylcellulose on content of added polyurethane[55], where σ_b is the tensile strength of the initial specimens and σ_{b_1} the tensile strength after exposure to ultraviolet radiation for 20 h.

Condensates of formaldehyde with respectively melamine, dicyanodiamide, urea, and thiourea have been suggested as stabilisers for polyacetals[47]. The molar ratio of the components in the condensation may vary within wide limits. The first two resins with a slight molar excess of formaldehyde (1.5–3.5 : 1) are acceptors of the formaldehyde liberated when the polymers are processed, and are thermally more stable. It is particularly noteworthy that polyacetals stabilised by the condensates do not discolour during processing. It is advisable to use these condensates mixed with known antioxidants and photostabilisers[47–50]. The thermal stability of polyformaldehyde is enhanced by the addition of polyacetalamides (M = 1000–10 000).[51]

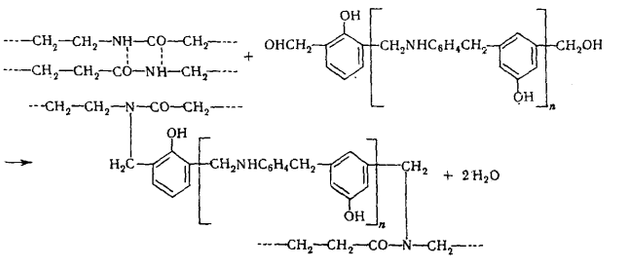
The use of copolymers of acrylamide (5–80 mole %) with styrene, alkyl acrylates, vinyl ketone, vinylnaphthalene, etc. has been proposed[52,53] for the thermal stabilisation of polyoxymethylene. The stabilised polyoxymethylene remained homogeneous and transparent.

The heat-resistance of polyurethane foams can be increased considerably by means of cyclic polyisocyanates obtained from aniline and formaldehyde or their derivatives[54].

The presence of polyurethanes—products of the condensation of tolylene di-isocyanate with ethylene glycol and of naphthylene di-isocyanate with triethylene glycol—diminishes appreciably the evolution of gas when acetylcellulose is exposed to ultraviolet radiation[55,56]. The variation in the tensile strength of exposed specimens indicates that the stabilising effect is considerably greater than could have been expected solely from the light-filtering action of the polyurethanes (Fig. 1). These products were more effective stabilisers for acetylcellulose than the phenyl salicylate usually employed industrially.

On ultraviolet exposure the polyurethane molecules are easily excited to a biradical triplet state (presence of phosphorescence in the luminescence spectra), and therefore become traps for free radicals formed by photolysis of the acetylcellulose. At low polyurethane contents this mechanism of stabilisation is decisive. In addition, the photodegradation of polyurethanes yields products having a system of conjugated bonds which exert a light-filtering effect. This latter mechanism of the stabilisation of acetylcellulose becomes dominant at high polyurethane contents. During exposure to ultraviolet the efficiency of polyurethanes as stabilisers does not diminish but, on the contrary, increases as degradation products accumulate. In principle any polyurethanes based on di- and polyisocyanates and polyhydroxy-compounds (glycols, polyethers) have a stabilising action. However, the energy of excitation of polyurethane molecules to the triplet state and the compatibility of a polyurethane with the polymer to be stabilised depend on the chemical structure of the polyurethane.

An aniline–phenol–formaldehyde resin has been suggested[57,58] for stabilising polyamide films. The stabilising effect is obviously due to the ability of the resin to react chemically with polyamides[59,60]:



which probably explains its efficiency as a photostabiliser. One cause of the aging of a polyamide film is the increase in the crystallinity of the polyamide with keeping. It may be supposed that the number of hydrogen bonds and the degree of crystallinity of the polyamide decrease in the presence of the ternary resin (1–2 wt.%).[61] Furthermore, the presence of phenolic and amine groups favours the appearance of inhibiting properties in the aniline–phenol–formaldehyde resin under certain conditions. This ternary resin, unlike other stabilisers (especially aromatic amines), does not increase the light absorption of polyamide films.

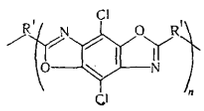
Polymeric antioxidants, whose efficiency has been tested in unfilled mixtures based on natural rubber, have been obtained by the reaction of a butadiene–methacrylaldehyde copolymer containing active aldehyde groups with

aniline and di-t-butylphenol[40]. A kinetic study of vulcanisation of the mixtures revealed that these products increase the degree of structuring of the mixtures. The explanation is that, in reacting with the peroxy-macroradicals of the rubber and forming complicated intermediate compounds, the polymeric antioxidants cross-link the molecular network of the vulcanised rubber, as it were, thereby stabilising it during oxidative degradation. Investigation of thermal aging showed polymeric antioxidants to be more effective than the usual stabilisers. They were found also to lengthen the induction period in the oxidation of pure and vulcanised rubber, as a consequence of their action on hydroperoxides. The similar chemical structure of polymeric antioxidants makes them readily compatible with vulcanised rubbers, with the absence of surface "blooming".

A few other examples of the use of oligomeric nitrogen-containing compounds as stabilisers should be mentioned. The elasticity and the heat-resistance of poly(vinyl chloride), poly(vinyl acetate), and their copolymers are improved by introducing a polyglutamate (M = 500–10 000)

$$[-NH-CH_2-(CH_2CH_2COOCH_2R)\,CO-] \qquad \text{(VII)}$$

where R = C_6H_5 or Alk (C_{5-21}).[62] Polymeric and simpler benzobisoxazole derivatives of the type



(VIII)

where R′ represents an alkylene or a phenylene radical, have been prepared[63,64]; they can be used as heat-stabilisers for halogenated polyalkenes.

4. Phosphorus-containing Polymers and Oligomers

Organophosphorus compounds have recently been proposed as thermal stabilisers and antioxidants. Phosphorous esters have become widely used. The stabilising effect of tervalent phosphorus compounds is due to their great reactivity. These stabilisers can take part in various processes underlying the stabilisation of polymers —in inhibiting oxidative processes, suppressing the degenerate branching of an oxidation chain, breaking down chromophoric groups, and also suppressing the harmful action of derivatives of metals of variable valency, which are often present as impurities in polymers[65–68].

The stabilising action of phosphites in poly(vinyl chloride) at high temperatures (80–200°C) consists mainly in combining with the hydrogen chloride catalysing breakdown of the polymer

$$(RO)_3P + HCl \rightarrow (RO)_2POH + RCl,$$

and in reacting with polymeric peroxides to prevent degradation of the main chain of the polymer

$$R'OOR' + (ROP)_3 \rightarrow (RO)_3P\begin{matrix}OR'\\OR'\end{matrix} \rightarrow R'OR' + (RO)_3P{=}O.$$

Furthermore, chemically combined phosphorus is detected in the polymer on the thermal decomposition of poly(vinyl chloride). This is explained by the reaction

$$\cdots\underset{\displaystyle Cl}{\overset{|}{CH}}\cdots + (RO)_3P \rightarrow RCl + (RO)_2\overset{\cdots CH\cdots}{\overset{/}{P}}\!\!=\!\!O$$

(the Arbuzov rearrangement), which may be catalysed by the alkyl chloride formed from the phosphite and hydrogen chloride. The rearrangement results in the replacement of labile chlorine atoms in the α-position to a double bond by groups more firmly bound to the polymer[69–73]. The efficiency of stabilisation increases with increase in the chain length of R.

Polymeric phosphites possess still more efficient inhibiting properties[74–78]. Polyphosphites of formula

$$[-O-\underset{\displaystyle OR_1}{\overset{|}{P}}-O-R-O-]_n \qquad \text{(IX)}$$

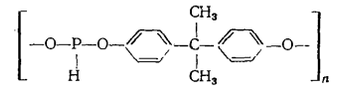
where

$$R{=}CH_2{-}CH_2,\ CH_2{-}CH_2{-}OCH_2{-}CH_2,\ C_6H_4,\ -C_6H_4-\overset{\displaystyle CH_3}{\overset{|}{C}}(CH_3)-C_6H_4-;$$

$$R_1{=}C_2H_5,\ C_4H_9,\ C_6H_5,\ ClC_6H_4;\quad n{=}2{-}10,$$

blend well with many polymers (polyalkenes, poly(ethylene terephthalate), rubbers) and are firmly retained in them[79]. This confers on polyphosphites valuable properties not possessed by the usual antioxidants (alkyl aryl phosphites). Polyphosphites have been obtained by transesterification of such esters with dihydroxy-compounds[76,79], but the products hydrolyse in air, which makes their use difficult in practice. Polyphosphites obtained by transesterifying complete and mixed esters of phosphorous acid with alkylated bishydroxyphenyl sulphides are free from this defect. The inhibiting action of sulphur-containing polyphosphites has been assessed from the change in the rate constants for the chemical relaxation of tension, which is an unambiguous measure of the resistance of vulcanised butadiene–styrene rubbers to thermo-oxidative degradation. The polyphosphite obtained by transesterifying triphenyl phosphite with bis-4-hydroxy-2-methyl-5-t-butylphenyl sulphide, in which the oxygen-phosphorus bonds are shielded by t-butyl groups and are stable to hydrolysis, was especially effective[80].

Not only complete polyphosphites but also intermediate structures, e.g.



(X)

have been proposed for the stabilisation of poly(ethylene terephthalate). Addition of 1 wt.% to about one-quarter reduces the thermo-oxidative degradation of the polymer at ~ 260°C. The effectiveness of this stabiliser is probably due to the presence of oxidisable P–H bonds[81].

The colour of solutions of a copolymer of vinyl chloride with acrylonitrile is preserved in the presence of mixtures of alkylene oxides with polymeric organic phosphites of general formula

$$(RO)_2PO\,[-R'-O-\underset{\displaystyle OR}{\overset{|}{P}}-O-]_n-R'-OP\,(OR)_2 \qquad \text{(XI)}$$

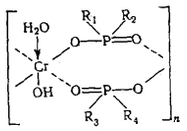
or with organic polyphosphonites of the type

$$RO-PO\,[-R'-O-\underset{\displaystyle C_6H_5}{\overset{|}{P}}-O-]_n R'-O\underset{\displaystyle C_6H_5}{\overset{|}{P}}-OR \qquad \text{(XII)}$$

where R = Alk (C_{1-10}) or C_6H_5, R′ is a residue of a saturated aliphatic diol, and n = 1–8. The use of lower alkylene oxides combined with polymeric organic phosphites and phosphonites improves the stability of resin solutions[82,83].

Halogenated resins have been stabilised by salts (cadmium, barium, lead, calcium, magnesium, zinc,

aluminium, tin, etc.) of organic or inorganic polyphosphoric acids[84]. Polymeric chromium phosphinate



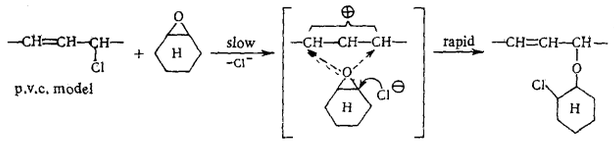
$(R_1-R_4 = Ph, Me; n > 1)$ (XIII)

provides good protection for vinyl chloride polymers from ultraviolet radiation[85].

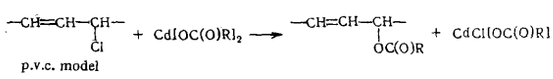
5. Polymers and Oligomers containing Epoxy-groups

The main types of epoxide stabilisers are glycidyl ethers—condensates of epichlorohydrin with phenols and aliphatic alcohols—and epoxidised esters of higher fatty acids.

The stabilising effect of epoxy-compounds and of their mixtures with the salts of aliphatic acids with Group II elements has been studied on model compounds—mixtures of 4-chlorohex-2-ene and 2-chlorohex-3-ene—that simulate a degraded poly(vinyl chloride) unit[86]. At 150°C the model compounds decomposed with the evolution of hydrogen chloride. Degradation was greatly retarded by the introduction of stabilising additives (cyclohexene oxides with cadmium–barium or calcium–zinc carboxylates). The labile chlorine atom in the allyl position was thus detached without formation of a new double bond, so that autocatalytic decomposition reactions did not develop:



p.v.c. model

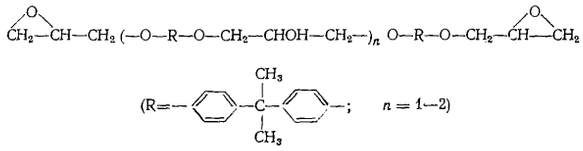


p.v.c. model

$(R = CH_3, C_7H_{15})$

Furthermore, epoxy-compounds evidently retard chain oxidations by inhibiting breakdown of the intermediate hydroperoxides. The model reaction of t-butyl hydroperoxide with cobalt octanoate shows that a mixture of an epoxide resin and a cadmium soap is more efficient than its components in inhibiting the decomposition of a hydroperoxide. The mixture approaches dibutyltin dilaurate in the efficiency of its action[87,88].

The lower glycidyl ethers have the disadvantages of being volatile and causing dermatitis, so that the non-volatile and less toxic epoxide resins are preferred for stabilising polymers. The glycidyl polyether



(XIV)

obtained by condensing a bisphenol with epichlorohydrin, has been suggested[89] for stabilising vinyl halide polymers.

Polyalkylene glycol ethers RO.[AO]n.R′, where R′ = 2,3-epoxypropyl, A = alkylene (C_6), and n = 2–4, also have a stabilising effect[90]. Dialkyltin epoxysuccinates (n = 1–20) blend well with vinyl halide polymers, do not decompose with the liberation of toxic products when processed, and ensure that compositions should have prolonged thermal stability and good light stability[91].

Products obtained by the reaction of epichlorohydrin with sulphones of formula HO.R.SO_2.R′.OH (R and R′ = C_6H_5 or $C_6H_5CH_2$) have been recommended for stabilising vinyl polymers[92,93]. Epoxidised esters of higher aliphatic acids present in compositions based on poly(vinyl chloride) have not only a stabilising effect but also a plasticising action[94–98]. They are generally used as a secondary stabiliser with magnesium, calcium, and zinc stearates, organotin stabilisers, and phosphites[99–111]. Extremely stable compositions have been obtained by introducing into polyalkenes products of the reaction of polymers containing epoxy-groups with various organic hydroxy- and thio-acids and hydroxyl-containing compounds[112–118].

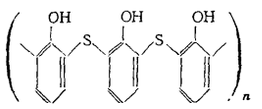
Rubbers modified by furan resins possess enhanced thermal and chemical stability[119].

6. Macromolecular and Oligomeric Sulphur-containing Compounds

Compounds containing sulphur effectively inhibit the thermo-oxidative breakdown of many polymers.

Products obtained by the action of sulphur on atactic polypropylene have been used to stabilise isotactic polypropylene[120–122]. The sulphurised atactic polymer blended well with isotactic polypropylene, was retained in it for a long time, and was not washed out by water. Products of the action of dibenzothiazolyl disulphide (Altax) on atactic polypropylene surpass the sulphurised atactic polymer in their stabilising action[123]. The inhibiting activity of products of the reaction of atactic polypropylene with sulphur or with Altax depends on the period of contact between them. The initial products contain mainly thiol and polysulphide groups, which are converted during the reaction into monosulphide and thioketone groups[124–126]. The greatest stabilising activity is possessed by the initial products, which are as good as certain industrial antioxidants, e.g. isobornylmethylphenol. The high activity of low concentrations of the initial products is due to the rapid conversion of polysulphides into sulphoxides and the involvement of mercapto-groups in chain-terminating reactions. However, thiyl radicals are highly reactive, and are able to initiate oxidation; for this reason the inhibiting activity of the initial products decreases as their concentration increases[127]. If ionol is also added, the thiyl radicals are stabilised, hence secondary initiation is absent, and the efficiency increases[121]. The final products of the interaction of atactic polypropylene with sulphur contain predominantly monosulphide and thioketone groups, which are oxidised to sulphoxides with greater difficulty than is explained by their insignificant stabilising activity[128]. The inhibiting power of the reaction product of polystyrene with sulphur exceeds many times that of sulphurised atactic polypropylene: addition of the former protects polypropylene at 200°C for 110–150 min, whereas the latter guarantees protection for only 7–12 min[129].

Other suggestions for the stabilisation of polyalkenes are a polydisulphide based on decane-1,10-dithiol combined with carbon blacks[130], oligomers obtained by the reaction of phenols with sulphur monochloride or dichloride[131]



$(n = 1-4)$ (XV)

and polyesters based on aliphatic thiodicarboxylic acids mixed with antioxidants of phenolic type [132,133]. Sulphur-containing stabilisers for poly(vinyl chloride) resins are generally used mixed with stabilisers that are acceptors of hydrogen chloride, an example being a mixture of an organic derivative of tin or zinc with a liquid polythiopolythiol

$$HS(CH_2CH_2OCH_2OCH_2CH_2SS)_nCH_2CH_2OCH_2OCH_2CH_2SH \quad (n = 3-6)^{134-136}. \quad \text{(XVI)}$$

The thermo-oxidative degradation of poly(vinyl chloride) resins is presented by polyester condensates of mercapto-alcohols and dicarboxylic acids mixed with lead silicate [137-139].

III. POLYMERS WITH A SYSTEM OF CONJUGATED DOUBLE BONDS

Polymers having systems of conjugated double bonds have recently been proposed as stabilisers for macromolecular compounds. These polymers are able to form relatively inactive biradicals on excitation to a triplet state, and thereby prevent the development of chain decomposition processes in the degradable polymer. The activation energy for the addition of radicals to conjugated polymers is less the lower the energy of excitation of the latter to the triplet state.

Polymers with systems of conjugated double bonds comprise a set of homologous polymers differing in conjugation energy in the transition state, in activation energy, and in energy of excitation. Therefore the use of these conjugated polymers as stabilisers of macromolecular compounds makes it possible in principle to inhibit chain breakdown processes over a wide range of temperatures or energies of exposure. In this connection the use of conjugated polymers is especially promising for raising the limiting operating temperature of known organic and heteroatomic polymers.

Polymers having an acyclic chain of conjugation—polyphenylacetylene, an equimolecular *p*-diethynylbenzene-phenylacetylene copolymer, and dehydrochlorinated poly(vinyl chloride)—inhibit the dehydrochlorination of poly(vinyl chloride) at 175–180°C and retard its breakdown under the influence of ultraviolet radiation. They can be used either independently or mixed with other stabilisers. When polyphenylacetylene is used alone (1 wt.%), the rate of evolution of hydrogen chloride from poly(vinyl chloride) at 175°C diminishes to one-third; the action of polyphenylacetylene is far more effective when mixed with lead silicate [140-142].

Polymers with aromatic rings in the conjugated chain—polyphenylene, polyazophenylene, polyphenyleneaminoquinone—have also been examined as stabilisers for poly(vinyl chloride). Their stabilising action is different from that of polymers having an acyclic conjugated chain. Aromatic conjugated polymers become more effective with rise in temperature, but acyclic conjugated polymers become less effective. The reason for this is that the energy of excitation to the triplet state is higher for polyphenylene than for polyvinylenes; therefore the inhibiting action of the former develops at higher temperatures. The effectiveness of the stabilising action of conjugated polymers is strongly dependent on the conditions of the thermal degradation of poly(vinyl chloride). Comparison of the rates of dehydrochlorination of the latter in nitrogen and in the presence of oxygen shows that aromatic conjugated polymers suppress only the thermo-oxidative degradation of poly(vinyl chloride). This is explained by the greater activity of biradicals of conjugated polymers in reactions with *O*-radicals than in reactions with atomic chlorine and *C*-radicals [143,144].

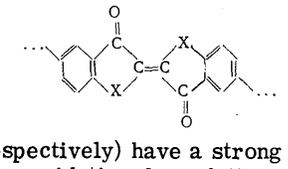
Conjugated polymers—polyphenylene, polyazophenylene, polyphenylacetylene, polydiphenylacetylene—have solved the problem of the thermal stabilisation of three-dimensional polymers based on polyether–acrylates. Addition of a conjugated polymer (5 wt.%) almost completely suppresses the thermo-oxidative degradation of hardened polyether–acrylates at 200°C, without impairing their physicomechanical properties. In the absence of stabilisers 30–35% of the initial polyether–acrylate is degraded under the same conditions [145-148].

Conjugated polymers retard the high-temperature oxidation of polyarylates [149], phenol–formaldehyde resins [150], and polycarbonates [151].

Examination of a large number of conjugated polymer inhibitors reveals that the most active contain in the main conjugation chain heteroatoms with a lone pair of *p*-electrons, such as polyquinonedioxins [152] (Table 1). Polymers having a ladderlike structure—(XX)–(XXIII), (XXV), (XXVI)—as well as polymer (XIX) possess the characteristic properties of conjugated systems: i.e. the *p*-electrons of their heteroatoms are conjugated with the π-electrons of the quinone and aromatic rings. In polymers (XVII), (XVIII), and (XXIV) conjugation is weakly developed, being least in (XVII), for which a tautomeric transition is impossible.

The thermo-oxidative degradation of polycarbonates was conducted at 300°C and an oxygen pressure of 500 mmHg. The efficiency of stabilisers against degradation was determined from the kinetics of the absorption of oxygen and from viscometric measurements in dichloromethane. An industrial polycarbonate may be contaminated with sodium chloride, which accelerates considerably the high-temperature degradation of the polymer (it reacts with terminal phenolic hydroxyls to evolve hydrogen chloride, which catalyses hydrolysis of the ester bonds in the polymer). Polyquinones inhibit degradation of an unpurified polycarbonate. Polymers of ladderlike structure containing two heteroatoms per monomer unit are especially effective; the inhibiting power of linear polymers is considerably lower (Fig. 2). The stabilising effect is strengthened by increasing the addition of polymeric quinones to 2 wt.%. [153-158]

Polymeric colorants such as polyindigo and polythioindigo



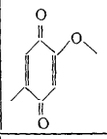
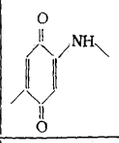
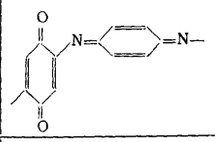
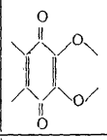
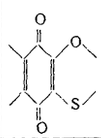
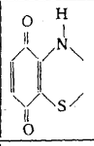
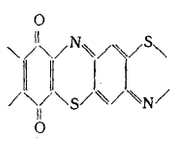
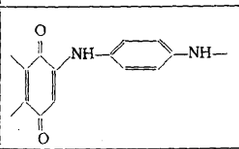
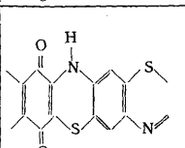
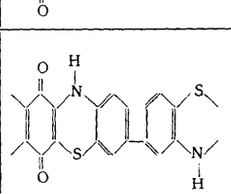
(XXVII)

(X = NH and S respectively) have a strong stabilising effect against the thermo-oxidative degradation of polyamide fibres [159]. When a fibre has been treated with such a dye or an analogue of low molecular weight, not only does its strength not diminish during degradation, but may even increase in some cases. The stabilising effect is most clearly evident in Kapron [6-polyamide] fibre, when the effectiveness diminishes in the sequence

polymeric dyes > lower analogues > Indanthren dyes

This can be attributed to completion of the supermolecular structure of the fibres under the influence of polar compounds deposited on their surface. Furthermore, a polymeric dye containing systems of conjugated bonds acts as an inhibitor of chain oxidation [159].

Table 1. Polyquinones investigated as stabilisers of polycarbonates[152].

Polymer	Monomer unit	Mol. wt.	Terminal groups	E.s.r. signal
(XVII)		1600	Br*	very weak
(XVIII)		1300	NH_2	weak
(XIX)		1400–1700	H, Cl	signal
(XX)		2200–2500	OH, Cl	signal
(XXI)		1800	Br*	signal
(XXII)		1600–1700	—	signal
(XXIII)		1600–1900	H, Cl	signal
(XXIV)		1500–1800	H, NH_2	weak
(XXV)		2000–2300	—	signal
(XXVI)		2000–2200	—	signal

*Branched chain.

Berlin considers that paramagnetic centres of polyconjugated systems play an activating part in the thermooxidative degradation of polymers (local activation effect).

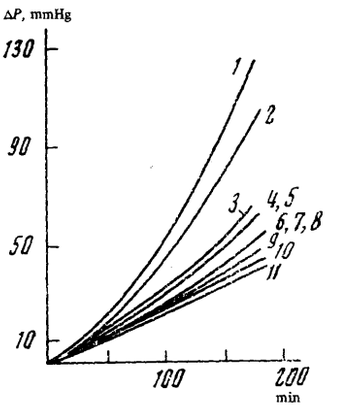


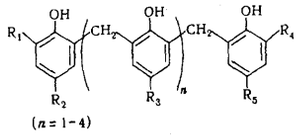
Figure 2. Rate of fall of pressure in the thermooxidative degradation of an unpurified polycarbonate in the presence of polymeric stabilisers (1 wt.%)[152]: 1) no addition; 2) (XIX); 3) (XXI); 4) (XXIII); 5) (XVIII); 6) (XVII); 7) (XX); 8) (XXIV); 9) (XXV); 10) (XXII); 11) (XXVI).

At high temperatures the diamagnetic conjugated polymer molecules undergo oxidative dehydropolycondensation, with an increase in their degree of conjugation and denser packing of the molecules in aggregates. This favours excitation of the diamagnetic molecules to the biradical state under the influence of the paramagnetic centres of the conjugated polymer, with the subsequent formation of charge-transfer complexes with peroxy-radicals. Further reactions of the complexes lead to the appearance of inactive products[160–166].

IV. MACROMOLECULAR AND OLIGOMERIC ANALOGUES OF STERICALLY HINDERED PHENOLS

Antioxidants of phenolic type have been widely used in industry because of their great effectiveness and the absence of toxicity[167]. They have the advantage of not discolouring the stabilised polymer. The mechanism of their action has now been studied quite thoroughly. Various sterically hindered phenols have been prepared and examined. Their effectiveness depends on several factors —including the nature of nuclear substituents and their bulk, the ease of free-radical detachment of hydrogen from the phenolic hydroxyl and the stability of the resulting phenoxyl radicals, as well as certain other factors—an aspect which has been reviewed in some detail[1,168–170]. The oxidation products of phenolic antioxidants also possess inhibiting properties, though less pronounced than those of the original phenols[171,172].

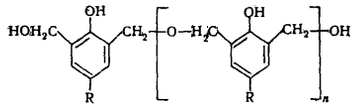
While exhibiting all the valuable features of phenolic stabilisers of low molecular weight, the polymeric analogues of sterically hindered phenols are considerably less volatile and soluble. Polyphenols of formula



(XXVIII)

($n = 1-4$)

(R^1–R^5 = alkyls and $n = 1-4$) have been prepared and found to be effective antioxidants for polyalkenes [173]. The phenolic polycondensate may consist of various aromatic monomer units—isopropylidene-*pp'*-diphenolic, s-butylidene-*pp'*-diphenolic, bisphenol sulphone, bisphenol sulphoxide, etc.—joined together by methylene, ethylene, ethylidene, di-isopropenylbenzene, and other groups [174–180]. A synergetic effect is observed when polyphenols are used mixed with bisdodecyl or bisoctadecyl thiodipropionate [181]. Polyhydroxyphenylalkanes also are effective antioxidants. Polypropylene has been stabilised with a mixture of a polyhydroxyphenylalkane (2,2,5,5-tetrakis-*p*-hydroxyphenylhexane) and bisoctadecyl thiodipropionate: the time at 140°C before darkening occurred was 180 h, but in the absence of a stabiliser 24 h. [182] Phenol–formaldehyde oligomers have been used to stabilise polyether-urethanes [183] and poly(vinyl chloride). [184] A method of stabilising poly(vinyl chloride) towards light and heat uses mixtures of a polyoxybenzyl ether



(XXIX)

($n > 1$; R = CH_3, $C(CH_3)_3$, C_6H_5, etc.) or a polyoxybenzyl alcohol with lead stearate or silicate as acceptor of hydrogen chloride. These inhibitors blend well with poly(vinyl chloride). The thermal stability of the latter is trebled by adding the polyoxybenzyl ether (1 wt.%). [185,186]

V. MACROMOLECULAR AND OLIGOMERIC ANALOGUES OF BENZOPHENONE

Derivatives of hydroxybenzophenone are widely used for the photostabilisation of polymers. Apart from the light-filtering effect, the decisive process with benzophenone derivatives is the resonance dipole–dipole interaction, leading to a radiationless transfer of the electronic excitation energy from the polymer to the photostabiliser [187–190].

Polymeric and oligomeric analogues of benzophenone have been proposed for protecting polymers from ultraviolet radiation. Polyalkenes and poly(vinyl chloride) resins have been stabilised with homopolymers of 2-hydroxy-4-methacryloylbenzophenone and 2-hydroxy-4-(meth)acryloylacetophenone. Poly(vinyl chloride) film yellowed and cracked after exposure to ultraviolet radiation for 200 h, but a film stabilised with poly-4-acryloyl-2-hydroxybenzophenone remained for 600 h without change. The photostability of poly(butyl acrylate) improved in the presence of poly-2-hydroxy-4-methacryloyl-5-t-butylbenzophenone [191]. Polymers of 2-hydroxy-4-(2-hydroxy-3-methacryloylpropoxy)benzophenone (XXX), 4-(3-acryloyl-2-hydroxypropoxy)-2,2'-dihydroxybenzophenone, etc. [192] and also the copolymer of (XXX) with phenyl 2-hydroxy-5-methacryloylmethoxybenzoate [193] have been recommended for the photostabilisation of a copolymer of vinylidene chloride with ethyl acrylate.

The homopolymers of acrylic and methacrylic derivatives of 4-alkoxy-2-hydroxybenzophenones have been used for the photostabilisation of polystyrene, poly(vinyl chloride), poly(methyl methacrylate), etc. Fig. 3 shows that poly(benzophenone acrylate) is more effective than the corresponding methacrylate as a photostabiliser for polystyrene, which is explained by the better compatibility of the former with the polymer. A copolymer of styrene with benzophenone methacrylate and a mixture of polystyrene with poly(benzophenone acrylate) have roughly the same stability towards light. Poly(benzophenone methacrylate) is an effective photostabiliser of poly(vinyl chloride) (Fig. 4). [194]

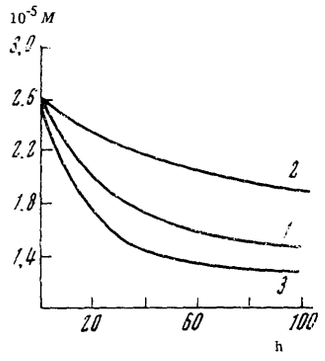


Figure 3. Dependence of molecular weight of polystyrene on time of illumination in the presence of polymeric stabilisers [194]: 1) poly(benzophenone methacrylate); 2) poly(benzophenone acrylate); 3) control specimen.

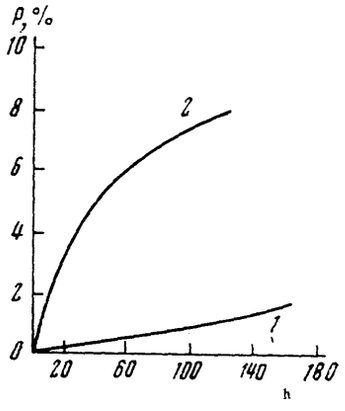
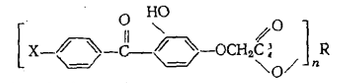


Figure 4. Dependence of content of gel fraction on time of irradiation of poly(vinyl chloride) [194]: 1) with added poly(benzophenone methacrylate); 2) no addition.

Oligomeric hydroxylated polyesters

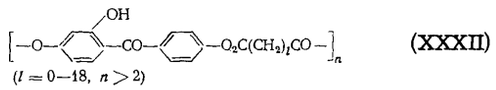


(XXXI)

(where X = H, AlkO (C_{1-4}), R = residue of aliphatic (C_{2-10}) polyhydric alcohol with $n = 2-6$ OH) have been

recommended as light-protective additives, which are well preserved in the polymer. They were obtained by reaction between 4-benzoyl-3-hydroxyphenoxyacetic acid and a polyhydric alcohol (ethane-1,2-diol, n-decane-1,10-diol, etc.). Tests in air for 10 weeks showed that the polymeric stabiliser was completely preserved in films, whereas the concentration of hydroxybenzophenones diminished considerably [195].

Products of the condensation of 2,4,4′-trihydroxybenzophenone with dicarboxylic acids (succinic, glutaric, adipic) or with their acid halides



(XXXII)

($l = 0$—18, $n > 2$)

have been proposed as photostabilisers which are well preserved in polyalkenes [196].

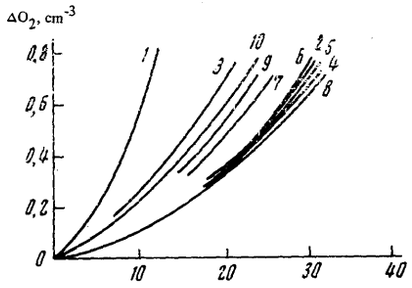
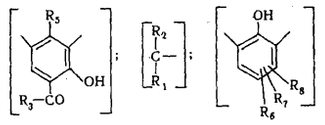


Figure 5. Photo-oxidation of stabilised polypropylene films at 60°C (distance from lamp to film 7 mm, with 2—mm Pyrex filter) with different stabilisers (0.0184 mole kg^{-1}): [197] 1) no additive; 2) 2-hydroxy-4-octyloxybenzophenone; 3) as (2) after extraction; 4) condensate (XXXIV); 5) as (4) after extraction; 6) condensate (XXXIII); 7) as (6) after extraction; 8) condensate (XXXV) before and after extraction; 9) condensate (XXXVI); 10) as (9) after extraction.

Polypropylene stabilised with various polycondensates—of 2-hydroxy-4,4′-bis-β-hydroxyethoxybenzophenone with thio-ββ′-dipropionic acid (XXXIII), 2,4,4′-trihydroxybenzophenone with a mixture of thio-ββ′-dipropionic (0.7 mole) and isophthalic (0.3 mole) acids (XXXIV), 2,2′-dihydroxy-4,4′-β-hydroxyethoxybenzophenone with thio-ββ′-dipropionic acid (XXXV), and 2,2′,4,4′-tetrahydroxybenzophenone with a mixture of isophthalic (0.7 mole) and adipic (0.3 mole) acids (XXXVI)—has been subjected to photodegradation before and after extraction with chlorinated hydrocarbons [197]. Fig. 5 shows that photo-oxidation is appreciably affected by extraction only with the relatively simple stabiliser 2-hydroxy-4-octyloxybenzophenone (curves *2* and *3*). The polycondensation product (XXXIII) is also partly extracted from polypropylene (curves *6* and *7*). The remaining stabilisers are almost unaffected by extraction. The most effective are polycondensates containing thio-ββ′-dipropionic acid—(XXXIV) and (XXXV)—probably because sulphur-containing groups are involved in the breakdown of hydroperoxides [198] formed during irradiation in air.

Halogenated polyalkenes have been stabilised by introducing an oligomeric product (M = 500) of the reaction of formaldehyde (or benzaldehyde) with *o*-hydroxybenzophenone (or acetophenone). The product absorbed intensely in the ultraviolet (340 nm) and exhibited high stabilising activity [199,200].

Polycondensates [201–203] with $M \geqslant 400$ and consisting of the units



(A) (B) (C)

(XXXVII)

(where R^1 and R^2 = H, Alk (C_{1-6}), chloroalkyl, furyl, vinyl, propenyl, phenyl; R^3 = Alk (C_{1-6}), Ar; R^4 and R^5 = H, OH, Hal, AlkO, Alk; and R^6, R^7, R^8 = H, OH, Hal, Ar, ArO, cycloalkyl) stabilise vinyl polymers towards heat and light. The molar proportions of the components are 1 : 2 : 1. Table 2 gives the test results.

Table 2. Stability of vinyl polymers containing added polycondensates towards heat and light [201].

Initial components of polymeric stabiliser			Polymer	Thermal stability*	Ultraviolet stability**
I	II	III			
o-Hydroxyacetophenone	formaldehyde	dodecylphenol	polypropylene	not discoloured	5
2-Hydroxy-4,6-dimethylbenzophenone	acetone	*m*-butylphenol	polyethylene	not discoloured	3
2,4-Dihydroxybenzophenone	furaldehyde	octadecylphenol	polyethylene	not discoloured	4
4-Chloro-2-hydroxybenzophenone	butyraldehyde	3,5-dichloro-4-methylphenol	poly(vinyl chloride)	discoloured	3
2-Hydroxy-4-methoxybenzophenone	benzaldehyde	octylphenol	ethylene–ethyl acrylate copolymer	not discoloured	3
o-Hydroxybenzophenone	formaldehyde	phenol	poly(vinyl fluoride)	not discoloured	4

*Under the test conditions (210°C for 30 min) the control specimen—the polymer without a stabiliser—is discoloured.

**The ratio of the time for the stabilised film to disintegrate to the corresponding time for the control film.

Macromolecular analogues of *o*-hydroxybenzophenone, obtained by the Fries rearrangement of polyarylates, have been proposed for the photostabilisation of various vinyl polymers [204]. The polymeric stabilisers possess low volatility, blend well with many polymers, and are as good as *o*-hydroxybenzophenone in effectiveness. Comparison of the infrared spectra of samples of poly(vinyl fluoride) film containing 1–2 wt.% of such a polyketone before and after being heated in a vacuum (0.1 mmHg) at 100°C for 3 h showed hardly any change in the content of polymeric stabilisers in the film, whereas the content of *o*-hydroxybenzophenone in a control specimen had decreased significantly. The effectiveness of the polymeric stabilisers was maintained even after exposure of the film at 60°C to ultraviolet radiation for 2 months.

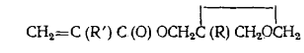
VI. OTHER MACROMOLECULAR AND OLIGOMERIC COMPOUNDS

Various macromolecular compounds containing an open chain of carbon atoms have been suggested for stabilising polymers. Macromolecular hydrocarbons, alcohols, acids and their salts, esters, ethers, etc. have found application.

Thermal stabilisation of poly(vinyl halide) resins has been effected by additions of polyethylene (0.5–2.0 wt.%),[205,206] which eliminated charring or any decomposition of the material during processing. The stabilising effect of polyethylene is explained, in the Reviewers' opinion, by two factors. Polyethylene is able to combine with atomic chlorine formed in the thermal degradation of poly(vinyl chloride), thus preventing development of free-radical degradation processes in the polymer and in the corresponding segments of vinyl chloride copolymers[1]. Such explanation seems probable, since polyalkenes are easily chlorinated at ~150°C even in the dark[207]. On the other hand, hydrogen chloride catalyses the thermal breakdown of poly(vinyl chloride).[208–211] It has been shown recently that the thickness of the specimen has a great influence on the rate of breakdown of this polymer. There exists a critical size, beyond which the elimination of hydrogen chloride becomes autocatalytic[212]. This indicates that polyethylene acts as a stabiliser also by diminishing the contact between hydrogen chloride and the polymer macromolecules, diminishing the relative importance of autocatalytic processes in the polymer degradation, and hence decreasing the overall rate of breakdown. Polyalkenes also stabilise polyoxymethylene. Its thermal stability is improved by polybutene and by an ethylene–vinyl acetate copolymer[213,214]; polyethylene and polypropylene are less efficient in stabilising polyoxymethylene. Oligomeric polyphenylenes—derivatives of toluene, *o*-, *m*-, and *p*-xylene, etc.—show promise for the thermal stabilisation of isotactic polypropylene. The effectiveness of these stabilisers is greatly increased by the addition of bisdodecyl thiodipropionate[215].

A polyol (a polyethylene glycol) has been used[216] in combination with sodium tellurite or selenite to improve the thermal stability and the transparency of poly(vinyl chloride). Polymers containing nitrile groups are stabilised by the addition of a polyhydric alcohol based on polyoxypropylene having a hydroxyl number of 60–700 and molecular weight 400–3000.[217]

A linear acrylic ternary polymer (M = 150 000 to 2 000 000), comprising monomer units of methyl methacrylate, ethyl acrylate, and an ester of an alkoxy-acid of formula



(XXXVIII)

(where R = Alk (C_{1-4}) and R′ = H, CH_3) stabilises poly(vinyl chloride) of intermediate or high molecular weight[218]. Pure poly(methyl methacrylate) has no effect on the rate of breakdown of poly(vinyl chloride).[219]

The introduction of oligoether–acrylate segments into the poly(methyl methacrylate) chain improves its physico-mechanical properties and enhances the thermal stability[220].

The polymeric salt obtained by the reaction of a copolymer of styrene and maleic anhydride with ammonium hydroxide protects poly(vinylidene chloride) from the action of ultraviolet rays[221].

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Affinity Chromatography of Enzymes

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The main principles and fields of application of a new method of enzyme chromatography, the so called "affinity" chromatography, are discussed. The method is based on the employment of an insoluble ligand of the enzyme (substrate, inhibitor, cofactor, etc.), that is sorption takes place owing to specific forces associated with affinities which constitute the basis of the biological function of the enzyme. The use of sorbents based on such ligands permits a more selective and effective isolation of pure enzymes from various sources compared with the usual types of sorbents, for example ion-exchange resins. In addition the review considers certain other techniques employing the specific affinity of the enzyme for the ligand in enzyme chromatography. Affinity chromatography can also be used to fractionate the products of chemical modification of enzymes and to investigate the physicochemical properties of enzyme-ligand complexes.
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I. INTRODUCTION

Numerous studies based on the selective binding of enzymes to ligands (substrates, inhibitors, coenzymes, etc.) for the purification of enzymes by adsorption (mainly chromatographic) methods have been published recently in scientific periodicals. Since the enzyme forms a complex with the ligand due to the so called affinity forces, the method has been given the name of "affinity" chromatography (from the Latin root "affinis"—related to, bearing a relation to), i.e. chromatographic separation of enzymes in accordance with their affinity for the substrate.

The tendency to seek selective sorbents for enzymes is itself quite understandable, since the usual types of chromatography, for example ion-exchange or gel chromatography, are not specific to the nature of enzymes; the purification of enzymes with the aid of these methods constitutes a multistage procedure and usually gives a low yield of the pure product. On the other hand, affinity chromatography normally makes it possible to extract enzymes from complex mixtures in a single stage with a high degree of purity and with a nearly quantitative yield.

Moreover, affinity chromatography is one of the most direct and at the same time simplest methods for the investigation of the formation of enzyme–ligand complexes, so that it can be used for a detailed elucidation of the physicochemical aspect of enzymatic catalysis.

The present review attempts to summarise and give a systematic account of studies in this field and to assess the potentialities of the method.

II. GENERAL PROBLEMS OF AFFINITY SORPTION

According to modern ideas, an enzymatic reaction can be represented by the following general equation

$$E + S \rightleftarrows ES \rightleftarrows EP \rightleftarrows E + P,$$

where E, S, and P are enzyme, substrate, and reaction product respectively. The equation shows that the elementary step in the simplest enzymatic reaction involves the formation of two complexes, namely the enzyme–substrate and enzyme–product complexes.

The first stage of the enzymatic reaction—the formation of the enzyme—substrate complex—take place as a result of specific interaction forces between the enzyme and substrate molecules, called the enzyme–substrate affinity. The few data obtained so far on the structures of enzymes and enzyme–substrate complexes[1-4] show that, in the binding of the enzyme to the substrate a number of non-covalent bonds of various types (hydrogen bonds, polar and non-polar interactions, etc.) are formed between them. Such multi-site contact between the enzyme and substrate molecules, leading to a high selectivity of interaction, is ensured by a specific spatial distribution of the functional groups of the enzyme, which is determined by its unique structure. In this case one usually speaks of the complementarity of the molecular structures of the enzyme and the substrate.

The enzyme–product complex is formed as a result of a chemical transformation of the substrate. Since in the course of this transformation the substrate remains bound to the surface of the enzyme molecule, evidently the enzyme–product complex is in general stabilised by the same forces (or involves the same interactions) as those involved in the stabilisation of the enzyme–substrate complex.

Apart from the complexes with the substrate and the reaction product, many enzymes form, by virtue of their functional specificity, extremely stable complexes with other types of ligands. These include coenzymes, allosteric activators, inhibitors, etc.

When the ligand is in a solid insoluble phase, it can be used as a specific sorbent for the corresponding enzyme. Like any sorbent used in chromatography, the affinity sorbent must have a fairly large surface area, a relatively high mechanical strength, and should not show a tendency to form either dense aggregates or conversely colloidal solutions. In a chromatographic column, the sorbent must allow an eluent flow rate acceptable in practice.

If the natural ligand satisfies these requirements, it can be used directly as the sorbent. However, the number of such sorbents is small and they are restricted to certain

biopolymers, mainly the substrates of digestive enzymes (starch, elastin, cellulose, etc.). In most cases ligands are soluble substances and are converted into an insoluble state by an artificial method. Here the following procedures are possible: (a) the ligand is modified chemically by the introduction of hydrophobic groups which make it insoluble; (b) the ligand is converted into an insoluble state by incorporation in an insoluble polymer which is polymerised for this purpose in a solution containing the ligand; (c) the ligand is attached (covalently or non-covalently) to an insoluble carrier. The procedure involving covalent attachment of the ligand is most frequently employed.

The main requirement which must be met by the affinity sorbent is sorption specificity. In principle, the affinity sorbent should contain only functional groups which ensure the selective binding of one specific enzyme in the absence of sorption of other substances. When the natural ligand is employed, the problem reduces to a test of its homogeneity and native properties, i.e. the absence from it of functional groups non-specific to the given ligand which may appear as a result of chemical side reactions, for example in purification or on storage.

The preparation of a synthetic sorbent requires a correct choice of the ligand, the carrier, and the method of joining the ligand to the carrier. The specificity and strength of the binding of the ligand to the enzyme may be estimated by preliminary tests using various methods, for example kinetic methods.

In order that the ligand which is bound effectively in solution should retain this capacity when attached to the carrier, it is necessary that the attachment should involve groups not participating in the interaction with the enzyme. Exact information about this may be obtained by the X-ray diffraction analysis of the corresponding enzyme – ligand complexes. These data are important for practical affinity sorption, since they constitute the basis for the most complete utilisation of the affinity forces and help to avoid an empirical search in the preparation of the sorbent. However one should note that information of this kind is still extremely limited [1-4].

When the ligand is attached to the carrier, one should also make sure that the functional groups responsible for complex formation are not only free but also accessible for binding to the enzyme in solution. Here we are concerned with possible steric hindrance in the approach of the enzyme molecule to the active surface of the sorbent. In particular, such hindrance may arise if the site of attachment of the ligand to the carrier is in the immediate vicinity of its functional groups involved in binding to the enzyme. In such cases it is desirable to attach the ligand to the carrier via intermediate reagents with a suitable length of molecular chains which function as a kind of "arm" which separates the active groups of the ligand from the surface of the sorbent.

In choosing the carrier one should bear in mind that it must not have a significant influence on sorbent specificity, i.e. that it must not contain functional groups which might give rise to the sorption of extraneous substances. The fact that the ligand is bound to the enzyme as a rule via several non-covalent linkages itself guarantees to some extent a minimal binding of impurities by such a sorbent, in which the ligand is attached to a fairly neutral carrier. Carriers of this type may include, for example, molecular sieves (Sephadex, Biogel, etc.) the very principle of whose action is designed to ensure the absence of non-specific sorption of proteins. Moreover, the choice of the neutal carrier makes it possible not only to eliminate the sorption of impurities but also to avoid a possible non-specific binding of the enzyme itself. In practice the specificity and efficiency of synthetic and natural sorbents must be tested experimentally in each case.

The next problem concerns the conditions governing the sorption and desorption of the enzyme. As stated above, the formation of an enzyme–ligand complex is due to the specific steric structure (conformation) of the enzyme protein molecule, which may change when the conditions in the medium are altered. Therefore it is extremely difficult to assess beforehand the optimal sorption and desorption conditions. On the basis of general considerations, one may expect that the optimal sorption of the enzyme on an affinity sorbent will occur close to the conditions governing its optimal catalytic activity and any departure from these conditions will lead to a weakening of the stability of the enzyme–ligand complex and to desorption of the enzyme.

If electrostatic interactions between the ionogenic groups of the enzyme and the ligand are important for their mutual binding, the stability of such a complex will vary with the pH of the medium and will decrease with increasing ionic strength. The stability of hydrogen-bonded complexes is probably an inverse function of temperature. Moreover, the stability of such complexes decreases in the presence of agents capable of forming hydrogen bonds (for example urea, guanidine, etc.). A similar approach is evidently applicable also to complexes stabilised by "hydrophobic" contact. Thus one of the desorption procedures consists of the weakening of individual types of bonds between the enzyme and the ligand in the complex. In the presence of bonds of different types, the decomposition of the complex requires a combined action of a variety of factors; one must bear in mind that the desorption conditions can then be very severe and can lead to denaturation of the enzyme.

Another desorption procedure, which is more appropriate to enzyme–ligand complexes, involves a weakening of the overall affinity of the enzyme for the ligand by altering the conditions in the medium (pH, ionic strength, temperature, etc.); for example, the conformation of the enzyme can be altered reversibly from complementary to non-complementary. Since the conformation of the protein molecule is as a rule senstive to the medium and the changes in it are of a cooperative type, these reversible conformational changes can occur under extremely mild conditions where the native structure of the enzyme is preserved. In addition, the sorbed enzyme may be desorbed competitively under the influence of the free ligands present in solution.

It is noteworthy that the study of the effect of each individual factor in the medium on the binding of the enzyme to the ligand can result in certain cases in definite deviations from the above general sorption and desorption rules. In principle, the attainment of optimal results in experiments on the isolation and purification of enzymes requires such preliminary study for each individual enzyme. In this case the optimisation of the conditions in the medium can not only ensure an efficient absorption and desorption of the enzyme itself but can also promote the elimination of possible impurities.

Yet another problem concerning the stability of the sorbent must be examined. This includes, first, the stability in relation to the conditions in the medium and, secondly, the resistance to the action of the enzyme. The first factor can be as a rule neglected since the choice of the conditions in the medium is determined in the first place by the stability of the enzymes themselves; it can be

taken into account only in the stage where the sorbent is prepared for the experiment or during its regeneration, which, when necessary, can be carried out under more severe conditions than sorption and desorption†.

As regards the stability of the sorbent to the enzyme, one should consider that it can be chemically transformed under the influence of the enzyme in those cases where a sorbent based on the substrate is employed. Evidently increased contact time between the sorbent and the enzyme can significantly decrease the capacity and specificity of the former although this factor is not common to all enzyme–substrate systems. In particular, one cannot rule out the possibility that under certain conditions in the medium the enzyme retains fully its affinity for the substrate but does not exhibit catalytic activity. In general preference should be given to sorbents where the ligand employed is not the substrate but a competitive inhibitor, which forms with the enzyme a so called "non-productive" complex (i.e. a complex which does not undergo a chemical transformation).

Resistance to enzyme action is important not only for the preservation of the sorption properties of the sorbent but also for the choice of the sorption procedure. The procedure can be static ("in a reservoir") or dynamic (chromatography). If a sorbent based on the substrate is employed, the sorption of the enzyme may be accompanied by a chemical transformation of the substrate with liberation of the reaction products to the surrounding solution. Since the reaction products also show affinity towards the enzyme and form fairly stable complexes with it, the result may be a competitive inhibition of the binding of the enzyme to the sorbent and the retention of part of the enzyme in solution. In those cases where the substrate reacts fairly rapidly and a static sorption procedure is employed, the inhibiting effect of soluble reaction products on the sorption of the enzyme can be very considerable. On the other hand, under dynamic conditions the products formed are continually removed by the stream of eluent flowing through the sorbent bed and have much less effect on the sorption of the enzyme. Therefore the static procedure can be used only with sorbents resistant to enzyme action or the sorption must be carried out under conditions where the enzyme is catalytically inactive; in other cases, the dynamic method is preferable.

The conditions governing the preparation and application of sorbents based on ligands discussed above apply in general also to sorbents based on enzymes. These are sometimes referred to as "enzymatic resins". Sorbents based on enzymes can be used to isolate and purify the corresponding ligands and also to investigate the binding of the ligand to the enzyme (although sorbents based on ligands are more suitable in this case). In view of the relative structural lability of enzymes, one must maintain conditions in the preparation and use of these sorbents which rule out irreversible denaturation of the enzyme.

The next section deals with studies based on using the affinity of the enzyme for the ligand, mainly for preparative purposes, and also data on the preparation of sorbents. A systematic account of the data described below may be based on the differences in the choice of the "sorbent–sorbate" system, which appears to be the most useful classification according to the general postulates concerning affinity sorption.

†In the operating cycle of the sorbent the author distinguishes its preparation for the experiment, the sorption and desorption of the enzyme, and sorbent regeneration (Editor).

III. THE USE OF ENZYME–LIGAND AFFINITY FOR PREPARATIVE PURPOSES

1. Natural Sorbents for Enzymes

The sorption of an enzyme on an insoluble substrate was first observed in 1910 by Starkenstein [5]—this was the sorption of liver amylase on potato starch. Later similar data were published by Ambard [6] for saliva amylase, by Chodat and Philia [7] for malt "diastase", and by Boekestein [8] for pancreatic amylase; in the last study, potato, rice, and wheat starches were tested as the sorbents.

Subsequently sorption on starch was widely used to isolate and purify amylases from various sources [9–20]. It was found that starch is a selective sorbent for α-amylase and does not sorb β-amylase. Thus Holmberg [9,10] discovered that malt α-amylase can be separated from β-amylase by sorption on starch from 50% ethanol solution in the presence of maltose; according to Holmberg's data, the sorbability of α-amylase increased as the concentration of alcohol was raised and the pH and temperature reduced. α-Amylase is an endoglycosidase, i.e. it cleaves the glycosidic linkages within the starch chain, in contrast to β-amylase, which splits off maltose residues from the non-reducing end of the carbohydrate chain. Therefore maltose, being a product of the activity of β-amylase, might have inhibited its binding to starch.

In a study of the sorbability of malt α-amylase on various starch and glycogen ("animal starch") specimens, Schwimmer and Balls [14] established that starch freshly precipitated with alcohol is the most effective sorbent; however, the sorbability of α-amylase on glycogen was highest. Bearing this in mind, Schwimmer and Balls [14] concluded that the efficiency of the sorption of α-amylase is determined by the area of the sorbent formed by maltoside chains with a length equivalent to 8 — 10 units and accessible to the enzyme in solution.

Schwimmer and Balls [15] purified malt α-amylase by chromatography on a column with wheat starch. The sorption was carried out at 5°C in the presence of 40% ethanol and calcium salts; the enzyme was desorbed with water saturated with calcium sulphate at room temperature. α-Amylase was isolated from the eluate in a crystalline state.

Thayer [17] separated the α- and β-amylases from *Pseudomonas saccharophila* by chromatography on a column with a mixture of potato starch and Celite. When the culture liquid was passed at 4°C through a column washed with water, only α-amylase was sorbed. Buffer solutions at different pH and with different calcium salt and maltose contents did not elute the sorbed enzyme. Elution was achieved using a concentration gradient of soluble starch and was very effective: the enzyme emerged in a sharp peak (3 ml of the eluate contained 75% of the total amount of the sorbed enzyme) and was concentrated by a factor of 100 compared with the initial solution. It is interesting to note that both amylases had the same pH activity optimum but differed sharply in their capacity for sorption on starch [17].

Markowitz et al. [18] reproduced Thayer's method [17] and obtained a highly purified crystalline preparation of α-amylase from *P. saccharophila*. A variant of this technique was employed by Neumann et al. [20] to isolate amylase from dog liver; the enzyme was purified by a factor of 23–147 with a yield of 45–75%.

Comparatively recently Vainer and Shul'man [21] published a report on the possibility of using starch to isolate amylase for practical purposes.

Leloir et al.[22] observed that insoluble starch can also be used as a sorbent for the purification of bean starch synthetase. Akazawa and Murata[23] and Tanaka and Akazawa[24] showed that starch synthetase is bound preferentially to amylose (a linear polysaccharide) rather than to the branched chain of amylopectin; the maximum sorption of starch synthetase on amylose occurred at a neutral pH and a low temperature but decreased sharply as the pH was reduced (to pH 5.0) and the temperature raised (above 25°C).

De la Haba[25] used sorption on starch for the purification of glycogen phosphorylase from rabbit muscle. When the whole muscle extract was passed through a column with potato starch at 3°C, the enzyme was completely bound to the sorbent; desorption was achieved by eluting the column with the soluble substrate (0.4% glycogen solution) and by raising the temperature simultaneously to 14°C. The enzyme was purified in this way by a factor of 33 with a yield of 100%; the specific activity of the resulting preparation corresponded to the activity of the doubly recrystallised enzyme. De la Haba[25] notes that the behaviour of glycogen phosphorylases *a* and *b* was identical under the conditions tested.

Hanabusa and Kohno[26] described a variant of the de la Haba method[25] in which the enzyme was desorbed solely by increasing the column temperature; they found this procedure more convenient, since it yields the enzyme without an admixture of glycogen and further purification is not needed.

Selinger and Schramm[27] studied the binding of glycogen phosphorylase to glycogen. They found that at pH 6.8 and a temperature of about 0°C phosphorylase *a* forms an insoluble enzyme–substrate complex with glycogen (up to 62% of the enzyme was precipitated). A similar complex was not formed with dextran, mannan, and levan, which indicated the specificity of the binding of phosphorylase *a* to glycogen. When the pH was changed to 5.0 or 9.0, the complex remained stable but at pH 4.0 it decomposed with loss of enzyme activity. An increase of temperature promoted the dissociation of the complex. It is interesting that the addition of α-amylase to the insoluble complex even at 0°C resulted in its complete decomposition in several minutes. According to the authors[27], this implies that phosphorylase *a* forms an insoluble complex only with native glycogen but not with its amylase-catalysed hydrolysis products, among which there are high-molecular macrodextrins resistant to the action of amylase[28]. Under comparable conditions, phosphorylase *b* was precipitated only in the presence of magnesium salts[27]. (This finding can probably be used for the separation of phosphorylases *a* and *b*.)

Leloir and Goldemberg[29,30] used the selective coprecipitation of glycogen synthetase with glycogen for the purification of specimens of this enzyme obtained from different sources. Rat liver glycogen synthetase was purified in this way by a factor of 300 and contained as impurities only small amounts of glycogen phosphorylase and amylase; however, the yield of the enzyme was low (only 12%).[29]

Loyter and Schramm[31] found that glycogen is able to bind α-amylase and used this property to isolate and purify the enzyme. The maximum coprecipitation of α-amylase with glycogen occurred at pH 8.0, a temperature of 0–3°C, and after the addition of ethanol up to a concentration of 40%. Subsequently Schramm et al.[32] found that not only glycogen but also macrodextrins, which are produced by the amylase-catalysed hydrolysis of glycogen and are resistant to the further action of amylase[28], are also capable of forming an insoluble complex with amylase. It is interesting that calcium ions, required for the enzymatic activity of α-amylase, were also necessary for its binding to glycogen and macrodextrin. Thus, when calcium ions were removed from solution by ethylenediaminetetra-acetate, an insoluble complex was not formed. Strontium and barium ions showed a similar activating effect, but cadmium and magnesium ions lacked this capacity. Schramm et al.[32] suggested that calcium ions are required either to maintain the active conformation of the enzyme or are involved directly in the binding of the substrate.

The above data on the binding of enzymes active towards the α-(1 → 4)-glucosidic linkage (i.e. capable of cleaving or synthesising this linkage) to various α-(1 → 4)-polyglucosides show that such binding is extremely selective. For example, starch effectively sorbs α-amylase but not β-amylase; starch synthetase, which is bound to amylose but not to amylopectin, exhibits a definite selectivity towards the polysaccharide. On the other hand, the selectivity is not absolute. Thus, apart from α-amylase, starch sorbs effectively starch synthetase and glycogen phosphorylase; similarly, glycogen ("animal starch") binds glycogen synthetase and α-amylase in addition to glycogen phosphorylase.

One might have expected that all the enzymes acting on α-(1 → 4)-polyglucosides would exhibit similar functional properties in relation to binding of the substrates in view of the similarity of the chemical properties of the latter. Apparently this happens to some extent although the selectivity characteristic of enzymes, depending on the steric structure of the substrate molecules and possibly on supermolecular structural factors, is shown in many cases. Moreover, the conditions in the medium where optimal binding takes place are different for different enzymes, which is evidently due to the individual characteristics of the structure of their protein molecules. This factor probably makes it possible to isolate in a pure form any enzyme without admixtures (or with minimal amounts of admixtures) of other related enzymes.

Natural sorbents have been used to isolate and purify a number of other enzymes. Jeuniaux[33–35] isolated a chitinase from soil streptomycetes by selective sorption on chitin from whole culture liquid. After the chitinase had been bound, the chitin with the sorbed enzyme was extracted and washed. The enzyme was not desorbed; instead the chitin was subjected to total hydrolysis by the chitinase and the soluble hydrolysis products were removed by dialysis. The chitinase was purified in this way by a factor of 70 with a yield of 27%. The resulting preparation contained no proteases, cellulases, pigments, and reducing sugars and the amount of protein impurities without chitinolytic activity was less than 5%.

The study by Grant and Robins[36] on the purification of elastase from pig pancreas showed that not only the active enzyme but also zymogen (proelastase) are bound with equal efficiency to elastin; this observation enabled the authors to reach the very important conclusion that the substrate binding centre, specifically the catalytic centre in the elastase molecule, is structurally autonomous. Gertler and Birk[37] purified proelastase using its adsorption on elastin.

Orekhovich et al.[38] investigated the binding of certain proteases (pepsin, trypsin, chymotrypsin, and papain) to comminuted sheep wool and silk fibroin. The experiments were performed at two pH values (3.9 and 7.9). Under these conditions, pepsin and papain were not bound either to wool or to silk. Trypsin and chymotrypsin were

bound fairly satisfactorily to both sorbents and at both pH values (the amounts of bound trypsin and chymotrypsin reached 83 and 75% respectively). Trypsin was desorbed using a solution of cysteine in the presence of urea and chymotrypsin using a solution of histidine in the presence of sodium chloride. Probably the differences in the behaviour of the proteases investigated reflect differences in their specificity.

Ogawa and Toyama [39] used chromatography on a column with powdered cellulose to separate a commercial preparation of cellulase from *Trichoderma viride* into three active components, which differ in their affinities for the substrate.

Reese and Avigad [40] described a method for the purification of levansucrase based on a selective coprecipitation of the enzyme with levan. The enzyme was purified by a factor of more than 2000 with a yield of 31%. Other enzymes (cellulose, β-galactosidase, α-amylase, galactose oxidase, and ribonuclease) were not coprecipitated under these conditions, which confirms the specificity of the binding of levansucrase to levan. A similar procedure was employed by Bauer and Avigad [41] for the purification of fructan hydrolase.

Cherkasov and coworkers [42-44] investigated the conditions governing the formation and decomposition of the enzyme–substrate complex of lysozyme with chitin using the chromatography of the enzyme on a column with the substrate. Two types of complexes, depending on the pH of the medium, were observed. One of the complexes predominates in a weakly acidic medium and is stable only in the presence of salts in solution, decomposing in a salt-free medium. The other complex predominates in a weakly alkaline medium, is stable also in the absence of salts, but decomposes when the solution is acidified. On this basis, two procedures were proposed for the isolation of lysozyme from various natural sources: (a) by sorption at pH ~ 5 in a salt solution followed by desorption with water and (b) sorption at pH 8–9 followed by washing the column with water and desorption with dilute acetic acid. Chitin obtained by standard methods usually contains free amino-groups owing to its partial deacetylation during purification. The presence of amino-groups imparts to such chitin the properties of an anion exchanger and leads to non-specific sorption of acid proteins (such as albumins), which are desorbed with acetic acid. Therefore, when ordinary chitin is employed, only the first procedure is applicable [45,46]. Treatment of ordinary chitin with dilute nitrous acid, which results in the replacement of the amino-groups by neutral hydroxy-groups, eliminates the non-specific sorption and permits the employment of the second procedure, which has the advantage that at pH 8–9 lysozyme does not exhibit a hydrolytic effect on chitin and the complex formed is more stable [47,48]. Lysozyme was isolated by this procedure from hen egg white and from aqueous extracts of horseradish and turnip in almost quantitative yields [45-48]. Chromatography on chitin was also successfully employed by Jensen and coworkers [49,50] for the purification of phage lysozyme. The authors note that the method made it possible to concentrate vanishingly small amounts of the enzyme and at the same time to free it from inhibitors which interfere with the determination of activity in the unpurified solution obtained by the lysis of phages. Thus the yield of lysozyme when isolated by this method was 300%, judging from the activity balance, which can only be explained by the liberation of the enzyme from inhibitors [50].

Among the studies discussed above, a typical adsorption technique was not always employed. For example, in the binding of enzymes to glycogen, the initial components were present in solution and yielded a precipitate only on interaction: this applies also to levansucrase and levan. However, the discussion of these investigations was useful not only because the method is similar to a variant of static adsorption but also because it is possible, in principle, to employ the data on the conditions governing the binding of the enzyme and substrate in experiments with synthetic adsorbents.

2. Synthetic Adsorbents for Enzymes

Erlanger [51] investigated the possibility of isolating and purifying chymotrypsin by binding it to a dipeptide inhibitor converted into a water-insoluble state: the benzyl ester of *N*-benzyloxycarbonyl-L-leucyl-D-phenylalanine (BECLP). It was rendered insoluble by introducing hydrophobic groups into the dipeptide molecule: the benzyl group (in the carboxy-group of phenylalanine) and the benzyloxycarbonyl group (in the amino-group of leucine). Bearing in mind the substrate specificity of chymotrypsin (chymotrypsin hydrolyses peptide bonds formed by the carboxy-groups of aromatic aminoacids), it might have been expected that BECLP would adsorb chymotrypsin. from solution. Indeed, Erlanger observed that chymotrypsin and chymotrypsinogen and pepsin were bound qualitatively to BECLP; trypsin and trypsinogen were also bound but less effectively. Other proteins tested (ribonuclease, human and bovine serum albumins, and β-lactoglobulin) were bound only in insignificant amounts. Erlanger believed that the approximately identical capacities of chymotrypsin and pepsin for binding to BECLP should have been expected in view of the similarity of their substrate specificities. However, the adsorption of trypsin (and trypsinogen) can hardly be due to a specific interaction, since this enzyme hydrolyses peptide bonds formed by the carboxy-groups of diamino-carboxylic acids (arginine and lysine). "Hydrophobic" ligands of the type employed by Erlanger have not found a wide application as sorbents.

Sorbents in which the ligand is linked covalently to an insoluble carrier acquired a greater practical importance for the sorption and chromatography of enzymes. Such sorbents were obtained for the first time by Lerman, who used them to isolate fungal tyrosinase [52]. Certain azophenols, known to inhibit tyrosinase, were chosen as ligands. They were linked to cellulose via an ether bond. Only sorbents whose ligands contain a *p*-hydroxyphenyl group at the free end, i.e. the group which is also present in tyrosine (the substrate of tyrosinase), showed a capacity for the selective sorption of tyrosinase:

1) cellulose —O—C_6H_3(OH)—N=N—C_6H_4—C_6H_4—N=N—C_6H_4—OH,
2) cellulose —O—C_6H_3(OH)—N=N—C_6H_4—N=N—C_6H_4—OH,
3) cellulose —O—CH_2—C_6H_4—N=N—C_6H_4—OH.

Sorbent (3), which was used for the chromatographic isolation of tyrosinase, proved to be the most effective. The enzyme could be purified by a factor of 61 with a yield of 56%.

Arsenis and McCormick [53] purified rat liver flavokinase by chromatography on flavin-substituted cellulose. 6-Amino-9-(1-D-ribityl)isoalloxazine, which is a substrate of flavokinase, and 7-amino-6,9-dimethylisoalloxazine, its

competitive inhibitor, were tested as ligands. In the reaction of these amines with chlorocarbonylmethylcellulose (the acid chloride of carboxymethylcellulose), the corresponding acetamide derivatives were obtained. Both adsorbents were found to be effective for the preparation of highly purified flavokinase.

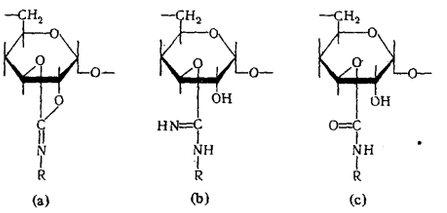
In another study, Arsenis and McCormick [54] investigated the possibility of purifying the apoenzymes of certain oxidoreductases containing flavin mononucleotide (riboflavin phosphate) as the coenzyme. The study was based on the observation that not only flavin mononucleotide but also its monomethyl ester can function effectively as the coenzyme of NADPH-cytochrome *C* reductase, pyridoxin (or pyridoxamine) phosphate oxidase, and glycolate oxidase. Bearing this in mind, the authors obtained esters of flavin mononucleotide with cellulose, phosphocellulose, and diethylaminoethylcellulose and tested them as adsorbents. It was found that, in column chromatography of the above apoenzymes on flavin-substituted cellulose, the enzymes are more firmly retained than on control specimens of celluloses, apparently due to the additional interaction between the apoenzyme and the coenzyme. Almost complete separation of the apoenzyme from impurities was achieved for apoglycollate oxidase; it was purified by a factor of more than 400 in a quantitative yield [54].

Lowe and Dean [55] purified oxidoreductases using adsorbents based on other coenzymes—nicotinamide-adenine dinucleotide (NAD) and nicotinamide-adenine dinucleotide phosphate (NADP) attached to cellulose. These adsorbents were found to be suitable for the isolation of glucose-6-phosphate dehydrogenase, lactate dehydrogenase, and threonine dehydratase, one chromatographic stage being sufficient for the separation of the enzymes.

Mosolov and Lushnikova [56] described a method for the purification of certain peptidohydrolases based on their selective binding to natural inhibitors of protein origin fixed on cellulose. The adsorbents were prepared by introducing the inhibitors into the azo-coupling reaction with *p*-diazobenzoylcellulose (this method presupposes that the protein inhibitors contain aromatic groups which are not essential for their functioning). Adsorbents based on the soya-bean trypsin inhibitor and the inhibitor of potato tuber proteases were obtained in this way. The adsorbent based on the trypsin inhibitor bound selectively and completely trypsin from solution at 0–3°C at pH 7.7 (1/15 M phosphate buffer); the enzyme was desorbed with dilute hydrochloric acid at pH 2.3; under these conditions, the enzyme–inhibitor complex is fully dissociated and the enzyme itself shows the maximum stability and does not undergo autolysis. Other proteins tested (bovine serum albumin, egg albumin, and ribonuclease) were bound to an insignificant degree, which indicated the specificity of the adsorbent. The efficiency of this adsorbent for the purification of trypsin is indicated by the finding that the specific activity of the crystalline trypsin preparation increased by a factor of 1.5–2 after adsorption and desorption, the preparation being completely free from autolysis products. The sorbent based on the inhibitor of potato tuber proteases was used [56] to purify the total protease preparation from *Actinomices fradiae*. After sorption and desorption, the proteolytic activity of the preparation also increased by a factor of 1.5–2; however, the solution retained an appreciable percentage of the activity, since not all the fractions of the preparation showed a sufficiently high affinity for the inhibitor.

The method of preparation of sorbents proposed by Porath and coworkers [57–60] has recently become most widely used. It consists of covalent binding of the ligand‡ to an insoluble polysaccharide carrier with the aid of cyanogen halides, for example bromocyanogen, and consists of two stages: (a) treatment of the polysaccharide with an aqueous alkaline solution of the cyanogen halide with formation of an intermediate reactive compound and (b) the coupling of the intermediate to the ligand in a neutral or weakly alkaline medium. The carriers can be starch, cellulose, and commercial products–Sephadex (cross-linked dextrin) and Sepharose (cross-linked agarose)—usually employed as molecular sieves. According to Porath and coworkers, the best carrier is Sepharose, which in aqueous solutions forms grains of an extremely porous gel so that not only its surface but also the inner space within the grains is accessible to enzyme molecules. As a result, adsorbents with a high capacity may be obtained on the basis of Sepharose.

An essential condition in the method of Porath and coworkers is the presence in the ligand of a free primary (aliphatic or aromatic) amino-group not required for binding to the enzyme, whereby the ligand can be attached to the carrier; if this group is absent, it must be specially introduced. The mechanisms of the reaction of cyanogen halide with the polysaccharide and of the subsequent stage where the primary amine is attached to the activated polysaccharide have not been finally elucidated. It has only been shown that, when a cyanogen halide reacts with the polysaccharide, a product containing additional nitrogen but not the halogen is formed; on the other hand, when this intermediate interacts with the amine, ammonia is liberated. Porath [59] suggests that this may involve the formation of the following structures:



The adsorbents obtained by the method of Porath and coworkers are quite stable in the pH range between 2 and 12, which includes the region of stability of almost all enzymes. In 0.1 *N* hydrochloric acid, only 1.81% of the attached ligand groups are split off from the carrier in 4 days, while in 0.1 *N* sodium hydroxide 42.7% of these groups are removed during the same period; in the latter case the losses probably occur owing to the decomposition of the carrier itself [60].

Despite certain limitations, the method of Porath and coworkers generally makes it possible to obtain a fairly wide and varied selection of starting materials for the coupling of the ligand to the carrier and in this sense it can be regarded as one of the most general methods for preparing affinity sorbents. The preparation and applications of sorbents by this method are discussed below [57–60].

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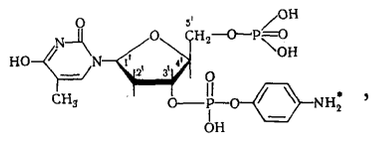
‡The method is used to attach to the sorbent not only the ligand but also the enzyme. In particular, it is used for the affinity chromatography of inhibitors, transfer RNA, and others—see the fourth International Fermentation Symposium, March, 1972, Kyoto, Japan, Abstracts, pp. 64–65 (Editor).

Cuatrecasas et al. [61] were the first to use this procedure to prepare sorbents for enzymes: the nuclease from *Staphylococcus aureus*, α-chymotrypsin, and carboxypeptidase A. The substrate of the nuclease is di-(*p*-nitrophenyl)thymidine 3′,5′-diphosphate. The nuclease readily splits off *p*-nitrophenyl phosphate from the 5′-position but has only a slight effect on the same group in the 3′-position. On the other hand, compounds with a free (not esterified) phosphate group in the 5′-position are powerful inhibitors of the nuclease. Bearing in mind these findings 3′-(*p*-aminophenylphosphoryl)deoxythymidine 5′-phosphate,

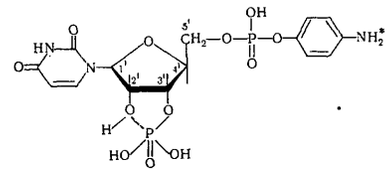


was chosen as the ligand for coupling with Sepharose. The inhibition constant for this substance, determined from kinetic data, is extremely low (10^{-6} M), which ensured a stable binding of the nuclease; the substance itself is stable in the pH range from 5 to 10; the p*K* of the amino-group is sufficiently low for effective interaction with Sepharose activated by bromocyanogen and the amino-group is sufficiently remote from the part of the ligand bound to the enzyme§. Nuclease from the whole culture liquid was isolated in quantitative yields in one stage by column chromatography using the sorbent obtained. The sorption was carried out at pH 8.0 (0.05 M borate buffer with added 0.01 M calcium chloride) and, after washing the column with the same buffer solution, the enzyme was desorbed with 0.01 M acetic acid.

In the preparation of a sorbent specific to chymotrypsin [61], an enantiomeric analogue of the substrate—the methyl ester of D-tryptophan—was chosen as the ligand. However, the resulting sorbent was not altogether satisfactory, probably because the small dimensions of the ligand produced steric hindrance to the approach of the enzyme to the active surface of the sorbent. In view of this, another ligand—the methyl ester of ε-aminocaproyltryptophan—was tested. In this ligand the tryptophan residue bound to chymotrypsin is much more remote from the site of attachment to Sepharose, so that it is much more accessible to the enzyme in solution. The resulting sorbent proved to be extremely effective both for the purification of chymotrypsin itself and for the elimination of admixtures of this enzyme from preparations of other enzymes, in particular ribonuclease. The sorption was carried out in 0.5 M tris hydrochloride buffer at pH 8.0 and the enzyme was desorbed with 0.1 M acetic acid. The yield of the pure enzyme was more than 90%. The dissociation constant of the chymotrypsin complex with this ligand is about 10^{-4} M, i.e. higher by 2 powers of 10 than the value for the enzyme—inhibitor complex of nuclease. Nevertheless, in this case too the adsorbability of the enzyme was sufficiently complete and stable. Thus the requirement for a very high stability of the enzyme—ligand complex is not strictly obligatory.

In the preparation of the sorbent for carboxypeptidase A, the dipeptide L-tyrosyl-D-tryptophan was employed as a ligand [61]. The sorption was carried out in 0.005 M tris-HCl buffer at pH 8.0 with sodium chloride added up to a concentration of 0.3 M (evidently in order to prevent the non-specific sorption of impurities by the free carboxy-groups of tryptophan residues). The enzyme was desorbed with 0.1 M acetic acid. The sorption of carboxypeptidase A (within the limits of the working capacity of the sorbent) and its desorption were quantitative. The specificity of the sorbent was demonstrated by the absence of binding of carboxypeptidase B under the same conditions.

Wilchek and Gorecki [62] described the preparation and application of a sorbent for ribonuclease. The ribonuclease substrates are ribonucleic acid and pyrimidine 2′ : 3′-cyclic phosphates; compounds such as cytidine 2′-monophosphate, cytidine 3′-monophosphate, and uridine 2′-monophosphate are known to be competitive inhibitors of the enzyme. However, the attempt to attach cytidine 2′-monophosphate to Sepharose by the method of Porath and coworkers was unsuccessful, probably owing to the low nucleophilicity of the amino-group in the 4-position. Therefore another class of inhibitors, namely 2′(3′),5′-diphosphates, was tested: firstly, only the 2′(3′)-phosphate group is important for their inhibiting activity and the group in the 5′-position can be modified; secondly, inhibitors of this type are the most powerful known (the inhibition constant determined from kinetic data is approximately 10^{-5} M). Therefore 5′-(*p*-aminophenylphosphoryl)uridine 2′(3′)-phosphate was chosen as the ligand:



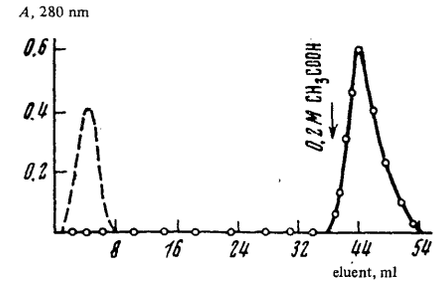


Figure 1. Affinity chromatography of ribonuclease A (after Wilchek and Gorecki [62]). The dashed line indicates the peak of ribonuclease inactivated by oxidation and reduction and also of enzymes with a different substrate specificity (trypsin and chymotrypsin). The arrow indicates the point where the eluent was changed. For details, see text.

The sorbent obtained firmly retained ribonuclease in 0.02 M acetate buffer at pH 5.2; the enzyme was desorbed with 0.2 M acetic acid (Fig. 1). With the aid of this sorbent, it was possible to free ribonuclease from various impurities, including phosphates of different types and also to eliminate selectively admixtures of ribonuclease from other preparations. The authors emphasise the importance of their method for the fractionation and purification of synthetic ribonuclease preparations [62].

§Here and henceforth the superscript* denotes the group attached to the carrier.

Porath and coworkers [63] synthesised a sorbent for asparaginase. The substrate of asparaginase is L-asparagine, while its enantiomeric form D-asparagine inhibits the enzyme. Therefore the ligand chosen was a product of the condensation of L(+)-β-chlorosuccinamic with hexamethylenediamine:

$$*H_2N-(CH_2)_6-NH-\underset{\displaystyle COOH}{\underset{|}{CH}}-CH_2-CO-NH_2\ .$$

The latter played the role of an "insert" between the functional groups of the ligand and Sepharose in order to eliminate the steric hindrance in the sorption of the enzyme. Optimum sorption occurred in 0.05 M borate buffer at pH 8.6 with sodium chloride added to a concentration of 0.3 M; at a higher ionic strength the enzyme was more weakly bound to the sorbent, while reduction of the ionic strength resulted in an increase of the sorption of impurities. The enzyme was desorbed with 0.001 M solution of D-asparagine in the same buffer. The specific activity of the asparaginase preparation obtained exceeded the activity of the preparations produced by other methods. The resistance of the sorbent to the action of the enzyme was entirely satisfactory.

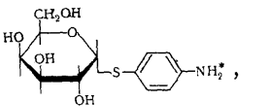
The sorbents obtained by the method of Porath and coworkers [57-60] have been used successfully for the isolation and purification of a number of other enzymes: chymotryptin-like enzymes [64], plasminogen [65], wheat proteases [66], papain [67,68], β-galactosidase [69], β-xylosidase [70], DNA polymerase [71], 3-deoxy-D-arabino-heptulosonate-7-phosphate synthetase [72], lecithin : chloesterol acyltransferase [73], acetylcholinesterase [74,75], and chorismate mutase [76]. Kasche [77] and Feinstein [78] obtained by this method a sorbent based on an inhibitor of soya-bean trypsin and showed that it binds not only trypsin but also chymotrypsin (cf. Mosolov and Lushnikova [56]).

Inman and Dintzis [79] described a method for the preparation of affinity sorbents based on Biogel (cross-linked polyacrylamide), used, like Sepharose, as a molecular sieve. In this procedure the carboxamide group of Biogel is converted by treatment with hydrazine hydrate into the hydrazide group, which in turn is converted subsequently into an acyl azide group by treatment with nitrous acid; the acyl azide group readily reacts with primary aliphatic and aromatic amines to form amides:

$$B-CO-NH_2 \xrightarrow{N_2H_4} A-CO-NH-NH_2 \xrightarrow{HNO_2} B-CO-N_3 \xrightarrow{R-NH_2} B-CO-NH-R.$$

Thus the method of Inman and Dintzis, like that of Porath and coworkers, requires the presence in the ligand of a free amino-group not required for binding to the enzyme; the difference is that polycrylamide has a carbon skeleton and in this respect is more stable than Sepharose or Sephadex.

Continuing the development of the methods of Porath and coworkers and Inman and Dintzis, Cuatrecasas [80-82] described the syntheses of various derivatives of Sepharose and Biogel, such that ligands can be attached to these carriers not only via the amino-group but also via the carboxylic, thiol, phenolic, and imidazole groups; also it is possible to vary the distance between the ligand and the carrier by interposing between them aliphatic chains with different numbers of atoms ("arms"). As mentioned above, the length of the "arms" is in some cases of decisive importance, for example in the synthesis of the adsorbent for chymotrypsin [61]. Another example described by Cuatrecasas [69,80] refers to bacterial β-galactosidase. *p*-Aminophenyl-β-D-thiogalactopyranoside



was employed as the initial ligand. When it was linked directly to Sepharose, the enzyme was not sorbed. When it was combined with the bromoacetamidoethyl derivative of Sepharose, a sorbent was obtained which only weakly retained the galactosidase:

$$\text{Sepharose}\ -NH-CH_2-CH_2-NH-CO-CH_2-NH-\ \text{ligand}\ .$$

On a sorbent with a longer "insert",

$$\text{Sepharose}\ -NH-(CH_2)_3-NH-(CH_2)_3-NH-CO-CH_2-CH_2-CO-NH-\ \text{ligand},$$

the enzyme was sorbed very strongly.

By comparing sorbents based on the same ligand but with different carriers, Cuatrecasas showed (using as an example the sorbents for nuclease [80] and β-galactosidase [80]), that the adsorbents based on Biogel have a lower capacity than those based on Sepharose, which is probably due to the lower porosity of Biogel.

3. Other Methods of Utilising the Affinity of the Enzyme for the Ligand in the Chromatography of Enzymes

Cavalieri and Caroll [83] showed that, by polymerising acrylamide in a solution containing DNA, it is possible to obtain a gel in which DNA is firmly incorporated and which is suitable for the isolation and purification of DNA polymerase.

In another method of employing ligands, a non-specific sorbent is saturated with a soluble ligand; for example, ligands containing basic or acid groups are attached to suitable ion exchangers. Such a procedure was described by Beers [84], who used it to purify polynucleotide phosphorylase on a column with polyadenylic acid attached to DEAE-cellulose. The properties of such sorbents have been hardly investigated and it is not clear whether the ligand molecules sorbed on the carrier retain the capacity for the selective binding of the enzyme. Bearing in mind the data of Cuatrecasas [61,69,80] concerning the role of the hydrocarbon "arm" between the ligand and the carrier, one must suppose that this capacity would be considerably weakened. In addition, it is evident that sorbents of this type are less stable than those with covalently bound ligands.

Yet another application of the affinity of the enzyme for the ligand in the chromatography of enzymes consists in a selective elution of the enzyme sorbed on a non-specific sorbent with a soluble ligand. Heppel [85] first showed that pyrophosphorylase sorbed on alumina gel is selectively and effectively eluted with a pyrophosphate solution. Subsequently this principle was used to purify fructose-1,6-diphosphatase [86-88], aldolase [87,89], malate dehydrogenase [90], nuclease [91], and pyruvate kinase [92]. Yoshida [93] isolated by this method glucose-6-phosphate dehydrogenase, pseudocholinesterase, lactate dehydrogenase, and alanine dehydrogenase. The chromatography of carboxypeptidase A on a DEAE-cellulose column in the presence of a competitive inhibitor (β-phenyl propionate) resulted in its resolution into five fractions differing in aminoacid composition and thermal stability [94].

IV. ANALYTICAL APPLICATIONS OF AFFINITY CHROMATOGRAPHY

An interesting analytical aspect of the application of affinity chromatography, described by Wilchek and coworkers [95], refers to the study of the active centres of enzymes by specific chemical modification. The specificity of the reaction in the region of the active centre (more precisely in the region of ligand binding) is achieved by employing in the reaction a ligand with a chemically reactive group. As a result, the ligand reacts with other groups of the enzyme in the region of ligand binding. Peptides obtained by the successive cleavage of the modified enzyme have been fractionated on a column with the native enzyme attached to an insoluble carrier¶. The column retains only the peptides which contain the modified amino acid residues—owing to the presence in them of the ligand group. By analysing these peptides, it is possible to locate the region of the active centre in the aminoacid sequence of the enzyme molecule. In the above study by Wilchek and coworkers [95], ribonuclease was azo-coupled with a diazotised inhibitor—5′-(*p*-aminophenylphosphoryl)uridine 2′(3′)-phosphate. This compound reacted with ribonuclease in molar proportions of 1 : 1. After the cleavage of the modified enzyme with trypsin, the mixture of peptides was fractionated on a column with native ribonuclease attached to Sepharose by the method of Porath and coworkers [57-60]. The chromatography was carried out at pH 5.0, which is optimal for the binding of the enzyme to the ligand [62]. The coloured product was firmly retained on the column and, after washing off the impurities, was desorbed with 0.8 M ammonium hydroxide solution. Analysis showed that the product is a single peptide incorporating aminoacid residues between 67 and 85 and containing the modified tyrosin residue. The authors note the rapidity and convenience of the method compared with ion-exchange chromatography and electrophoresis.

The same method, which has been called the method of "affinity labelling", was used by Wilchek [97] and Cuatrecasas [98] for the isolation of a modified peptide from staphylococcal nuclease. An affinity label was applied also to acetylcholinesterase [99], aspartate aminotransferase [100], lysozyme [101], and *β*-galactosidase [102].

Kravchenko and coworkers [103,104] used affinity chromatography to separate the products of the photochemical oxidation of lysozyme in the presence of Methylene Blue under the conditions of preferential oxidation of tryptophan residues. Chromatography on Amberlite CG-50 ion-exchange resin made possible only the separation of the overall photochemical oxidation products from the unchanged native enzyme (Fig. 2). Bearing in mind that the modification of tryptophan residues in lysozyme might affect its affinity for the substrate [1-4], the lysozyme was chromatographed on chitin [42,43]. The results of such chromatography are presented in Fig. 3. [103] The chromatogram shows clearly three peaks (*X*, *Y*, and *Z*), the *Z* peak emerging almost simultaneously with the front of the eluent. Since the peaks emerging with the front can have a complex composition, the *Z* peak was subjected to further analysis. When it was rechromatographed under conditions increasing the affinity of lysozyme for chitin (a higher ionic strength of the medium [43]), it was possible to separate it into several further fractions [104]. Kravchenko and Lapuk [105] showed that the main fraction of the *Z* peak consists of an individual modification product in which the tryptophan residue 28 was oxidised. It is interesting to note that the tryptophan residue 28 is remote from the active region of the enzyme and is not directly involved in the binding of the substrate [1-4]. Nevertheless, experiments showed that its oxidation leads to a significant decrease of affinity. Hence it follows that this aspect of affinity chromatography is not restricted to cases where the active region of the enzyme is modified.

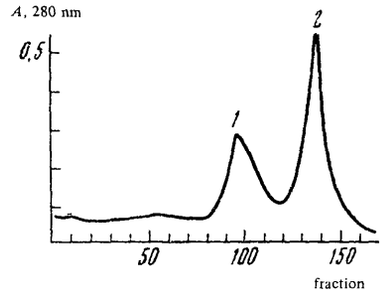


Figure 2. Chromatography of photochemically oxidised lysozyme on Amberlite CG-50 cation-exchange resin columns (after Kravchenko et al. [103]); 2.7 × 28.8 cm column; 0.2 M sodium phosphate buffer, pH 6.72; rate of elution 35 ml h^{-1}: 1) mixture of photochemical oxidation products; 2) native lysozyme. 10 ml fractions.

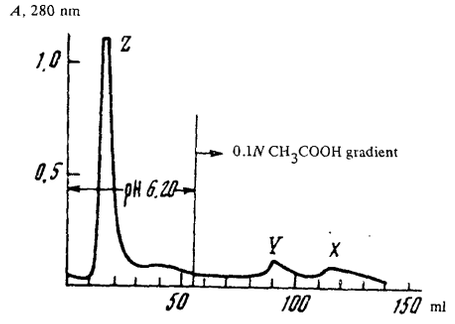


Figure 3. Chromatography of a mixture of products of the photochemical oxidation of lysozyme (peak *1* in Fig. 2) on chitin (after Kravchenko et al. [103]); 0.9 × 22.5 cm column with chitin dispersed to a 50 μm grain size; initial conditions: 1/15 M phosphate buffer, pH 6.20; volume of mixer for gradient elution 200 ml; rate of elution 15 ml h^{-1}.

¶There is an extensive literature on sorbents containing enzymes attached to insoluble carriers. The methods of their preparation and various aspects of their applications have been described in the reviews by Silman and Katchalski [96], Gryszkiewicz [141], and Goldman et al. [142].

A similar approach was employed by Kasche [77] to fractionate and characterise the functional properties of the products of the modification of heat-treated and γ-irradiated chymotrypsin on a column containing an inhibitor of soyabean trypsin attached to Sepharose by the method of

Porath and coworkers (Feinstein also reported [78] that, apart from trypsin, this type of sorbent is capable of specific binding of chymotrypsin). Native chymotrypsin showed an appreciable affinity for the inhibitor and lagged appreciably behind the eluent front. After heat treatment in solution, the enzyme was resolved into two fractions one of which emerged with the front and was completely inactive and the other corresponded to native chymotrypsin. After γ-irradiation, both in solution and in a dry state, two fractions were also obtained, one of which emerged with the front and was inactive. However, the second peak occupied an intermediate position on the chromatogram between the inactive and native enzymes. Measurements on the fractions showed that, as the enzyme emerges from the column, its enzymatic activity increases smoothly from 0 to 100%.

The use of affinity chromatography for analytical purposes is not as yet very common although this section has shown that there is a fairly broad base for such investigation and the few examples quoted demonstrate great possibilities of this method.

V. CHROMATOGRAPHIC CHARACTERISTICS OF THE PHYSICOCHEMICAL PROPERTIES OF THE ENZYME–LIGAND COMPLEX

Chromatography is one of the most direct and simplest methods for the investigation of the thermodynamics of sorption and complex formation [106–108].

Cherkasov and Kravchenko [109,110] were the first to employ this method for the investigation of the thermodynamic properties of the enzyme–substrate complex of lysozyme and chitin. Preliminary studies [42,43] showed that, depending on the pH of the medium, lysozyme forms two types of complex with chitin, with different conditions for their stability, as mentioned above (p. 895). Since the existence of two types of complex was not revealed by other methods, the chromatographic approach was employed for this purpose [109,110]. The equilibrium constant was found from the relation between the retention volume and the molar concentration of lysozyme at its peak on the output curve and the heat of complex formation was estimated from the relation between the retention volume and column temperature [106–108]. The determinations were made at pH 4.7 and 8.4, which correspond to the most favourable conditions for the two types of complex (at intermediate pH values lysozyme is distributed between the two complexes). The results obtained are listed in the Table which includes for comparison also data obtained by other methods at pH ~ 5 (there are no published quantitative data referring to pH 8–9; only graphical relations between the stability of the complex and pH, obtained by differential ultraviolet spectrophotometry [113] and fluorescence measurements [114,115], are available.

The Table shows that the results obtained by the chromatographic method at pH 4.7 agree very satisfactorily with those obtained at pH ~ 5 by other methods. Hence it follows that affinity chromatography is a fully valid method for the study of the thermodynamics of the binding between enzyme and substrate.

The data for the properties of the complex at pH 8–9 are contradictory. It follows from the work of Rupley et al. [113], Chipman et al. [114], and Lehrer and Fasman [115] that, on increase of pH from 5 to 8–9, the stability of the complex falls (the variation of other thermodynamic quantities with pH is not quoted in these reports). On the other hand, the results of the chromatographic determination show that the stability of the complex at pH 8.4 is higher almost by a factor of 10 than at pH 4.7 (cf. the values of ΔG° in the Table). The discrepancies are probably due to the inadequacy of the spectroscopic methods for the investigation of the complexes. Indeed these methods are indirect and are based on the detection of effects associated with changes in the conformation of lysozyme on formation of the enzyme–substrate complex.

Thermodynamic parameters of the formation of a lysozyme–substrate complex.

pH	$-\Delta F^\circ$, kcal mole^{-1}	$-\Delta H^\circ$, kcal mole^{-1}	$-\Delta S^\circ$, e.u.	Method	References
4.7	6.9	14.0	23.8	Chromatography	109, 110
5.0	7.0	12.8	19.7	Calorimetry	111
5.3	7.0	16.6	32.2	Kinetics	112
5.3	7.2	14.3	23.0	u.v. photometric	113
8.4	8.1	9.6	5.0	Chromatography	109, 110

On the other hand, analysis of the differences between the enthalpies and particularly the entropies of complex formation at pH 4.7 and 8.4 (see Table) shows that the conformation of lysozyme changes appreciably only when the complex is formed in an acid medium, but there is little alteration or none at all in an alkaline medium [110]. Thus, by virtue of the conformational properties of lysozyme, indirect methods evidently detect only the complex formed at pH ~ 5 and lead to the incorrect conclusion that the stability of the complex decreases as pH rises to 8–9. Similar situations can arise also in many other enzyme–substrate systems.

The applicability of kinetic methods for such purposes is limited to conditions where the enzyme exhibits its activity; for example, in the case of lysozyme and chitin these methods are applicable at ~pH 5 but not above pH 8.

Thus the direct method of affinity chromatography is more informative than the kinetic and spectroscopic methods now widely employed in this field.

The developments of recent years in the field of affinity chromatography show that the method can be fruitfully employed in a wide variety of different types of enzyme studies. On the whole, the present state of affinity chromatography shows it to be a promising analytical and preparative method in enzyme chemistry.

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During the preparation of the review for the press, reports appeared on the use of affinity chromatography for the purification of tyrosine hydroxylase [116], neuraminidase [117], dihydrofolate dehydrogenase [118–120], plasminogen [121–124], thrombin [125], pepsin [126], carboxypeptidase A [127,128], carboxypeptidase B [128,129], transaminases [130], trypsin-like enzymes [131], and certain proteases [132]. Figs. 4 and 5 present examples of the isolation and separation of carboxypeptidases A and B.

The method of "affinity labelling" of the active centre of the enzyme has been described for carboxypeptidase A [133,134] and aldolase [135].

Akanuma et al. [136] used affinity chromatography to investigate the properties of carboxypeptidase B complexes with various analogues of basic and aromatic amino-acids.

Wilchek et al. [137] reported certain changes in the functional properties of protein kinase in its chromatography on Sepharose to which cyclic adenosine monophosphate had been attached.

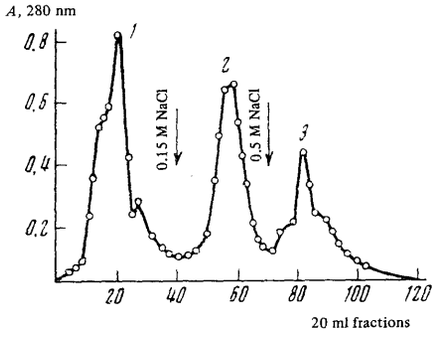

Figure 4. Separation of carboxypeptidases A and B by chromatography on Sepharose 4B with bound ε-aminocaproyl-D-tryptophan (after Reeck et al. [128]); initial eluent; 0.02 M tris-HCl buffer, pH 7.5, with added 0.05 M NaCl, followed by NaCl concentration gradient elution; the change of eluent is indicated by arrows: 1) impurities; 2) carboxypeptidase B; 3) carboxypeptidase A.

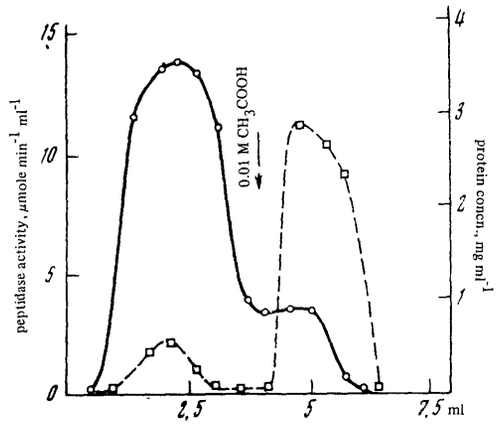

Figure 5. Isolation of carboxypeptidase A from a mixture of proteins by chromatography on porous glass with bound glycyl-D-phenylalanine (after Robinson et al. [127]). A column with granulated (200 mesh) porous glass (pore diameter 200 nm) was charged with a mixture of carboxypeptidase A, lysozyme, rubonuclease A, and bovine serum albumin. Initial eluent: 0.02 M tris-HCl buffer, pH 7.5, with added 0.2 M NaCl; the arrow indicates the change of eluent; continuous line—protein; dashed line—peptidase activity.

Mosbach et al. [138] and Weibel et al. [139] described the preparation of adsorbents for dehydrogenases with nicotinamide-adenine dinucleotide as the coenzyme.

The introduction of a new type of insoluble carrier—porous granulated glass—is noteworthy [127,139]. The porous glass is activated by treatment with aminosilanes, the amino-group introduced thereby being employed for the covalent binding of ligands.

Several reviews have been published on the affinity chromatography of enzymes and certain other bioorganic compounds [140,143,144].

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State of Water in Inorganic Crystal Hydrates and the Characteristic Features of Their Dehydration

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The state of water in inorganic crystal hydrates has been discussed, and the various distortions of the water molecule, as far as its dissociation, under the influence of the environment have been analysed. The reactions involved in the extensive dehydration of crystal hydrates have been examined from the viewpoint of the relationship between the state of water in the hydrate and the characteristic features of the dehydration processes leading to irreversible changes in the substance undergoing dehydration and to the decomposition of a complex oxo-anion. The bibliography contains 221 references.

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I. INTRODUCTION

The nature and state of water in hydrated compounds has recently been attracting increasing attention from research workers. This is due to the part played by hydrates in the solution of general problems of solid structure and also to the considerable practical importance of these compounds, since many substances can be obtained most readily and in purest form as the crystal hydrates. In technology and preparative chemistry, in addition to the original hydrates, extensive use is also made of their dehydration products. For example, one possibility being discussed is the provision of water for cosmonauts by the dehydration of water-containing non-terrestrial minerals.

The variety of substances capable of combining with and firmly retaining water to some extent predetermines the variety of ways in which water can be bound. Moreover, the way in which the experimental results from the study of hydrates are presented often depends on the methods used and the aims of the work. This has apparently been responsible for the extreme variety of terms characterising the nature and the state of water in inorganic hydrates, which has led almost to a state of crisis in the present nomenclature for the types of water in hydrates. The chief among these are: 1) sorbed or hygroscopic (adsorption and capillary) water [1-3]; 2) water of crystallisation [1,4,5]; 3) water of constitution [1,6-8]; 4) structural water [9-11]; 5) hydrolysis water [12]; 6) lattice and non-lattice [13]; 7) layer and inter-layer [14]; 8) combined [15] and chemically combined [16]; 9) constructional [17]; 10) zeolite [18]; 11) peripheral [19]; 12) high-temperature [20]; 13) hydrate [21]; 14) oxonium [22-24]; 15) intercrystal-polyamorphionic [12]; 16) coordination [25]; 17) clathrate hydrate water [26], etc. To these should apparently be added the various forms of "anomalous water" [27-29], which are apparently stable only in the layer next to the wall in

capillaries, so that they can also be regarded as a special type of combined water [30]. If allowance is made for the fact that the varied forms of water in hydrates differ significantly from one another only in the limit, the indefinite nature of each of the above terms becomes clear. This indefinite character leads to the temptation to create "one's own" new terms, characterising "most fully" the state of water in specific materials.

As far as dehydration reactions are concerned, a considerable amount of work, particularly early work, has been carried out without an analysis of the real state of water in the substance, and the "anomalies" frequently observed in experiments, for example the removal of fractional quantities of water, have been regarded as "contrary to common sense" and have therefore been ignored [31]. The discussion of the kinetics and thermodynamics of dehydration processes often does not make allowance for the structural and even chemical changes in the solid phase on dehydration. If however these changes are too obvious, attempts are made to create attractive thermodynamic models without allowance for the actual processes taking place in the solid substances on heating. At the same time, a fairly large amount of experimental material has now accumulated, showing that the water molecule is not always present in a hydrate as an individual structural unit, that dehydration is often accompanied by the partial or even complete decomposition of the salt, and that in many instances this process is the primary process and not, for example, the hydrolysis of the salt by water vapour. This leads to the conclusion that the water in a solid substance has a unique reactivity, and the behaviour of water in the dehydration of a hydrate is evidently determined to a considerable extent by its spatial and energetic structure in the original hydrate. Information of this type has become available chiefly in the last ten years, as a consequence of the fruitful application of modern physical methods of study to the examination of hydrates.

The present review attempts to summarise the available data and to establish the relationship between the state of water in an inorganic hydrate and the characteristic features of its dehydration. Recognising that it is not appropriate to include in the present review a large number of sharply differing classes of water-containing substance, we shall restrict ourselves to an examination of so called crystal hydrates, that is phases with definite compositions, exhibiting physical and chemical individuality, with molecular compositions usually represented in the form $X.H_2O$. Particular attention will be paid to hydrates containing an oxo-anion, to an analysis of the various distortions of water in a hydrate lattice under the influence of the crystal field and intermolecular interactions, as far as its dissociation, and also to the decomposition of the complex oxo-anion of a salt on the dehydration of its hydrate.

2. METHODS OF STUDYING THE STATE OF WATER IN CRYSTAL HYDRATES

The most important methods for studying the structure of crystal hydrates are X-ray diffraction and neutron diffraction, for which the achievements in the determination of the symmetry and molecular parameters of compounds are familiar. With reference to the problems being discussed, it may be noted that despite the fact that the position of the hydrogen atom in a hydrate is determined from X-ray diffraction data with a low accuracy or is derived from general geometric considerations, the results obtained in this way by careful work in most instances show good agreement with the results obtained by neutron diffraction. When comparing the numerical data obtained by these methods, however, it must be borne in mind that O–H distances determined by X-ray diffraction are always shorter than those determined by neutron diffraction [32]; this is due not to the error in the measurements but to the difference in the nature of the quantities measured. Moreover, the shortened O...O distance found by X-ray diffraction in water-containing substances (less than the sum of the van der Waals' radii) does not always provide a sufficient criterion for concluding that there is hydrogen bonding in the substance [33,34].

The state of water in a crystal becomes more definite when the results of a structural analysis are compared with the results obtained by measuring quantities directly related to the strength characteristics of the chemical bond; in this field, a leading position is rightly occupied by the vibrational-rotational spectra of molecules—the infrared absorption and reflectance spectra and the Raman spectra (RS)—since these reveal the characteristic frequencies of the molecular vibrations, which depend in definite fashion on the geometry of the molecules and the strength characteristics of the chemical bond. When the molecule is perturbed by some external influence, the force constants of the chemical bond are altered, and this brings about a regular displacement of the bands in the vibrational spectra. These methods have been found to be particularly useful in the study of water-containing compounds, because of the comparative ease of isotopic replacement of hydrogen and the large (~1.4) coefficient of isotopic displacement of the frequencies of the vibrations of the groups of atoms containing hydrogen.

The vibrational spectra of water in various states have been the subject of a fairly large number of reviews and monographs on the infrared spectra of water in inorganic substances in adsorbed, zeolite, crystallisation, constitutional, and free forms [35,36], the librational vibrations of water in solid hydrated compounds [37], the spectroscopy of hydrogen bonds involving water [38–42], and the spectroscopic manifestation of coordinated water [36,43–45]. For the purposes of further discussion, we shall deal briefly with the most characteristic manifestations of water in vibrational spectra in relation to its state.

The stretching vibrations of the O–H groups in the monomeric gaseous water molecule have frequencies of 3650 cm^{-1} (ν_1) and 3750 cm^{-1} (ν_3). Polymerisation by H-bonds in the gaseous phase or conversion into the condensed state leads to a displacement of the absorption bands towards longer wavelengths, accompanied by broadening of the bands until they merge. There are a large number of empirical and semi-empirical correlations between the values of the νOH frequency and the length of the H-bond, [38,46–49] between the length of the H-bond, the potential curves, and the hydroxyl frequencies [50]; between the magnitude of the displacement $\Delta\nu$OH and the energy of the H-bond; [39,51–53] and between the frequency νOH and the electronegativity of the hydrate-forming element [54]. In the calculation of the displacement of the bands, the origin is usually taken as the ν_3 frequency of the non-perturbed water molecule or the averaged value 3700 cm^{-1}, since even when there are two bands in the νOH region, a reliable assignment to ν_1 or ν_3 is difficult. Calculations by means of empirical equations relating the length and energy of the H-bond to the displacement $\Delta\nu$OH often give satisfactory results even in the study of substances of different types, differing in chemical character

and crystal structure, as a consequence of the marked sensitivity of νOH to the configuration of the H-bond. These relationships are usually linear, if the length of the H-bond lies in the range 2.5–2.8 Å. There is as yet no sufficiently convincing criterion for selecting the limiting O...O distance in a H-bridge, at which interaction of the H-bond type can be neglected, since $\Delta\nu_{OH}$ approaches zero asymptotically in the range 2.9–3.4 Å. The value 2.84 Å in the frequently used expression:

$$\Delta\nu_{OH} = 4.43 \cdot 10^3 \cdot (2.84 - R) \quad (1)$$

where R is the O...O distance, in our opinion, is too low, since a distinct displacement of the absorption bands is observed even for much larger distances. Bellamy[48] proposed the more appropriate value 3.35 Å, beyond which, according to various theoretical considerations, the energy of the interaction should not exceed 0.2–0.3 kcal mole^{-1}. This quantity appears in the semi-empirical expression

$$\Delta\nu(\text{cm}^{-1}) = 50\left[\left(\frac{d}{R}\right)^{12} - \left(\frac{d}{R}\right)^{6}\right] \quad (2)$$

used in calculations covering a wide range of H-bond lengths. The energy of the H-bond can be estimated with sufficient accuracy by means of a relationship established from a large number of results, according to which one unit of energy in kcal mole^{-1} is equivalent to a change in frequency of 50 cm^{-1}. More accurate values can be obtained only for groups of substances of the same type, and always require verification by some independent method.

In view of the highly characteristic nature of the stretching vibrations of the OH groups, this range of the spectrum does not make it possible to obtain unambiguous information on the nature of the oxygen–hydrogen group in a solid substance, since the ranges corresponding to the νOH bands of hydroxide ions OH^-, molecular water H_2O, and the hydrated proton $H_{n+2}O_m^+$ overlap. This problem can be resolved by analysing the bending vibrations of the hydrates, for which the frequencies lie below 1500 cm^{-1} for OH^-, in the range 1590–1680 cm^{-1} for H_2O, and in the range 1680–1800 cm^{-1} for the hydroxonium ion H_3O^+.[55,56] The frequency of the bending vibration of an isolated water molecule is 1595 cm^{-1}. On association, including that due to H-bonding, the absorption band corresponding to this vibration is displaced towards higher frequencies[57], but the displacement is much smaller than that for the stretching vibrations, and for the same perturbation amounts to 10–50 cm^{-1}. The number of components of the bending band coincides with the number of forms of water molecule in the original hydrate, but unfortunately this criterion can be used only when the degrees of binding of the molecules differ considerably, since in most instances, because of the small displacement of δ_{H_2O}, the bands due to different kinds of water are not resolved.

The above regular features apply qualitatively for all substances, irrespective of their nature and state of aggregation. In the analysis of the bonding of water in inorganic hydrates from their infrared spectra, however, it is necessary to make allowance for the fact that coordination of the water molecules to a metal ion influences the vibrations of the molecules in the same way as H-bonding. The displacement of the bands due to the stretching vibrations of water towards longer wavelengths for strong electrostatic complexes as a consequence of the coordination of water to a metal, according to calculations, may reach 600 cm^{-1}, and is determined by the polarising and electron-accepting properties of the cations[58]. A rigorous separation of the perturbing influence of each of these two factors on the vibrations of water molecules is hardly possible, since on the one hand, hydrates in which the existence of H-bonding might be excluded are as yet unknown, and on the other hand, the effects of coordination and H-bonding are closely related, since the polarisation of the O–H bond in the field of the cation, by increasing the proton-donating properties of water, leads to a decrease in the force constant of the bond, and this is equivalent to an increase in the strength of the H-bond and a correspondingly greater displacement of ν_{OH}. Definite progress in this direction has been made in a study of the infrared spectra of series of isomorphous perchlorates[59–61], since the perchlorate ion is one of the weakest proton acceptors. These results show that in this class of compound, the value of $\Delta\nu$OH resulting from the coordination of water, even for *d* elements, is not more than 150 cm^{-1}.

The introduction of water into the first coordination sphere of a metal leads to the production, in the vibrational spectra of the hydrates, of bands characterising the vibrations of $M(H_2O)n$ complexes, at comparatively high frequencies. The M–O stretching vibrations in these groups are observed in the range 300–500 cm^{-1} for a number of aquo-complexes[62], and at higher frequencies for small ions with high charges; for example, the bands for $[Be(OH_2)_4]^{2+}$ and $[Al(OH_2)_6]^{3+}$ lie at 860 cm^{-1} and 600 cm^{-1} respectively[63,64].

Promising possibilities for the theory of the energy of H-bonding are provided by the analysis of the vibrational spectra of the H-bond itself; these spectra are produced as a result of the loss of rotational or translational degrees of freedom by the molecules of groups of atoms on formation of the H-bond. The vibrations of the hydrogen bond are observed in the frequency ranges 100–200 cm^{-1} for the stretching vibrations, and 50–80 cm^{-1} for the bending vibrations. Unfortunately, since the use of long-wave infrared spectrometers is not yet widespread, work in this field has been carried out chiefly by Raman spectroscopy, and this has restricted the range of substances studied to solutions and single crystals. Attempts have been made[65–71] to compare the frequencies with the lengths of H-bonds, but the state of water of crystallisation in this range of the spectrum has as yet been insufficiently studied, and no definite generalisations can be reached.

Difficulties in the Interpretation of the Infrared Spectra of Water in Crystal Hydrates

A clear distribution of the vibrations of water in different states in different regions of the spectrum is characteristic only of limiting ideal situations. As already noted, the nature of the spectrum in the range of the stretching vibrations of the OH groups does not make it possible to determine the nature of the oxygen–hydrogen group in the substance. The production of several bands in this frequency range can be related not only to the existence of several kinds and states of water but also to the formation of H-bonds with different energies by the same molecule, and also to the production of overtone, combination, and resonance frequencies. In this instance, partial deuteration of the substance, which makes it possible to determine the nature of the splitting of the OH bands, is extremely useful. At the same time, the absence of appreciable structure in a band does not indicate uniformity of the binding of water in a substance, since the vibrations of groups of different character may not be resolved, as a

consequence of the large width of the band due to a hydroxyl group forming an H-bond. Moreover, it must be borne in mind that the band frequently observed at 3450 cm^{-1} may be due not to the substance being studied but to the absorption of water adsorbed by the substance, particularly for substances with a highly developed surface. Fortunately, the low sensitivity of the position of this band to the nature of the sorbing substance facilitates its assignment [72].

In our opinion, considerable care must be exercised in the use of the repeatedly recommended method for the quantitative determination of different types of water in a substance by partial dehydration until a particular component of the spectrum disappears [55,73]. This method can be adopted without significant reservations only for substances of the zeolite type, since, as will be shown below, the state of water changes during the dehydration of a salt. This is particularly true of aquo-complexes.

The bending vibrations of water in a number of hydrates may be observed at frequencies of ~1670 cm^{-1}, and their assignment to molecular water or the hydroxonium ion becomes difficult. In this instance an unambiguous interpretation can also be carried out by studying partly deuterated materials. Allowance must be made, however, for the fact that in a number of substances the degree of hydration of the proton may be greater than unity, and this is also reflected specifically in the nature of the spectrum and must be taken into account in its interpretation [74]. Situations more difficult to explain are those in which the frequency of the bending vibration of water in a hydrate is displaced towards longer wavelengths relative to its position for monomeric water, and the structural data exclude the possibility of formation of hydroxo-compounds [75-78]. This may be due to a significant change in the angular characteristics of the water molecules. Thus in magnesium sulphate monohydrate the distance between the protons is 1.65 Å compared with the usually observed 1.50–1.58 Å, [76,79] and for $CuCl_2.2H_2O$ the HOH angle increases to 111.36°. [80]†

Although the analysis of the spectra in the stretching and bending ranges has shown that the water molecule retains its vibrational individuality, this does not exclude the possibility that bending vibrations of M–OH groups are produced when water is present in the first coordination sphere of an electron-accepting metal and its position is determined by the nature of the complex-forming metal.

The interpretation of the characteristic vibrations of an aquo-complex is most complicated, since this range corresponds to the stretching and bending vibrations of a large number of oxo-anions, and more particularly since deuteration has little influence on the positions of the bands of an aquo-polyhedron.

NMR and other methods. Considerable progress in the study of the state of water in hydrates has been made in recent years by proton magnetic resonance (PMR) and ^{17}O nuclear magnetic resonance (NMR) spectroscopy [42,44,81-83].

† It may be that the vibrational spectrum of water in aquo-complexes with H-bonding does not correspond to the triatomic model usually employed, and that the production of several bands in the range 1400–1600 cm^{-1} is due to the production of additional degrees of freedom in the vibration of, for example, a penta-atomic fragment of the type $M-O\begin{matrix}H\ldots O^- \\ H\end{matrix}$.

The PMR method has given important information on the lifetime of the H-bond and, most important, it has confirmed directly that in systems with H-bonding there is proton exchange in the O–H...O group, with a comparatively low activation energy (2–7 kcal $mole^{-1}$) [84,85] and has shown that reorientation and rotation of a molecule of water of crystallisation as a whole are possible [86-89]. An important feature for the understanding of the mechanism of the dehydration of a number of compounds is that the mobility and free path of a delocalised proton along the chain of H-bonds in ice have been found to be much greater than those in liquid water [90]. These quantities are even greater in clathrate hydrates [91], that is the stabilisation of the bonds by the lattice facilitates proton transfer.

Since the PMR method gives information primarily on protons, its use for the study of the state of water as a whole is somewhat limited. In the determination of the coordination of water to a metal ion it is preferable to study ^{17}O NMR, and this method has been used, in particular, to study the hydrate numbers of a number of metal ions. Unfortunately, this information has been obtained chiefly for the liquid state. For solid hydrates, for which low-resolution resonance is chiefly employed, its achievements have been much more modest. For a restricted range of substances, various empirical correlations have been found between the inter-proton distance and the length of the H-bond [83], but these relationships require verification for a wider range of substances and by other independent methods (vibrational spectra, structural analysis, etc.).

Other methods for studying the state of water in a solid, for example measurement of the dielectric properties, spectroscopy in the visible and ultra-violet ranges, magnetochemical methods, and EPR spectroscopy, are much less specific, and their application to the problem being considered is limited to several individual instances. If water is coordinated to a cation, however, these methods may give extremely useful additional information, particularly for the hydrates of salts of the transition metals.

3. STRUCTURE OF CRYSTAL HYDRATES

The mechanical, physical, and chemical properties of crystal hydrates are determined to a considerable extent by the position and state of the water molecules in their structure. At this stage, therefore, a general classification of hydrates, taking account of all the properties of the water-containing substance, is hardly possible. Any attempt to generalise the properties of large groups of hydrates must be based primarily on the final aims of the generalisation. From this viewpoint, for a description of the geometric arrangement of the water molecules relative to the other components of the crystal, it is quite satisfactory to use the classification adopted in crystal chemistry [92], based chiefly on Bernal's theories [93]; in this classification, all hydrates are divided into the following groups: a) hydrates in which the water molecules are isolated from one another; b) hydrates with isolated unit structures, in which water forms independent groups; c) chain hydrates; d) layer hydrates; e) hydrates with three-dimensional frameworks formed by water molecules. In the examination of dehydration reactions, however, this classification can be taken only as a first approximation, since it does not reflect the variety of forms of water and the influence which this has on the chemical properties of a

real hydrate, in which the water molecules interact strongly with the cation and anion of the salt and with one another, undergoing much greater distortion not only relative to their configuration in the gaseous phase, but also relative to water in the solid and liquid states; for example, in aquo-complexes the M–OH_2 distance is extremely close to or equal to the M–O distance in the corresponding oxide [94].

Since in most instances the analytical data do not give information on the forms in which water is present in a substance, it is necessary first of all to have criteria for distinguishing water of crystallisation from water of constitution, that is water present in ionised form, for example as hydroxide or hydroxonium ions. Since neutron diffraction techniques are not widely available, and X-ray diffraction does not give unambiguous results when applied to water, a suitable criterion for an extremely wide range of substances is provided by the presence of the band due to the bending vibration of molecular water in the vibrational spectrum of a hydrate, since the position of this band is highly sensitive to the conversion of water into the ionised state. Thus crystal hydrates can be regarded as substances in which the water molecule retains its vibrational individuality.

For the discussion of the state of water in crystal hydrates in relation to their dehydration, it is convenient to divide them into the following groups: 1) substances for which the hydrate number (n) is greater than the coordination number (CN) of the metal in the given compound; 2) hydrates with n equal to the coordination number; 3) hydrates with n less than the coordination number. As proposed by Shishkin [95], hydrates with variable composition, of the zeolite type, form an independent group of hydrates containing molecular water.

Many hydrates with a large quantity of water of crystallisation can be represented as solid solutions of water and the corresponding anhydrous salt, since their structure, with some assumptions, can be interpreted as corresponding to the structure of ice in which the positions of some of the water molecules and the cavities are occupied by ions of the salt. The nature and position of the bands in the infrared spectra of these hydrates in the range of the water vibrations are close to those in the spectrum of ice, and their heats of dehydration are also close to the heat of sublimation of ice.

When n is greater than the coordination number by one or two units, two structurally non-equivalent types of water can be clearly distinguished: part of the water, in quantities corresponding to the coordination number of the metal, is present in its first coordination sphere, and the rest of the water is present at a considerable distance from the cation (~4 Å). This situation is observed in many metal heptahydrates and in copper salt pentahydrates, and has been confirmed by direct structure determinations, from the bands due to water in the infrared spectra, and by NMR. [96–100] The water not combined with the metal forms H-bonds with a coordinated water molecule, or, if the steric conditions are favourable, with the anion; the energy (~4.5 kcal $mole^{-1}$) and length of these bonds are often independent of the nature of the anion, as shown by the presence, in the infrared spectra of these hydrates, of a band at ~3400 cm^{-1}, close to ν_{OH} for molecules bound by H-bonds in liquid water. This molecule has a much greater mobility than coordinated water [101].

The properties of water from the immediate environment of a metal are determined chiefly by its interaction with the cation and anion, and to a smaller extent by the interaction with water outside the coordination sphere, so that they are of the same type as those of hydrates of the second group. Hydrates in which the hydrates numbers are equal to the coordination number and in which all the water is in the inner coordination sphere of the metal (aquo-complexes) make up a large group among known inorganic crystal hydrates. The energy of the H-bond formed by coordinated water can vary over a fairly wide range (the value of $\Delta\nu_{OH}$ sometimes reaches 1000 cm^{-1} [102,103]), depending on the nature of the cation and anion. Ionic aquo-complexes in a solid substance undergo various distortions under the influence of the crystal field and the H-bonds, so that the water molecules among themselves and the OH groups of an individual molecule can become non-equivalent; this is often accompanied by the production of different M–OH distances, the difference amounting to 0.02–0.2 Å for neighbouring water molecules [94,104]. If the symmetry of the crystal is sufficiently high or a large number of states of water molecules with similar energies are produced, this non-equivalence may not lead to splitting of the bands in the infrared spectra, and more or less broadened single bands are observed in the range of absorption of water. With marked distortion of the coordination polyhedron, however, for example as a consequence of the Jahn–Teller effect or on formation of H-bonds of different energies by the same water molecule, the bands due to the stretching and sometimes also the bending vibrations of water may be split, and the water becomes spectroscopically non-uniform.

The most complicated sets of possible energy states of water molecules and positions in the structure are shown by the hydrates of the third group, containing a small quantity of water of crystallisation. At the same time, this class of hydrate is of greatest interest for the solution of the problems of preparing anhydrous substances, since as a consequence of the stepwise nature of the reactions, the dehydration of higher hydrates in the final stages gives products with small and sometimes fractional hydrate numbers.

If the water in these hydrates is present in the first coordination sphere of the metal, the coordination polyhedron also contains some oxygen atoms of the anion, so that in addition to the M–OH interaction there may also be interactions of the H-bond type between water and the anion of another polyhedron, leading to marked distortion of the water molecule itself and of its environment. Thus for nickel nitrate tetrahydrate [105], eight different O–H...O distances have been found, and each of these bonds produces its own absorption band in the infrared spectra in the range 3525–3130 cm^{-1}, the dependence on RO...O being given by the empirical function (1). For a definite mutual spatial orientation of the water molecule and the anion, both hydrogen atoms of water may be joined to the same oxygen atom of an anion, and this leads to a decrease, relative to liquid water and ice, in the inter-proton distance and hence in the HOH angle [97,106,107]. On the other hand, one of the hydrogen atoms may remain almost free, whereas the other takes part in the formation of a strong H-bond [108]. The angular characteristics of the water then undergo distortions which are the opposite of those in the first example, and the vibrations of the two OH groups can be regarded as almost independent. Thus the above correlation between the length of the H-bond and the inter-proton distance may have only a limited application for systems of this kind.

Lower hydrates sometimes show anomalous values for the frequencies of the water vibrations [109], unusual coordination [110,111], and fractional hydrate numbers. All these facts indicate that many lower hydrates, particularly

those obtained by the dehydration of higher hydrates, are in a stressed state; this may be attributed to some lack of correspondence between the small size of the cation and its extensive coordination possibilities and the large radii of the complex oxo-anions. This lack of correspondence is removed to a considerable extent for aquo-complexes, as a consequence of the increase in the effective radius of the complex aquo-cation. On this basis it should be expected that the decrease in the hydrate number as far as the formation of the anhydrous salt should be accompanied not only by the distortions of the water molecule noted above but also by an increase in the extent of the perturbing influence of the lattice on the anion.

The distortion of the symmetry of an anion can be followed by direct structure determinations, and also from the splitting of degenerate absorption bands and the appearance of forbidden bands in the vibrational spectra. For example, on going from copper sulphate pentahydrate to the monohydrate, the symmetry of the anion decreases [112] from T_d to C_{3v}, or to C_{2v} in the dehydration of the double sulphates of various transition metals [113] and even to C_s for the selenate anion, with the same symmetry, on going from the hexahydrate to the dihydrate in double copper selenates [114]. This situation is typical, and has also been noted for rare earth metal bromates [115], phosphates [116], and many other salts. An increase in the complexity of the spectra in the range of the vibrations of the anion may naturally be due not only to a decrease in the symmetry of the anion but also to a decrease in the site symmetry of the crystal, but in a number of instances these effects can be distinguished fairly simply [117]. Moreover, for systems in which the influence of the symmetry of the lattice can in practice be excluded, for example for ion exchange films, decrease in the degree of hydration is accompanied by a sharp increase in the magnitude of the splitting of the bands due to the degenerate vibrations of sulphate and selenite anions [118]. A number of authors have not noted any significant differences in the infrared spectra of higher and lower hydrates [119] or have observed a decrease in the complexity of the spectrum in the range of the vibrations of the anion on going from hydrates to the anhydrous salts [120,121], and this has led to the suggestion that H-bonds have a decisive influence on the decrease in the symmetry of the anion. Calculation of the stability of solid systems with H-bonds [122] has shown, however, that the rupture of the O–H...O bond is energetically more favourable than distortion of the valency angles of the anion, despite the fact that the linear H-bond is the most stable [123]. In the limit, this leads to a situation in which some hydrogen atoms in crystals may not take part in the formation of a H-bond. It appears that H-bonding in a hydrate under favourable conditions intensifies the decrease in the symmetry of the anion brought about by more powerful interactions. This is confirmed by the fact that when an anion is coordinated to a metal ion, the splitting of the bands due to the degenerate vibrations is accompanied by their displacement towards longer wavelengths [113,124,125]. Thus those instances where the symmetry of an anion increases with decrease in the hydrate number are to be regarded as exceptions, particularly since the decrease in the complexity of the spectrum is often only apparent, as a consequence of the conversion of the substance to the amorphous state on dehydration.

On the basis of the nature of the interaction of water with a metal ion, it should be expected that the strength of the $M-OH_2$ bond should be determined primarily by the polarising and electron-accepting properties of the cation, that is by its size, charge, and outer electronic structure. In a series of elements of the same type, ν_{OH} for water decreases regularly with decrease in the radius of the ion or with increase in its charge [126,127]. When several factors change simultaneously, however, it becomes difficult to predict the relative strength of the interaction of water with the cation. Thus $\Delta\nu_{OH}$ is much greater for hydrated salts of aluminium and beryllium than for zirconium and hafnium compounds. For transition metals, the degree of binding of water is greater than might have been expected for a purely electrostatic interaction. Within the first transition series, $\Delta\nu_{OH}$ and hence the degree of perturbation of the water molecules in the salts of the doubly-charged ions decrease in the order: $Mn < Co < Ni < Cu > Zn$, which corresponds closely to the familiar Irving–Williams series for the stability of complex compounds. The magnitude of the splitting of the degenerate vibration of the anion changes in the same order, indicating that the mechanisms of the interaction of the cation with water and the oxo-anion are similar.

The extent of the distortion of water under the influence of the anion is characterised by the proton-acceptor properties of the latter. Study of the hydration of anions introduced into an ion-exchange film based on polystyrene (R) has shown that these properties change in the opposite order to the abilities of the corresponding acids to undergo protolytic dissociation [128], increasing in the order RSO_3^-, $RSeO_3^-$, RPO_3^{2-}, $RSeO_2^-$, RPO_2H^-. In accordance with this, ν_{OH} in the spectrum of their hydrates decreases from 3465 cm^{-1} to 3335 cm^{-1}, indicating that the strength of the H-bond increases in the same order. Unfortunately, an unambiguous interpretation of the influence of various cations and anions on the state of water is possible only for strictly isomorphous series, which is not always possible, or in the study of ion-exchange films, although in the last instance it is not always possible to achieve reliable control of the degree of hydration. Despite this, the order of change in the energy of the H-bond with change in the nature of the anion, observed by Karyakin and Muradova [103] for substances of different types, where the energy increases from 1.7 kcal $mole^{-1}$ to 8.5 kcal $mole^{-1}$ in the series ClO_4^-, NO_3^-, Cl^-, CO_3^{2-}, SO_4^{2-}, and PO_4^{3-}, shows satisfactory qualitative agreement with the above order for the polystyrene acids.

Thus if we take as a measure of the influence of the cation the change in ν_{OH} relative to ν_{OH} for a similar hydrate of an alkali metal salt, and as a measure of the influence of the anion the magnitude of $\Delta\nu_{OH}$ relative to the perchlorate of the same element (assuming that the effects of the two factors on water are additive), we find that for a series of hydrates the frequency of the stretching vibrations of water should be displaced to 3000 cm^{-1}, which corresponds to a H-bond energy of about 15 kcal $mole^{-1}$, that is a value close to the energy of a chemical bond. The state and reactivity of water combined in this way must naturally differ significantly from those for the free state.

This should lead primarily to a marked increase in the degree of protolytic dissociation of water. Hydrated metal ions in solution exhibit acidic properties to a greater or lesser extent, as a result of dissociation to form hydrogen ions and a complex hydroxoaquo-ion. According to Schwarzenbach [129], water in the inner coordination sphere of metal complexonates can be titrated with alkali. Water of crystallisation can react with metals with which liquid water does not react [130]; a remarkable feature is that compounds with small hydrate numbers are much more active than the higher hydrates.

Modern theories of the energetics of H-bonding and the structure of substances containing hydrogen bonds make it

possible in many instances to explain the state of water in a hydrate and to predict its possible chemical properties. For substances with strong intermolecular interactions we can expect in the limit the production of a symmetrical O...H...O band, so that the proton belongs with equal probability to the water molecule and the anion, and this formation should acquire the properties of an acid salt. From the general course of the relationship between O–H and O...O distances, it follows that this situation should arise for an H-bond length of about 2.3 Å. This value is assumed in the discussion of various models of "anomalous" water or poly-water [131,132] and appears to have been confirmed experimentally [133]. In a number of solid substances a symmetrical hydrogen bond has been assumed at much larger distances [134–137] (of the order of 2.4–2.5 Å). In systems with longer H-bonds there is also a definite probability of transfer of a proton from water to the anion, since the potential curve for an unsymmetrical bond has two minima for which the height of the potential barrier may be reached on thermal excitation, and the efficiency of this process can be increased by an appreciable factor by tunnelling of the proton along the H-bond. According to calculations [138], this process is probable for a distance between the minima reaching 0.8 Å.

If a system of H-bonds is formed by several water molecules, the energy barriers to the removal of a proton may be decreased by the positive heat of formation of oxonium ions. In accordance with this, the state of water in iron phosphate and arsenate dihydrates is more accurately represented by the formula $MXO_4.(OH)^-H_3O^+$ than by the classical formula with isolated water molecules [139,140]. Oxonium ions have been found in the solid state in a number of hydrates of inorganic acids and salts [103,141–145]. According to Zundel and Metzger [146], a proton is completely removed from polystyrene sulphonic acid at a degree of hydration equal to two, that is when the ion $H_5O_2^+$ is formed. This ion has also been detected in hydrogen chloroaurate tetrahydrate [147], where the distance between the potential wells is 0.62 Å, and in perchloric acid dihydrate [148], where it is assumed that there is only one minimum on the potential curve. It is suggested [149] that the oxonium ion is most stable in the form of the trisolvate and that its hydrate should have the structure $H_9O_4^+$. According to Lundgren and Olovsson [150], this ion is present in hydrobromic acid tetrahydrate. Hydrated hydroxonium ions with the composition $H_3O^+.(H_2O)_n$, where n reaches 10, have been detected by mass spectrometry in the gaseous phase. Despite the fact that the $H_9O_4^+$ ion has been assigned [154] the planar symmetrical structure $H_3O^+.3H_2O$ (H-bond energy 46.3 kcal mole^{-1}), the heats of hydration of the hydroxonium ion found from the mass-spectrometric data do not show an inflection at n = 3, but show a smooth change, and at n = 7 they approach the heat of evaporation of water from a flat surface [155]. The structure $H^+(H_2O)_n$ is therefore to be preferred. A remarkable feature is that the geometric structure and energetics of the hydrated proton and hydroxide ion almost coincide for equal degrees of hydration [156].

In these complex formations, despite the fact that molecules of water of crystallisation often retain their individuality as vibrational units, the proton is completely delocalised over the entire ion. In the limit, as shown by Shakhparonov [157,158], many properties of aqueous systems can be described by assuming that a conductivity zone exists for protons. Although the concepts of a proton gas have been applied chiefly to liquid systems [159], it will be shown below that they have proved useful for the explanation of various characteristic features of the dehydration of solid inorganic hydrates.

Finally, for the salts of multiply-charged readily hydrolysed metals, the water may be completely dissociated, and these compounds should be regarded as complex acids, and not crystal hydrates. Nevertheless, many substances of this type are still classified as crystal hydrates, apparently because of the difficulty of determining the true state of water in the materials. A number of properties of solid hydrates of various zirconium and hafnium salts, however, make it impossible to regard these compounds as crystal hydrates or as the corresponding acids, which exist in solution. For zirconyl chloride hydrates, structures with oxo-bridges or hydroxo-bridges, or structures with complex polynuclear ions of the type $[Zr_4(OH)_8.(H_2O)_{16}]^{8+}$, [160,161] have been proposed. A tendency for hydrated compounds of this type to form bridging groups and to acquire more strongly acidic properties is shown by tin phosphates [162], aquopolytungstates [163], metal borates, etc. In these limiting situations, the water is present as water of constitution, and the suggested criterion for estimating the state of water does not apply.

In most hydrates, however, the state of water is characterised by a greater or lesser displacement of hydrogen ions towards the anion, and the magnitude of this displacement is determined by the properties of the cation and anion, and also by steric factors. In this connection, the corrections to the formulae of hydrates proposed by a number of authors on the basis of the vibrational spectra [for example for magnesium carbonate trihydrate [164,165] $Mg(OH)^+(HCO_3)^-.2H_2O$] must evidently be understood not as corresponding to complete dissociation of the water molecule but as an illustration of the fact that the water molecule reacts so strongly with the anion that a change in its vibrational characteristics becomes possible. To the same extent this is also true of Lendormy's conclusions [166] that many transition metal sulphate monohydrates should be regarded as acid salts of the type MH_2SO_5.

The tendencies, noted above, for the state of water in crystal hydrates to change with change in the hydration numbers and the nature of the environment relate primarily to systems in which all or part of the water is in the coordination polyhedron of the metal. There are therefore some exceptions, where the water in lower hydrates is less firmly bound than that in higher hydrates. This situation is observed in calcium sulphate hemihydrate [167], in which the water must be regarded as zeolite water, since the structure remains unchanged on dehydration. The interpretation of the spectra of hydrates of this kind in the far infrared range has been based on a crystal structure model [168] in which water forms a molecular lattice which is quasi-independent of the ionic lattice of the salt.

4. DEHYDRATION OF CRYSTAL HYDRATES

The extensive range of dehydration reactions has produced a large number of papers on the study of these reactions, but up to the present there has been no sufficiently well-founded approach to the interpretation of many experimentally established features of these reactions in relation to their kinetics or to the problems of the thermal stability of the intermediate hydrate forms produced in the decomposition of the original hydrate. To some extent this can be attributed to the variety of forms in which water is combined in solid inorganic hydrates, and also to the specific nature of the problems studied and hence of the conditions under which the experiments have been

carried out, and this has made it difficult to compare the results of different studies, even of the same substance.

In their monographs, Young [169] and Garner [170] have discussed a large number of studies of the kinetic features of dehydration. In many of these, sufficient attention has not been paid to the possible influence of the formation of various intermediate hydrates on the kinetic characteristics. On the other hand, the operations involved in the isolation of individual hydrated phases and the determination of their thermodynamic functions make it necessary to take account of kinetic factors, because of the ease with which false equilibria are established in hydrates. Only in a few papers have the macro-kinetic characteristics of a reaction been related to the energetic and geometric structure of water in the hydrate lattice.

In most instances, dehydration takes place in stages, and the number of intermediate phases may be extremely large. Thus in the dehydration of magnesium sulphate heptahydrate, seven intermediate hydrates are formed [171,172]. It is only in a few instances, chiefly when water is not combined with the metal, that it can be removed from water-rich hydrates in a single stage. Most of the intermediate forms are generally produced in the final stages of the process, often with the formation of compounds with fractional hydrate numbers which sometimes are not submultiples of the original number. Fractional hydrate numbers are sometimes also encountered in hydrates precipitated from solution under normal conditions [173], for example $CdSO_4.\frac{8}{3}H_2O$, so that there are insufficient grounds for assuming that these compounds should be regarded as solid solutions of the anhydrous salt and the corresponding hydrate. The number and composition of the intermediate hydrates depends to a marked extent on the nature of the substance and the conditions under which the reaction is carried out. They may be different even for isomorphous substances, for example aluminium sulphates [174] and selenates [175], or rubidium and caesium tellurites [176]. Measurement of the vapour pressure over hydrated strontium oxalate showed that in the range of hydrate numbers from 2.5 to 2 there exists a series of non-stoichiometric hydrates, for which the heat of dehydration [177] increases from 12.7 kcal mole^{-1} for $n = 2.5$ to 17.7 kcal mole^{-1} for $n = 2$. An increase in the heat of dehydration with decrease in the hydrate number is a common feature of most hydrates. The effective activation energy of the reaction changes in the same order, and in many instances it is close to the heat of the reaction. The differences sometimes observed in these quantities, or their anomalously high values (particularly for ΔH calculated from the vapour pressure) are often related to the possibility of formation of unstable intermediate compounds or to the increased energy of the final dehydration product. The values of these quantities also depend to a marked extent on the particle size of the original crystals. Thus the dehydration of goethite [178] is endothermic for the coarsely-crystalline material, athermic when the particle size is about 100 Å, and exothermic for specimens with a smaller particle size. Engberg [179] has shown that if the activation energy and heat of dehydration are determined for monodisperse particles with the same dimensions, the values are almost equal.

The conditions of the process, particularly the pressure and composition of the gaseous phase, have a marked influence on the chemistry of dehydration. For example, with change in the external water vapour pressure from 10 mmHg to 80 mmHg, the number of stages and the composition of the intermediate phases in the dehydration of strontium oxalate changes three times [177]. Examples are known where processes become more complicated [174] or simpler [180,181] (with reference to the number of stages) in a vacuum and at atmospheric pressure. The temperature dependence of the equilibrium vapour pressure above all possible intermediate hydrates in a given system does not always make it possible to predict the sequence of stages for given specific conditions, since the influence of kinetic factors may lead to the production of thermodynamically unstable compounds as the chief product.

To some extent, the state of the dehydrated product also depends on the external pressure. It has been shown by a complex thermal and X-ray diffraction study [182] that in the dissociation of copper sulphate pentahydrate at pressures above 15 mmHg the loss of water is synchronous with the change in crystal structure; with decrease in pressure, the rate of crystallisation differs to an increasing extent from the rate of decomposition, and the product obtained in a vacuum is amorphous towards X-rays, but crystallises with the liberation of heat on subsequent heating. The formation of a product amorphous towards X-rays on dehydration under severe conditions is fairly common, and is not observed only in substances for which the lattice remains unchanged on the removal of water, for example zeolites, or when rearrangement of the structure takes place very rapidly. In our view, this is one of the chief factors preventing the fruitful application of thermodynamic and kinetic methods to the study of dehydration, since it leads to the production of such anomalous effects as the Smith–Topley effect in macrokinetics [170] or the departure of the temperature dependence of the vapour pressure from the logarithmic law for static measurements [183]. The excess of energy of the disordered phase for various substances varies in the range 3–7 kcal mole^{-1}. It is suggested that increase in the vapour pressure of water in the gas decreases the surface energy of the amorphous phase as a consequence of adsorption, and facilitates the formation of crystallisation nuclei. The residual water of intermediate hydrates or the "anhydrous" final products stabilises the disordered state, however. This is indicated, in particular, by the fact that in a number of instances [184-186] the temperature of removal of the last traces of water coincides with the temperature of the start of crystallisation of the reaction product. In condensed phosphates, the last few tenths of a percent of terminal hydroxyl groups are held extremely firmly [187] and are not removed completely in one month at 800°, preventing further polymerisation of the phosphates or their conversion into products with a ring structure.

Moreover, the kinetic characteristics of dehydration are influenced to a considerable extent by the degree of perfection of the crystals and the presence of macro- and micro-defects on their surface. Thus the rate of propagation of the reaction zone is different for the external surface and for a freshly exposed surface of a single crystal [188].

The above brief list of the most important characteristic features of dehydration demonstrates the sensitivity of these reactions to a great variety of factors, which makes it difficult to compare the thermal stabilities even for hydrates of the same type. For the same reasons, the discussion of the problems of predicting the direction of dehydration reactions on the basis of an analysis of the state of water in the original hydrate may lead to pessimistic conclusions, particularly in relation to the kinetic parameters of the process. A large number of results show that the number of stages in the reaction very seldom coincides with the number of kinds of water in the original hydrate. The chemistry of dehydration can be predicted

fairly unambiguously for hydrated zeolites and to a lesser extent for hydrates in which the water is not present in the coordination sphere of the cation. In the decomposition of aquo-complexes, however, the direction of the change in the structure of the coordination polyhedron of the metal is almost always unknown, so that the possible composition of the dehydration product also remains indefinite. The rearrangement of the structure on the formation of an intermediate hydrate also leads to a change in the initial state of the water and this evidently casts doubt on the method sometimes used to estimate the number of forms of water in a hydrate from the number of stages in its dehydration. In these instances, water fractions which are physically completely identical are removed in stages; this is also observed in systems with low hydrate numbers [189]. This provides evidence that the disordered phases formed in the dehydration have a microcrystalline structure, since otherwise we should not expect the formation of stable intermediate hydrates with a definite composition during dehydration.

An all-round approach to the analysis of the state of water in hydrates, however, makes it possible to explain most of the observed characteristic features of dehydration, and in a number of instances to predict their development. This applies particularly to the dehydration of hydrates in which the types of water differ sharply, for example many heptahydrates, for which the water molecule which is not present in the coordination sphere of the metal is removed first [180,190]. In the complex diphosphatoaluminate anion [191], four of the ten water molecules are coordinated to the metal and six are joined to phosphate groups, and in accordance with this, six water molecules are removed in the first stage of the dehydration.

From a large number of observations, albeit often only qualitative, it follows that dehydration is reversible only in its initial stages; the removal of the last water molecules is generally difficult and is most frequently irreversible. This irreversibility is usually attributed to kinetic factors, but some results indicate that in many instances it is due to irreversible changes in the salt, undergone in the dehydration of the original hydrate. Processes involving hydrolysis by water of crystallisation are familiar for various halogen systems and some nitrates [192-195]. A characteristic feature of these reactions is that the reactivity of the water of crystallisation does not show any clearly defined specific features, since hydrolytic decomposition of the anhydrous salts under the influence of water vapour is possible at the same temperatures. In accordance with this, the extent to which these reactions take place depends on the vapour pressure of water and the corresponding hydrogen halide over the substance undergoing dehydration.

In many instances, however, extensive dehydration is accompanied by changes in the substance which do not take place or which are even thermodynamically unlikely under the given conditions in the reaction of the anhydrous compound with water. It is not always possible to obtain an anhydrous salt with stoichiometric composition by dehydrating its hydrate. Qualitative information is available on the decomposition of the complex oxo-anion in the dehydration of carbonates [196], selenites [197,198], various sulphates [199-201], oxalates [202,203], and acetates [204]. These results were obtained for substances in which decomposition of the anion leads to the formation of volatile products, so that the simplest thermogravimetric methods can be used to establish that the process takes place. The study of the state of the solid dehydration product indicates that this phenomenon is much more widespread.

Our ideas on the dehydration of phosphates have altered radically in literally the last five years. The use of infrared spectroscopy [116,205,206], chromatography [207,208], and NMR [209] for the analysis of the solid phase has established that the extensive dehydration of both acidic and normal phosphates leads to extensive changes in the anion with the production of a mixture of condensed phosphates in the solid phase while the overall composition of the product remains constant. The final formation of crystalline ortho-, pyro-, or metaphosphates with increase in temperature results from secondary processes involving the reaction of oxides with higher phosphates.

The extent to which the anion decomposes may be different, but a large number of results indicate it is constant for a given substance and is almost independent of the conditions of the reaction, particularly the external water vapour pressure. Thus as in the case of metal halides, the theories of ordinary hydrolysis are evidently not applicable to these systems.

Mechanism of Dehydration of Crystal Hydrates

The widely encountered theories of the development of the reaction zone and the mechanism of thermal dissociation do not explain the above characteristic features of the extensive dehydration of solid inorganic crystal hydrates. They can be discussed from the viewpoint of the theories, examined in the previous section, of a unique "pre-dissociation" state of water in many lower hydrates. According to this, the first stage of this intracrystalline hydrolysis should be the transfer of the hydrogen of the water to the anion and the formation and possibly the stabilisation of acidic and basic groups in the substance on heating. In fact, these groups have been detected at definite stages of the dehydration in, for example, the dehydration of magnesium sulphate [200] or thorium oxalate [203]. Experimental data on the possibility of reorientation and rotation of water molecules, the high mobility of protons in solids, and the low height of the potential barrier for the migration of a proton along an H-bond makes this conversion extremely probable. When an acid salt is dehydrated, this process may lead to the formation of appreciable quantities of free acid in the substance [208]. Thus up to 15% of free phosphoric acid has been detected in the dehydration products in separate stages of the dehydration of calcium [206] and strontium [208] hydrogen phosphates. These results indicate that the formation of linear and cyclic polyphosphates is a secondary process in the dehydration of orthophosphates.

Theories of the energetics of hydrated compounds were used by Dombrovskii [210-213] to provide a qualitative explanation for various kinetic features of dehydration. The increase in the reaction rate on the addition of proton-donating substances and its decrease by proton acceptors indicate that dehydration involves proton transfer and not electron transfer, and results from the migration of protons in the lattice and on the surface of the crystal. The reversible decrease in the intensity of ν_{OH} with increase in temperature for a number of hydrates is also related to proton delocalisation, and the activation energy for the transfer of the proton to the conductivity zone has been estimated [214] as 2 kcal mole^{-1}. Increase in temperature leads to an increase in the mobility of the water molecule [215,216] and in the concentration of free protons in the lattice; this is accompanied by an increase in the proton conductivity when the substance is heated below its decomposition temperature [217].

The subsequent stages of the dehydration lead to the separation of metal oxides and the decomposition products of the corresponding ion in the gaseous or solid states; the temperatures of this decomposition of the anion may in a number of instances be lower by hundreds of degrees than the decomposition temperature of the anhydrous substance. The concentration of metal oxide in excess may reach several percent, so that care must be taken in the use of dehydration for preparative purposes, for example to obtain anhydrous substances and to determine their thermodynamic functions, particularly if allowance is made for the fact that on further heating, the oxides may react with the normal salt to form basic compounds.

If the anhydrous salt is not sufficiently stable to heat, it is impossible to distinguish processes of extensive dehydration and dissociation. This is due primarily to the lability of the disordered dehydration products. The water-containing formations, amorphous towards X-rays, are characterised by high proton mobility even at room temperature [209]. Thus on heating, partial dehydration is accompanied by fairly rapid rearrangement of the solid phase into a new quasi-stable state with a higher thermal stability than the original state. If allowance is made for the fact that the residual water stabilises the state amorphous towards X-rays, this continuous series of changes leads to the production of a dehydration temperature range which can extend to extremely high temperatures (700 to 800°) for compounds stable to heat. This scheme is confirmed by the extremely rapid decrease in the rate of dehydration in the final stages and by the temperature dependence of the degree of dehydration [218]. As expected, the temperature coefficient of the reaction rate corresponds to the temperature coefficient of diffusion in the solid, and this casts doubt on the commonly encountered suggestion that this course of the process is due to diffusion restriction of the removal of the gaseous product. The temperature dependence of the vapour pressure is not logarithmic, however, but is close to linear; this also is not contradictory to the scheme discussed.

The estimation of the relative probability of this "intracrystalline" hydrolysis of a salt can be based on a comparison of the extents of the influence of the cation and anion on the water. In actual fact, almost all known examples of the partial decomposition or rearrangement of a complex oxo-anion on dehydration involve substances containing an anion with clearly defined proton-acceptor properties and a strongly polarising electron-accepting cation. The substances for which the temperature ranges of dehydration and subsequent dissociation of the anhydrous salt are fairly clearly distinguished are chiefly the phosphates, selenites, and tellurites of transition and light metals forming multiply-charged cations. The relative extent of this decomposition of the anion changes qualitatively in the same order as the degree of distortion of the water molecule in the hydrate. For example, in the dehydration of normal zinc phosphate [206], almost no production of poly-forms is observed, whereas they are observed in appreciable quantities for the analogous compounds of cobalt, nickel, and copper.

The possibility that reactions of this kind also take place with substances which bind water less strongly cannot be neglected, however. For example, the rate of dehydration of beryllium sulphate tetrahydrate is influenced considerably by the presence of sulphuric acid on the surface of the crystal, although the decomposition takes place according to the stoichiometric equation [219].

The introduction of theories of the change in the state of water under the influence of only the cation and anion provides a qualitative explanation for the nature of the experimentally observed effects. For quantitative conclusions this approximation in a number of instances is insufficient, and it becomes necessary to make allowance for the influence of energetically weaker interactions on the water. For transition metal salts these may be interactions of the ferromagnetic or antiferromagnetic type between the cations, leading to some rearrangement of the electronic structure of the aquo-polyhedron. Thus in the dehydration of $CuSeO_3.\frac{2}{3}H_2O$, every sixth SeO_3^{2-} anion is decomposed, with the liberation of selenium dioxide into the gaseous phase [197]. The EPR spectra show that every sixth copper ion remains relatively isolated in this hydrate [220], and the rest take part in exchange interactions of the antiferromagnetic type, as confirmed by measurement of the temperature dependence of the magnetic susceptibility. The participation of the copper ions in exchange interactions leads to a redistribution of the electron density with a decrease in the strength of the M—O bond and a corresponding decrease in the energy of the H-bond formed by the water molecules coordinated to these ions. A water molecule joined to an isolated copper ion is therefore deformed to a greater extent, and this leads to decomposition of the anion on dehydration, by the mechanism examined above. The difference in the energies of the hydrogen bonds formed by the two types of water, determined by infrared spectroscopy, is ~1.2 kcal $mole^{-1}$, in good agreement with the energy of the magnetic interactions in di- and polynuclear complexes of copper with anomalous magnetic properties. The relationship between the effective magnetic moment and the frequency of the νCuO vibrations [221] confirms that weak interactions have a significant influence on the thermal dissociation of the substances.

The material examined leads to the conclusion that many characteristic features of thermal dehydration are determined by the state of the water in the lattice of the inorganic hydrate. The relative probability of decomposition of a complex oxo-anion can be estimated from data on the degree of distortion of the water molecules under the influence of the environment. The extent of this distortion is determined by the strength of the interaction of the water molecules with the cation and anion, and depends on the polarising and electron-acceptor properties of the cation and the proton-acceptor power of the anion.

The mechanism of these processes can be explained on the basis of theories of the dynamic nature of hydrogen bonding and the partial delocalisation of the protons when the hydrate is heated.

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Kinetics and Mechanism of the Dehydration of Crystal Hydrates

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The present review considers experimental data and the results of theoretical studies of the dehydration of crystal hydrates. The data have been systematised according to the stages of the reaction in the light of modern theories of the kinetics and mechanism of chemical reactions in solids. Attention has been drawn to a number of unsolved problems. It has been shown that the dehydration of crystal hydrates may prove a convenient model system in topochemistry for the solution of these problems. The bibliography contains 102 references.

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1. INTRODUCTION

Modern theories of the mechanism and kinetics of topochemical reactions are based to a large extent on experimental studies of the dehydration of crystal hydrates, since these processes provide a convenient model system which can be used to study the regular features of an important class of topochemical thermal decomposition reactions of the type:

$$A_{(solid)} \rightarrow B_{(solid)} + C_{(gas)}.$$

Moreover, the study of these processes is of independent interest, since many dehydration reactions (for example the dehydration of gypsum, alum, and metal sulphate penta- and heptahydrates) have important applications and are used in chemical technology, the technology of building materials, the metallurgical industry, etc.

Initially, the attention of many research workers was drawn to crystal hydrates by the apparent simplicity of their decomposition. As experimental data accumulated, however, it became clear that dehydration is in fact much more complex than previously supposed, and many facts relating to its mechanism have still not been explained. For example, it is not known why in many instances dehydration, having started at some point on the surface of a crystal, continues to develop at the same point (autocatalysis of the reaction); the factors responsible for the catalysis of dehydration by various additives, including the solid product, have not been determined; the relationship between the original structure and the structure of the product has been little studied, etc. Thus new studies of the mechanism and kinetics of the thermal decomposition of crystal hydrates are urgently required.

The aim of the present review is to systematise available data on the nature of dehydration and to draw attention to some problems which are not yet fully resolved.

Modern theories of the kinetics and mechanism of chemical reactions in the solid phase[1,2] show that the processes occurring in the dehydration of crystal hydrates can be divided into three groups: 1) the production of nuclei of the reaction product (prenucleation period); 2) the formation and growth of reactive nuclei; and 3) the overall kinetics of the process and the overall mechanism of the reaction.

It is obvious that this division is to some extent arbitrary, and that in real situations these three stages are mutually related. Nevertheless, we shall use it in the present review, chiefly for convenience in the presentation of the material.

2. PERIOD PRECEDING THE FORMATION OF NUCLEI OF THE REACTION PRODUCT

The study of the processes preceding the production of observable growing nuclei of the reaction product has been the subject of a comparatively small number of papers; this is due not to lack of interest in the study of this phenomenon, but to the complexity of the investigations. Most of the published papers, therefore, are concerned with the verification of theories regarding which imperfections in the crystal are responsible for the production of nuclei.

Existing theories of nucleation[3-5] relate chiefly to the thermodynamic conditions for their production and show little relation to the physicochemical features of the crystal. Almost no experimental studies of the factors responsible for the production of nuclei have been carried out, although they are of considerable interest.

In 1954, Garner and Jennings[6] suggested that as the water is removed, the defects formed on the surface of the crystal diffuse into its volume and accumulate at dislocations. In their opinion, the aggregates of defects formed in this way might act as centres for nucleus formation. The experimental test of this theory carried out by these authors using the dehydration of chrome alum showed, however, that the rate of diffusion of defects through the crystal is too low to have any significant influence on the rate of movement of the boundary between the starting material and its solid dehydration product.

Macdonald[7] pointed out that for reversible reactions, such as dehydration, it is difficult to imagine that the reaction can begin in the interior of a crystal. Even if such an act took place, the marked hindrance of diffusion at the point of development of the reaction would finally establish an equilibrium pressure, and the reaction would stop. Thus water molecules evaporating from the surface

at the points where they are least firmly bound to the crystal (point defects, impurities, dislocations, etc.) will form vacancies. The formation of nuclei in this instance will take place as a result of the migration of water molecules over the surface and their volatilisation at the points where vacancies were formed in the earlier stages.

The influence of dislocations on dehydration has been studied by many workers. As a result of such studies, Thomas and coworkers[8-10] concluded that if dislocations do have an influence on the dehydration of $NiSO_4.7H_2O$, they do so only in the earliest stages of the reaction. These early stages are naturally of particular interest in investigating the factors responsible for the production of nuclei, but it has not been possible to detect any significant correspondence between the points of emergence of the dislocations on the surface of a crystal and the points at which decomposition nuclei appear[8-11]. Moreover, it should also be noted that even if such a correlation were established, it would not provide an unambiguous answer to the question of whether the dislocations are themselves responsible for the production of nuclei, since dislocation pits in most instances consist of other point defects, impurity centres, etc.

Nevertheless, a relationship between the nuclei and the various imperfections in a crystal apparently does exist. This is indicated by experiments on the dehydration of $NiSO_4.7H_2O$,[12] in which a marked scatter was observed in the times at which the first nucleus appeared. Under the given conditions, in one of the experiments, the first nucleus (which usually appeared during the first hour) appeared only 495 min after the start of dehydration in a high vacuum. In another experiment, no nuclei appeared even 32 h after the start of the observations. On the other hand, if the surface of carefully prepared copper sulphate pentahydrate crystals is rubbed with a crystal of the monohydrate of the same salt, nuclei appear immediately in large quantities over the whole of the treated surface[13].

These few papers apparently contain all the available information which might provide an answer to the problem of the factors responsible for the production of nuclei. There is as yet insufficient experimental material to make it possible to relate the production of nuclei unambiguously to specific properties of a crystal and to predict the law governing the time dependence of the formation of nuclei.

3. KINETICS OF THE FORMATION AND GROWTH OF NUCLEI

The regular kinetic features of the appearance and growth of nuclei of the reaction product have been studied to a greater extent than the factors responsible for their formation. After the existence of nuclei had been clearly established, it was suggested that the induction period which is always observed in the dehydration of freshly prepared crystal hydrates is due chiefly to the anomalously slow rate of growth of the nuclei in the initial stages of the reactions[14,15].

To verify this theory, the rate of increase in the linear dimensions of the nuclei on $CuSO_4.5H_2O$ and $NiSO_4.7H_2O$ was measured[12,16]. It was found to be constant and approximately equal to the rate of propagation of the surface of separation, calculated from kinetic measurements of the loss in weight using the equations for a compressed parallelepiped (see below, section 5). The nuclei grew at a constant rate, however, only when the dimensions reached values of $(2-5) \times 10^{-3}$ cm. An analogous picture was observed in the study of chrome alum. In this instance, two kinds of nucleus were observed, each of which had its own constant rate of growth[17]. An induction period was also observed in this instance[18]. Table 1, taken from the paper of Cooper and Garner[17], gives data on the rates of growth of nuclei at different temperatures.

Table 1.

Temperature, °C	Rate of growth of nuclei $\times 10^6$, cm s^{-1}
35	8.64—8.89
30	6.04—5.85
25	4.03—3.84
20	2.22
15	1.20—1.11

It would be of interest to determine whether the nuclei grow into the interior of the crystal at the same rate or whether they have a planar shape and grow only over the surface of the crystal. From the kinetic viewpoint these two situations should differ fundamentally[2]. To resolve this problem for the dehydration of chrome alum, the extent of the development of nuclei was observed in a direction perpendicular to the surface, by cleaving the crystal and measuring directly the depth of penetration of the nuclei in partly dehydrated crystals. Two of these experiments on the dehydration of chrome alum at 30° gave rates equal to 7.8×10^{-6} cm s^{-1} and 5.9×10^{-6} cm s^{-1}, which agree with the values obtained by following their development over the surface (compare the data in Table 1). These results indicate that in some systems the rates of growth of the nuclei in directions normal to and parallel to the surface are equal.

In a study of the dehydration of potassium hydrogen oxalate hemihydrate, Hume and Colvin[19] observed the interesting phenomenon of an arrest in the movement of the surface of separation; this could not be explained at the time. In their experiments, the nuclei of the product grew at a constant rate until they reached a certain size, after which growth stopped. After 5–10 min, growth of the nuclei began again, and the rate of growth was equal to that before the arrest.

A constant rate of growth of the nuclei has been observed in almost all studies of the decomposition of crystals. The kinetics of the growth of nuclei is thus described by a linear function of time, beginning from dimensions of $\sim 10^{-3}$ cm.

It was noted above[12] that a marked scatter is observed in the times at which the first nucleus appears on different single crystals of the same substance. Despite this feature, however, the curves obtained by plotting the number of nuclei against time are smooth (Fig. 1). These curves are described to a high degree of accuracy by the equation

$$\lg N = k \lg (t - t_i),$$

where t_i is the time at which the first nucleus appears. The existence of this relationship suggests that although the appearance of the first nucleus is apparently a random process, depending on a large number of factors, the crystal apparently subsequently undergoes irreversible changes which predetermine the times at which the second, third, etc. nuclei appear. In other words, the

time at which the $(n + 1)$th nucleus appears is determined unambiguously by the presence of the n nuclei previously formed on the surface of the crystal.

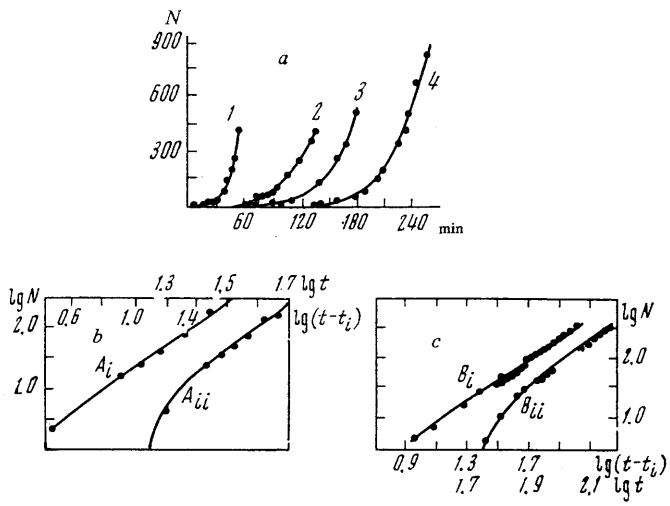

Figure 1. Time dependence of the number of nuclei at different temperatures: 1) 22°; 2) 15°; 3) 8°; 4) 1° (a), and the same curves on logarithmic coordinates: A_i, B_i—plots of $\lg N$ against $\lg(t - t_i)$ (b); A_{ii}, B_{ii}—plots of $\lg N$ against $\lg t$ (c).

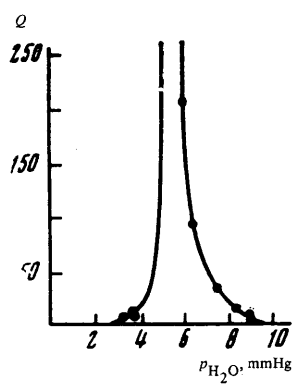

Figure 2. Dependence of the ratio of the maximal rate of formation of nuclei at a given water vapour pressure to the rate of nucleus formation in a vacuum (Q) on the water vapour pressure.

The presence of water vapour alters the rate of formation of nuclei on different crystal hydrates in different ways. If a crystal is treated with water vapour after it has been kept for some time in a vacuum, the rate of nucleus formation at first increases, and then decreases, passing through a maximum. This has been observed for $KCr(SO_4)_2.24H_2O$, $NH_4Cr(SO_4)_2.24H_2O$, and $CuSO_4.5H_2O$.[6] All these hydrates showed a sharp increase in the number of nuclei when the vessel was evacuated again. This effect has not been explained, although it is of undoubted interest. It is difficult to relate it to the blocking action of water vapour on the crystal surface, if we consider the nature of the relationship between the water vapour pressure and the ratio of the maximal rate at a given water vapour pressure to the rate of nucleus formation in a vacuum, given in Fig. 2 for the example of chrome alum. In contrast to the situation for chrome alum, the rate of nucleus formation in the dehydration of, for example, potassium aluminium alum is almost independent of the water vapour pressure in the space surrounding the crystal.

The influence of water vapour on the rate of movement of the surface of separation or, which is the same thing, on the rate of increase in the linear dimensions of the nuclei will be discussed below.

4. INFLUENCE OF VARIOUS FACTORS ON THE OVERALL KINETICS OF DEHYDRATION

In the kinetic approach to the study of solid-phase reactions, the degree of transformation of the substance (from the loss in weight or liberation of gas) during decomposition is usually measured. The curves obtained in this way are integral with respect to all parameters except time. More complete studies of reactions of this type have shown that the rate of dehydration depends markedly on a large number of factors. Some of these factors are structural (the dependence of the rate on the crystal habit, the degree of dispersion, the defect character of the lattice, etc.), and their influence on the decomposition has been described[20,21]. Another group of factors which must be taken into account in the study of the kinetics of the decomposition of solids is directly related to the general regular features of solid-phase reactions. In the present section, we shall examine these features as they apply to the dehydration of crystal hydrates.

Self-cooling. All crystal hydrates which have been studied lose water in a markedly endothermic process. As a consequence, on dehydration in a vacuum, when heat exchange between the specimen and the thermostat takes place chiefly by radiation, the temperature at which the removal of water takes place may generally speaking not be equal to the temperature of the thermostat. This feature has been pointed out by many workers. The effect has been described as self-cooling, and calculations based on the theory of black-body radiation have been proposed to take account of it. For example, in the dehydration of $CuSO_4.5H_2O$, Smith and Topley[22] suggested that the temperature of the crystal be calculated by means of the expression:

$$\lambda\left(-\frac{dm}{dt}\right) = S \cdot 1.38 \cdot 10^{-12}[T^4 - T'^4]$$

which allows for the physical characteristics of the crystals. Here λ is the heat of the reaction, $(-dm/dt)$ the mass rate of the reaction, S the external surface area of the specimen, and T and T' the temperatures of the thermostat and the specimen respectively.

An analogous equation was used by Cooper and Garner[17] in a study of the dehydration of alum:

$$\lambda\delta\Delta = k\Delta_0[T^4 - T'^4]$$

where k is Planck's constant, Δ_0 the initial surface area from which radiation takes place, Δ the surface of separation at a given moment of time, and δ the reaction rate

in g $cm^{-2}s^{-1}$. The self-cooling effect is not small enough to be neglected without distorting the true decomposition picture. The magnitude of this effect, calculated from the equation for chrome alum[17], is given in Table 2.

Table 2.

Cooling Δt, deg	Temperature of thermostat, °C
11.8	35
8.8	30
6.2	25
4.1	20
2.3	15

The results show that even at 15°, the extent of the self-cooling is much greater than the generally accepted limits of temperature stability in an isothermal process. Neglect of this effect may lead to significant errors in the determination of the kinetic parameters of a reaction.

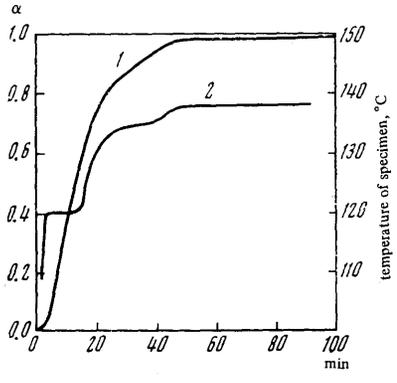

Figure 3. Simultaneous change in the loss in weight (1) and temperature (2) on the dehydration of $CaSO_4.2H_2O$ (temperature of thermostat 138°).

The question of the true conditions under which a reaction takes place naturally requires the most thorough analysis. For this purpose, experiments have been carried out in which the temperature of a specimen and its degree of transformation were recorded simultaneously[23,24]. An example of the results is given in Fig. 3. The simultaneous recording of the temperature and the degree of decomposition was carried out for the dehydration of $CaSO_4.2H_2O$. A noteworthy feature is that the temperature of the thermostat (138°) was not attained even as $\alpha \to 1$. Most of the specimen (see Figure) decomposed at an almost constant rate at ~ 120°. In this instance, equalisation of the thermal fluxes—the rate of supply of heat from outside and the rate of absorption of heat in the reaction—apparently took place. This conclusion appears the more correct since the reaction takes place at the surface of separation between the original hydrate and its decomposition product, so that heat exchange takes place through a surface which is also the reaction zone.

In this example, the dehydration of gypsum was carried out at a water vapour pressure equal to 200 mmHg. Despite the presence of a gaseous atmosphere facilitating heat exchange between the specimen and the thermostat, however, the effects of self-cooling were significant in this instance also. There thus appears to be little justification for the assertion[22] that in a gaseous environment the effect of self-cooling can be neglected.

In most instances, the curves for the topochemical decomposition of solids are S-shaped[1]. The latest studies[25,26] apparently prove that for reactions with marked endothermicity, such as the dehydration of crystal hydrates, the magnitude of the induction period on the $\alpha(t)$ curves depends to a large extent on the conditions of heating of the crystals.

Special mention must be made of the determination of the rate of dehydration from the rate of movement of the boundary of separation between the phases. In most instances this has been determined from some kinetic equation for a fixed value of α and has been related to a temperature calculated for the given value of α with allowance for the effect of self-cooling. This determination is correct, however, only if quasi-steady-state conditions obtain for the process. In other words, the change ΔT in the temperature of the specimen within a certain small time interval should be sufficiently small compared with the corresponding change $\Delta\alpha$ in the degree of transformation of the specimen during the same time interval:

$$\frac{\Delta T}{T} \ll \frac{\Delta\alpha}{\alpha}$$

where T and α relate to the middle of the time interval. If this condition is not observed, thermographic conditions will be established, so that the values of the kinetic parameters will differ from those obtained under isothermal conditions[26,27].

Influence of the gaseous atmosphere. The gaseous atmosphere in which the dehydration of crystals takes place may be inert or contain water vapour. Direct experiments have established that an inert atmosphere, up to pressures of 3–4 mmHg, has no significant influence on the rate of dehydration[28]. Above this pressure, diffusion control begins to have an effect, and perturbations associated with the presence of the inert atmosphere in the system become significant. It is very difficult to establish the nature of this influence, since it is superimposed on other effects and cannot be isolated in pure form.

Under dynamic conditions, the extent of the influence of an inert atmosphere depends on the rate of gas flow in the reaction zone. This problem has not been studied systematically, although there are indications that the rate of dehydration increases with increase in the rate of gas flow[29-31].

The presence of water vapour in the reaction zone influences the observed rate of dehydration. This is observed first because the rate of dehydration represents the difference between the actual rates of the forward dissociation and back reactions, and secondly because these opposed rates are themselves functions of the concentration of molecules in the reaction zone. They are determined by adsorption equilibrium. The relationship between the reaction rate constant (or constants) and the partial pressure of water vapour may therefore be very complicated, and it is complicated even further by the fact that water vapour may have a direct catalytic effect on the dehydration and also on the subsequent crystallisation of the product.

Topley and Smith[32], and Volmer and Seydel[33], in studies of the dehydration kinetics of manganese oxalate dihydrate, observed a complex relationship between the rate constant and the partial pressure of water in the reaction system, characterised by the presence of a maximum and a minimum on the plot of rate against H_2O pressure. Other crystal hydrates usually showed only a smooth decrease in rate with increase in pressure[34].

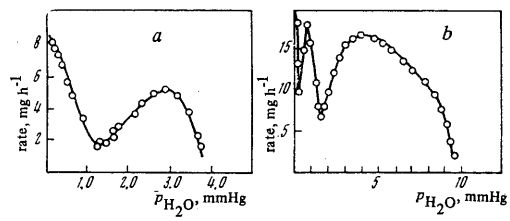

Figure 4. Dependence of the rate of dehydration on the water vapour pressure for $MnSO_4.4H_2O$ (a) and $ZnSO_4.7H_2O$ (b).

For a long time, manganese oxalate was regarded as unique in this respect. A systematic study of the phenomenon showed, however, that with increase in the water vapour pressure, most crystal hydrates behave in approximately the same way as manganese oxalate, and in some instances in even more complex fashion[35-37]. The relationships for the crystal hydrates $MgSO_4.4H_2O$ and $ZnSO_4.7H_2O$ are given in Fig. 4. For zinc sulphate, the rate of dehydration passes through two minima and two maxima with increase in the water vapour pressure, whereas magnesium sulphate tetrahydrate shows approximately the same behaviour as manganese oxalate.

A study[37] of the dehydration of various crystal hydrates at a fixed water vapour pressure in the surrounding atmosphere showed that at a certain pressure after the initial act of nucleus formation the reaction stopped completely (Fig. 5).

It is difficult to find an unambiguous interpretation of this complex behaviour of crystal hydrates on dehydration in the presence of water vapour. The shape of the curves obtained by plotting rate against pressure is usually attributed to competition between the accelerating action of water on the crystallisation of the product and the retarding action on the movement of water through the layer of product into the surrounding space[34,35]. In some instances the phenomena associated with the presence of water in the reaction zone are attributed to the formation of porous structures in the decomposition zone[38]. The difficulty of finding an explanation is due chiefly to the lack of experimental data on the adsorption equilibrium of water during the decomposition.

The existence of gaseous catalysis has been verified experimentally[39] for $CuSO_4.5H_2O$. Study of the dehydration in a stream of hydrogen in the presence of small quantities of water and HCl showed that the reaction rate is increased considerably (by a factor of 5–7). Analysis of the partly decomposed crystals showed that HCl is adsorbed by the surface of the crystals. These experiments demonstrate again the need for a study of the phenomena of adsorption and desorption of water by the surface of crystal hydrates during their decomposition.

The "impedance" of the layer of product. As the reaction develops into the interior of a crystal, the layer of product may finally become so thick that diffusion controls the removal of water molecules into the surrounding space from the surface of separation of the phases, which is also the place where the reaction is proceeding. This effect has been detected by many authors[22,28,39,40] in the study of dehydration, and has been called "impedance".

The magnitude of the impedance effect is measured as the difference between the observed rate of movement of the surface of separation into the interior of the crystal for a given layer thickness and the corresponding rate for zero thickness. Since the rate of movement of the surface of separation at zero layer thickness cannot be measured directly, it is found by extrapolation to zero layer thickness[41]. Strictly speaking, this extrapolation should be not to zero thickness but to the thickness corresponding to the maximal rate of movement of the surface of separation, since in the initial period after their production, the nuclei grow at an anomalously slow rate. This applies equally to the development of the reaction zone into the interior of the crystal in the initial stages of the reaction.

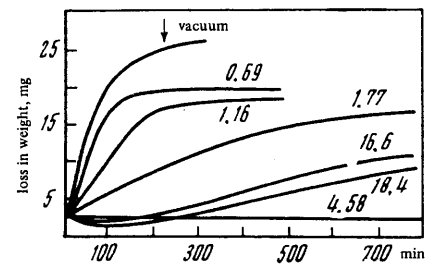

Figure 5. Dehydration curves for $MgSO_4.7H_2O$ at various water vapour pressures (given by the figures next to the curves). Decomposition does not take place at p_{H_2O} = 4.58 mmHg.

Despite the importance of an understanding of the phenomenon of impedance in the study of the kinetics and mechanism of dehydration, there is still lack of agreement on this subject. Taylor and Taylor[42] found that the product obtained in a comparatively thin layer has a high porosity, so that it could hardly have had a significant influence on the reaction rate. Nevertheless, they do not reject the possibility that water molecules adsorbed on the surface of the product may hinder considerably the removal of water from the reaction zone into the free volume. This may in turn be responsible for an increase in the water vapour pressure in the reaction zone and hence a decrease in the reaction rate.

Generally speaking, all explanations put forward for the origin of the impedance reduce in one way or another to a displacement of the equilibrium at the surface of separation between the starting material and the product. From the kinetic viewpoint, this question is probably closely related to the range—kinetic or diffusion—in which the reaction takes place.

We noted above that theories of the competition between the catalytic action of water on the crystallisation of the product and the retarding influence (as a consequence of diffusion) of the layer of product have been used to explain the "strange" dependence of the rate of dehydration on the water vapour pressure. From this it may be concluded that the diffusion and adsorption properties of the product cannot be neglected, but the extent to which they are significant is not yet known.

The phenomenon of impedance has also been used many times to explain the familiar so-called autocatalytic course of the curves for solid-phase decomposition (see Vorontsov's review[43]). The impedance effect possibly does not always apply, as far as can be judged from experiments on the measurement of the rate of growth of nuclei into the interior of a crystal[18]. Finally, it should be noted that for strongly endothermic dehydration, a decrease in the rate of propagation may also be due to a change (decrease) in the flow of heat supplied to the reaction zone as a consequence of differences in the thermal conductivity of the starting material and the product. An amorphous product in this instance may even act as a heat insulator.

The above examination shows that impedance is a complex phenomenon. Despite its small magnitude, neglect of the effect in the study of the dehydration of crystal hydrates may lead to significant errors in kinetic determination and to incorrect interpretation of reaction mechanisms.

Formation of Labile Phases and Intermediate Liquid Hydrates

Partington in 1911 suggested[44], and a large number of subsequent studies subsequently proved[33,39,45,46], that the dehydration of crystal hydrates, particularly at low partial water vapour pressures, gives an intermediate product amorphous towards X-rays. The absence of lines on the X-ray diffraction patterns for specimens dehydrated in a vacuum can be due entirely to the true amorphous character of this product. On the other hand, as pointed out by Roginskii[47], the product formed on dehydration in a vacuum may consist of a disordered assembly of very fine crystals (up to 10^{-7} cm in cross-section), and this would also lead to the absence of lines on the X-ray diffraction patterns, because of the insufficient sensitivity of the apparatus. Subsequent electron-microscope studies by Roginskii and coworkers[48] showed, however, that despite marked dehydration of $Na_2SO_4.10H_2O$ and $MgSO_4.7H_2O$ crystals at a pressure of 10^{-4} mmHg, the external form of the crystal and its ultramicroscopic structure initially remain unchanged.

It was only on prolonged irradiation that cavities were produced on the surface and a tendency for new cavities to be produced close to those previously formed (localisation) was observed. Some time after the start of the appearance of the cavities, the crystal consisted of a fine network of solid material surrounding the cavities produced, that is a skeletal structure appeared, indicating an amorphous intermediate product, rather than a submicrocrystalline product.

The problem of the formation of intermediate unstable phases has been most fully studied by Khomyakov[49] and Frost and coworkers[50]. Thus Khomyakov observed that partly dehydrated crystals of $CuSO_4.5H_2O$, immediately after the experiment was stopped, liberated a quantity of heat (4824 cal $mole^{-1}$) approximately equal to the difference between the heats of the dehydration of the freshly prepared and partly decomposed $CuSO_4.5H_2O$ crystals. According to Thomsen[51], these heats are −17334 cal $mole^{-1}$ and −12519 cal $mole^{-1}$ respectively, and their difference does indeed differ little from the heat determined by Khomyakov. This effect was not observed on repeated dehydration.

Frost carried out analogous experiments and followed the quantitative change in the amorphous product during the reaction at different water vapour pressures. He found that after the removal of water, the product remaining liberated heat for a definite time interval. This thermal effect was attributed to rearrangement of the structure from an amorphous state to a crystalline state corresponding to the structure of the product. Thus it was found that the intermediate amorphous products are rich in energy, and are metastable phases. The values of the heats of the transformation from the intermediate state to the final state, taken from a paper by Frost and coworkers[38], are given below:

$ZnSO_4.H_2O$(amorphous) → $ZnSO_4.H_2O$(crystalline); ΔH = −7600 cal $mole^{-1}$
$CuSO_4.H_2O$(amorphous) → $CuSO_4.H_2O$(crystalline); ΔH = −7170 cal $mole^{-1}$
$MgSO_4.H_2O$(amorphous) → $MgSO_4.H_2O$(crystalline); ΔH = −6550 cal $mole^{-1}$
$NiSO_4.H_2O$(amorphous) → $NiSO_4.H_2O$(crystalline); ΔH = −4720 cal $mole^{-1}$
$CoCl_2.H_2O$(amorphous) → $CoCl_2.H_2O$(crystalline); ΔH = −1390 cal $mole^{-1}$

(it is indicated in parentheses whether the compound is in the amorphous or crystalline state).

It was found that from a certain pressure, almost no amorphous product is produced on dehydration in water vapour. The values of these critical pressures are very close to those corresponding to the minimal rate on the plots of the rate of dehydration against H_2O pressure. Not all of the crystal hydrates form an amorphous intermediate product even on dehydration in a vacuum. For example, salts such as $NiNO_3.6H_2O$, $Mg(NO_3)_2.6H_2O$, and chrome alum, on dehydration in a vacuum, form a crystalline lower hydrate with an extensive internal surface due to formation of capillaries, whereas dehydration in the presence of water vapour at ordinary pressures, as with the other crystal hydrates, gives normal crystalline aggregates. An attempt to classify hydrates according to this characteristic was made in a review by Dell and Wheeler[52].

All the phenomena described above can be explained as follows: within a certain temperature range, the lattice framework is preserved even after the crystal (for example $CuSO_4.5H_2O$) has lost four water molecules. This also favours the flow of the water diffusing through the layer of product. The lattice framework is preserved until nuclei of the new stable phase appear. The production of these nuclei depends on the decrease in the flow of water through the layer of monohydrate and also on the temperature and surrounding pressure of water vapour.

Studies of the nature of the amorphous product and its role in the decomposition of crystal hydrates are of particular interest in relation to theories of the localisation of the reaction in a narrow zone at the surface of separation between the starting material and the product. Since the specific volumes of the original hydrate and final product are not always the same, the layer of amorphous product then will always compensate the structural stresses and ensure the structural change from the starting material to the reaction product.

The existence of intermediate lower hydrates has been established from vapour pressure isotherms[53,54], and their formation on thermal dehydration has been detected

in a large number of thermographic [55,56] and X-ray diffraction [57-70] studies.

The importance of thermographic investigations in the study of the kinetics of dehydration should not be overemphasised. Reisman and Karlak [58] showed that small changes in the conditions under which thermographic experiments are carried out produce a marked scatter in the experimental results obtained. This is in fact the reason for the frequently encountered lack of agreement in the thermographic results obtained by different authors. Thermographic studies are of greatest value in the discussion of the mechanisms of the dehydration of crystal hydrates, when, as we shall subsequently see, it is absolutely essential to allow for the formation of intermediate lower hydrates during the decomposition.

The intermediate hydrates are extremely unstable, and this explains the almost complete lack of information on the kinetics of their dehydration in pure form. Nevertheless, Cooper and coworkers [71] were able to study the kinetics of the dehydration of copper sulphate trihydrate. The kinetic curve which they obtained differs little from the usual curve for solid-phase decomposition.

Influence of the addition of the solid product. Since dehydration takes place at the surface of separation between the original hydrate and its product (usually a lower hydrate), the possibility of direct contact between the starting material and the amorphous or crystalline lower hydrate cannot be excluded. In this connection, the possible catalysis of the dehydration by solid decomposition products is of undoubted interest. Studies of this kind have been made by Rae [14], Skramovsky [55,72], and Vallet [30], and later by Sakovich [73] in an examination of the decomposition of hydrated salts of copper, cobalt, and magnesium.

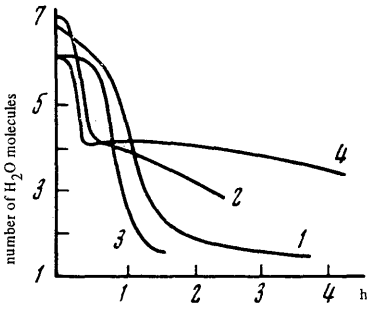

Figure 6. Dehydration curves for $CoSO_4.7H_2O$ and $CoSO_4.6H_2O$ in the pure state and with the addition of anhydrous salt: 1) $CoSO_4.7H_2O$; 2) $CoSO_4.7H_2O$ + 5% $CoSO_4$; 3) $CoSO_4.6H_2O$; 4) $CoSO_4.6H_2O$ + 5% $CoSO_4$.

These studies showed that the addition of a lower hydrate increases the stability of that intermediate hydrate and at the same time increases the rate of the stage leading to the formation of the salt added. This is illustrated by the curves, taken from Feitknecht's paper [69], for the dehydration of cobalt sulphate hexa- and heptahydrates containing 5% of the anhydrous salt (Fig. 6). According to Sakovich [73], the observed accelerating action of the added product on the dehydration of crystal hydrates is due to their interaction at the points of contact with the surface layer of the starting material. This interaction is due to the affinity of the reaction product for water vapour, the pressure of which is always greater above the original hydrates than above their dehydration products. Introduction of the additive produces regions of the reaction zone are produced even at room temperature, and this apparently leads to an increase in the rate of the process. This explanation is supported by a comparison of these experiments with Garner's observations of the formation of nuclei on the surface of copper sulphate pentahydrate treated with the monohydrate of the same salt, when nuclei appeared almost instantaneously.

The partial stabilisation of the intermediate hydrates added to the starting material, observed by Vallet [30], can be attributed rather to a simple increase in the quantity of intermediate phase.

The problem of the mechanism of the accelerating action of the added product is closely related to a more general problem in the chemistry of solids—the mechanism of the influence of various heterogeneous additives on solid-phase reactions. This problem is at present far from being solved, despite its obvious importance for topochemistry.

5. THEORETICAL DESCRIPTION OF THE KINETICS OF DEHYDRATION

The problem of the satisfactory description of the kinetics of dehydration has faced research workers since the earliest studies of these processes, and cannot be regarded as fully resolved. The first attempts to provide a quantitative description of dehydration were based, strangely enough, on the idea of autocatalysis [74,75]—an idea which has in fact been revived recently [76]. Historically, however, the development of modern topokinetics originated in the successful application of Langmuir's idea [77] that the surface of separation between the phases is the point at which reaction takes place to the description of the kinetics of decomposition of various hydrates [41].

In fact, the possibility of describing the kinetics on the basis of simple geometric representations of the form of nuclei and their number appeared very attractive. This simplicity proved to be deceptive, however. Hume and coworkers [78] examined three examples of topochemistry, differing radically in their mode of description. In the first, nuclei are formed immediately and cover the surface of the particle almost completely. The process is then described by the equation of a "contracting" sphere, parallelepiped, etc., depending on the shape of the crystal. In the other extreme case, when the frequency of formation of the nuclei is low compared with the rate of movement of the surface between the phases, the reaction obeys a unimolecular law, as for example in the conversion of monoclinic into orthorhombic sulphur. The example of greatest interest for topochemistry is the intermediate situation, where the ratio of the rate of production of nuclei to the rate of movement of the surface between the phases is such that at sufficiently small degrees of conversion, each particle will contain at least one nucleus. In this instance the reaction rate will pass through a maximum and an S-shaped curve will result. It is this third possibility which is usually realised in the decomposition of crystal hydrates.

One of the first equations used for the description of the kinetics of dehydration was an equation in which the

mass rate, divided by the original surface area of the crystal[22], was taken as the rate constant. Subsequently transformed into the equation of a compressed parallelepiped, it was used successfully by Hume and Colvin[28] to describe the kinetics of the dehydration of copper sulphate pentahydrate. A number of other equations[29,40,78], some simpler, some more complex, including the Polanyi–Wigner equation, have been applied to various reactions, with varying success.

With the development of the formal kinetics of reactions in the solid phase, more complex equations based on various physical models of the reactions have appeared. Thus a more important problem, in our view, is the applicability of the kinetic method of analysis to the determination of the mechanism of a reaction, or in other words the problem of the correspondence between the model used in the derivation of the kinetic equation and the real physical picture of the decomposition. Molony and Ridge[80], in a study of the kinetics of the dehydration of calcium sulphate dihydrate, found that the experimental results are described equally effectively by the equations

$$A - B(1-\alpha)^{1/3} = kt$$

and

$$A - B(1-\alpha)^{1/2} = kt$$

(naturally, with different constants). The correlation coefficients calculated for the two equations were −0.969 and −0.983 respectively, that is they almost coincided. In the opinion of these authors[80], this result provides an example of a situation in which applying the equations of formal topokinetics in itself cannot provide as a criterion for the unambiguous selection of one of two or more proposed reaction mechanisms. This conclusion applies not only to dehydration, but to topochemical reactions in general, and forms the basis of a contradiction between a real process and the method used to describe it. The efforts of many research workers have been directed towards the elimination of this contradiction. Some have adopted the approach of increasing the accuracy of familiar equations by including the distribution of particle sizes[81,82], by making allowance for mass and heat transfer in the crystal[83], by using the activated-complex theory[84], etc. Others consider that there is no point in trying to describe the entire decomposition curve by means of a single equation, since different stages of the process correspond to different mechanisms[85]. Despite all efforts in the field of the kinetics of dehydration, however, two of the anomalies noted by Garner[86] as early as 1938 have not yet been explained satisfactorily.

a. The reaction rate in a large number of examples of the decomposition of solids, including the decomposition of crystal hydrates, increases as a very high power of time. The exponent is much greater than might have been expected from simple theoretical considerations based on the theories of the boundary of separation.

b. The reaction rate in the initial stage is proportional to the mass of sample decomposed, and not its area.

It may therefore be definitely stated that the problem of an adequate description of dehydration is generally speaking a part of topokinetics, which is at present largely unsolved.

6. MECHANISM OF DEHYDRATION

We noted above that the dehydration of crystal hydrates involves the formation of intermediate amorphous or crystalline lower hydrates. This feature determines the possible decomposition schemes.

The transitions between the different stages of the reaction have been studied most fully for $CuSO_4.5H_2O$ and $CaSO_4.2H_2O$. When the reaction takes place in a single stage, for example from copper sulphate pentahydrate to the monohydrate, the reaction scheme can be represented in the form shown in Fig. 7.[17,40,87]

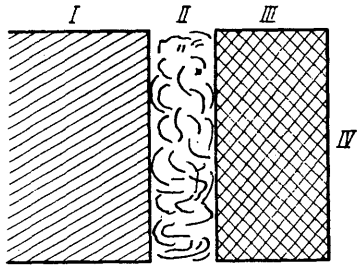

Figure 7. Dehydration of crystal hydrates: I) reagent; II) intermediate layer; III) product, undergoing slight recrystallisation; IV) open space (vacuum or water vapour).

Garner and Pike[88], referring to data on the structure of $CuSO_4.5H_2O$,[89] point out that dehydration in a vacuum, which always gives the monohydrate, corresponds to the loss of four water molecules coordinated to the copper atom. The fifth water molecule is not coordinated, and the strength of its bonding is apparently different. Their non-equivalence in the $CuSO_4.5H_2O$ lattice is also indicated by experiments on isotopic exchange[90].

In the presence of water vapour, the decomposition is complicated considerably, chiefly because of the production of the trihydrate as an intermediate compound. According to Colvin and Hume[34], the overall scheme for the dehydration of copper sulphate pentahydrate can be represented in the form:

$$CuSO_4 \cdot 5H_2O \rightarrow \underset{\text{amorphous}}{CuSO_4 \cdot 3H_2O} \begin{cases} \xrightarrow{I} CuSO_4 \cdot H_2O + 2H_2O \\ \xrightarrow{II} \underset{\text{crystalline}}{CuSO_4 \cdot 3H_2O} \xrightarrow{III} CuSO_4 \cdot H_2O + 2H_2O \end{cases}$$

The amorphous trihydrate formed in the decomposition, when treated in a vacuum, immediately loses two more water molecules (route I) and is converted into the monohydrate. The presence of water vapour may direct the reaction along route II → III, since water facilitates the crystallisation of the amorphous trihydrate.

The activation energy for the dehydration of $CuSO_4.5H_2O$ and $CuSO_4.3H_2O$ has the values E_1 = 16–18 kcal mole^{-1} [17] and E_2 = 15.6 kcal mole^{-1} [71] respectively, that is the difference is not large.

The various stages in the dehydration of $CaSO_4.2H_2O$ are given in the following scheme[91]:

$CaSO_4 \cdot 2H_2O$ (monoclinic)

Dehydration, possibly including topotaxy ↓ ↑ Recrystallisation without topotaxy

$CaSO_4 \cdot \frac{1}{2}H_2O$ + water (rhombohedral)

Quasi-zeolite dehydration of the lattice without recrystallisation ↓ ↑ Adsorption of water from vapour, quasi-zeolite reaction

$CaSO_4$ Soluble anhydrite.

↓

$CaSO_4$ Orthorhombic anhydrite

This compound is also of interest since the mechanism of its complete dehydration is complicated by an additional transformation between the two crystalline forms of the anhydrous salt[92].

It is impossible to give here all the crystal hydrate decomposition schemes which have been proposed: the number is greater than the number of hydrates. The examples given show sufficiently clearly the importance of making allowance for the stepwise character of the overall process and the formation of various intermediate compounds in the description of dehydration.

7. NEED FOR A STUDY OF THE LOCALISATION OF THE DEHYDRATION OF CRYSTAL HYDRATES

We have already mentioned various unsolved problems in the chemistry of crystal hydrates. In the present section we would like to consider particularly the problem of the localisation and auto-localisation of the process. As already mentioned in the introduction, we are referring to the interesting property of crystal hydrates and other topochemical systems of decomposition with the formation and growth of nuclei. It is extremely important to answer the question of why this takes place and to find methods of controlling this process. The importance stems primarily from the large number of practical applications of crystal hydrates on the one hand, and also from the considerable theoretical importance of the problems of localisation in topochemistry on the other hand, since the concept of nuclei forms the chief distinguishing feature of topochemical reactions.

An example of the practical utilisation of the results of these studies is provided by the production of catalysts by the dehydration of crystal hydrates. Partly dehydrated crystal hydrates are at present used as catalysts for a large number of industrial reactions[93,94]. In this connection, the control of the formation and growth of nuclei would open up the possibility of controlling the properties of the catalysts obtained, through the directed production of the catalytically active materials. This of course is not the only field in which it is important to find ways of controlling localised processes. They are equally important in photography, metallurgy, etc.

The problem of localisation naturally is not specific for dehydration alone. It can be applied equally successfully to any solid-phase reactions involving the formation and growth of nuclei of the product. It is convenient, however, to distinguish crystal hydrates from most other similar systems since it is at present difficult to find a class of substances which have been studied in such detail. In addition to a very large number of studies of the kinetics and mechanism of the dehydration of crystal hydrates, detailed structural studies have been made[70], the infrared spectra have been studied[95,96], dehydration has been studied by NMR[97] and dielectric spectroscopy[98], and data have been obtained by isotopic substitution[99] and from proton conductivity in crystal hydrates[100] and from the influence of ultrasonic radiation on the dehydration[101]; the absolute velocities of water molecules leaving a crystal surface on dehydration have also been measured[102]. These studies have been so extensive and varied because crystal hydrates provide one of the best model systems in topochemistry, by means of which it may be possible to come close to a solution of the problem of localisation; the importance of this problem in theory and practice has already been emphasised.

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Oxygen Compounds of Iron(VI, V, IV)

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Published information on the chemistry of oxygen compounds of iron—the ferrates(VI, V, IV)—has been reviewed briefly. The methods of preparation, chemical properties, thermal decomposition in air and in O_2, the kinetics and mechanism of decomposition in solution, methods of analysis, structural, spectroscopic, and magnetic studies, the nature of the covalent bonding, and the uses of the ferrates(VI, V, IV) have been described. The bibliography contains 108 references.

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I. FERRATES(VI)

Compounds of sexavalent iron in the form of salts of ferric acid ($MFeO_4$) have been known for a long time [1,2]. About twenty to thirty of these compounds have now been prepared; only the ferrates(VI) of potassium, rubidium, caesium, strontium, and barium have been obtained in the pure crystalline state, and the others are known in solution or have been isolated from solution in the solid state but with a considerable amount of impurity. The difficulties associated with the preparation of pure crystalline ferrates(VI) are due chiefly to their instability.

Preparation. The alkali metal ferrates(VI) can be prepared by the following methods: 1) by heating to red heat a mixture of iron filings and potassium nitrate or a mixture of iron oxide, alkali, and potassium nitrate [1-3]; 2) by oxidising, by heating in a stream of O_2, solid phases consisting of an alkali metal oxide, peroxide, or hydroxide with iron (or its oxide) in the ratio $M_{alk}:Fe = 2:1$; [4-8] 3) by the electrochemical dissolution of an iron anode in alkali solutions [9-12]; 4) by oxidising iron salts or the freshly prepared hydroxide with various oxidising agents (Cl_2, Br_2, NaOCl etc.) in a strongly alkaline medium [13-19]; and 5) by double decomposition [20].

Methods (1) and (2) are the simplest, but the ferrates(VI) obtained by these methods are usually contaminated by traces of the starting materials and side products of the reactions, and these cannot be removed without decomposition of the chief product. Method (3) gives only solutions of the alkali metal ferrates(VI), the concentration of which increases with increase in temperature to 50°, or with increase in the alkalinity of the solution and the current density.

Method (4), which has been used to prepare the pure crystalline ferrates(VI) of K, Rb, and Cs, is of particular interest. These ferrates have a limited solubility in saturated solutions of the corresponding alkalis. This property is used to precipitate them from solution. A product with a purity of 98–100% is obtained by recrystallising the precipitated ferrates(VI) and washing with alcohols [21]. The high solubility of Li_2FeO_4 and Na_2FeO_4 in concentrated alkalis makes it impossible to isolate them from solution in the crystalline state [22]. Solid Li and Na ferrates(VI) can be obtained by method (5), by the double decomposition of $LiClO_4$ or $NaClO_4$ with K_2FeO_4 with subsequent vacuum-drying of the filtrate [20]. The products, however, have a purity of only 15–69%. The ferrates(VI) of Na and more particularly Li decompose much more rapidly than the ferrates(VI) of the other alkali metals during preparation and purification.

As far as the alkaline earth metal ferrates(VI) are concerned, it should be noted that unlike the ferrates(VI) of Ca and Mg, the ferrates(VI) of Sr and Ba are sparingly soluble in water and are precipitated when K_2FeO_4 solution is treated with Sr or Ba nitrates, chlorides, or acetates [10, 16,23,24]. It has been possible to obtain pure crystalline $SrFeO_4$ and $BaFeO_4$† only at 0° in the complete absence of CO_2. In the moist state they decompose fairly rapidly by reacting with CO_2. [17] Solutions of Ca and Mg ferrates(VI) have been obtained by the double decomposition of Ca and Mg sulphates, carbonates, or oxalates with $SrFeO_4$. [23]

The ferrates(VI) of other metals have been obtained by double decomposition from solutions of the metal nitrates and a suspension of $BaFeO_4$ in water [25]. Solid ferrates(VI) of Pb, Cu, Ag, Hg, Al, Zn, Th, Co, Ni, Fe^{II}, and Fe^{III} have been isolated in this way. Most of these compounds decompose on drying or with a slight increase in temperature (30–40°).

Attempts to replace oxygen in ferrate(VI) by fluorine by fluorinating K_2FeO_4 [26] or a $4KO_2 + Fe_2O_3$ mixture [27] were unsuccessful.

Physicochemical properties. The dry crystalline ferrates(VI) of K, Rb, Cs, and Sr are stable in air and can be kept in closed vessels. Barium ferrate(VI) in the moist state with a water content of 4–5% is spontaneously converted into $BaFeO_3$ at room temperature [17,28]. The decomposition corresponds exactly to the equation

$$BaFeO_4 \cdot aq = BaFeO_3 \cdot aq + \frac{1}{2} O_2$$

At a moisture content of 1–2%, $BaFeO_4$ has an almost unlimited stability.

When heated, all ferrates(VI) decompose with the liberation of O_2 and the final formation of tervalent iron compounds. The decomposition of ferrates(VI) in air takes place at different temperatures: 150–400° for K_2FeO_4, 80–600° for $SrFeO_4$, and 105–800° for $BaFeO_4$. [29] The liberation of active oxygen in the thermal decomposition is not accompanied by the immediate reduction of Fe^{VI} to Fe^{III}, but involves the conversion of the ferrates(VI) through intermediate reduction states to

†$SrFeO_4$ is less stable than $BaFeO_4$. The maximal purity of Sr ferrate(VI) obtained did not exceed 95–97%.

ferrates(III).[17,30,31] For example, the decomposition of K_2FeO_4 in a stream of O_2 from 200° to 700° involves the formation of potassium ferrate(V) and ferrate(III) by the reaction:

$$2K_2FeO_4 = K_3FeO_4 + KFeO_2 + O_2$$

Above 700°, after the complete disappearance of K_2FeO_4, decomposition of K_3FeO_4 begins:

$$K_3FeO_4 = KFeO_2 + K_2O + \frac{1}{2}O_2$$

Pure $KFeO_2$ is obtained at 1000°, after the volatilisation of K_2O.

Sr and Ba ferrates(VI) decompose in a stream of O_2 as follows: at low temperatures (~200°) vigorous liberation of active oxygen takes place with the formation of ferrates(III); oxidation of Fe^{III} to Fe^{IV} begins at about 400°, reaching a maximum (~90% Fe^{IV}) at 700–900° with the formation of $SrFeO_3$ and $BaFeO_3$.[32]

The red-violet aqueous solutions of ferrates(VI) are unstable and gradually decompose according to the scheme:

$$2FeO_4^{2-} + 3H_2O = 2FeO(OH) + \frac{3}{2}O_2 + 4OH^-$$

Study of the rate of decomposition by measurement of the change in pH with time in solutions with different K_2FeO_4 concentrations[33] has shown that dilute solutions of ferrates(VI) are more stable than concentrated solutions. For example, after standing for 1 h, 0.02–0.025 M solutions still contained 89% of the FeO_4^{2-} taken initially, whereas 0.05–0.086 M solutions decomposed completely.

The decisive factors influencing the stability of ferrate(VI) solutions are temperature and alkalinity[34]. The rate of decomposition of ferrates(VI) decreases considerably at low temperatures. Thus the rate of decomposition of 0.01 M K_2FeO_4 solution at 25° is five times that at 0°. The influence of alkalinity on the decomposition of ferrate(VI) solutions is complex and depends on the magnitude of the surface area of the $Fe(OH)_3$ formed in the decomposition[35]. The properties of the latter are determined by the concentration of alkali. Thus in 10% and 40% alkali solutions the $Fe(OH)_3$ precipitate is bulky and settles very slowly. In this instance the ferrate(VI) solutions decompose rapidly. In 20% alkali solutions, in which $Fe(OH)_3$ is precipitated in a compact form and rapidly produces a binding film on the walls of the vessel, ferrate(VI) solutions decompose much more slowly.

The addition of salts to ferrate(VI) solutions influences their stabilities in different ways. Potassium periodate[37], metaphosphates, pyrophosphates, and borates[36] produce a sharp increase in their stability. The addition of alkali metal cations to a ferrate(VI) solution, on the other hand, increases the rate of decomposition in the order Li^+, Na^+, K^+, Rb^+, and Cs^+, the increase being greater, the greater the concentration of the added cation[38].

The decomposition may take place in different ways, depending on the initial ferrate(VI) concentration[39]. In dilute solutions the decomposition is homogeneous and corresponds to the kinetic equation $dx/dt = k(a-x)^2/x$. When the active form of iron hydroxide appears, the reaction rate increases and corresponds to fractional-order kinetics. In concentrated solutions (greater than 0.01 M) iron hydroxide is formed immediately on decomposition, and the reaction is heterogeneous almost from the start.

The decomposition of ferrates(VI) in highly concentrated alkali solutions is monomolecular and gives $Fe(OH)_3$ with the intermediate formation of ferrates(IV).[35,40,41] The first stage of the decomposition is characterised by the complete decolorisation of the violet ferrate(VI) solutions and the precipitation of dark-blue or black Na and K ferrates(IV) respectively. The composition of the latter has not been determined. In the second stage the unstable ferrates(IV) decompose, the decomposition being slow in concentrated alkali solutions and immediate on dilution with water.

Recent studies[42] have established that the decomposition of ferrates(VI) in alkali solutions (like the decomposition of permanganates and perrhenates) is catalysed by traces of nickel and cobalt always present in the reagents. It has been proved experimentally that the rate of decomposition of alkali ferrate solutions prepared from highly pure reagents is extremely low. On the addition of nickel or cobalt salts (10^{-6} M) the stability of these solutions decreased sharply. The influence of other salts, or of $Fe(OH)_3$, was slight, however. This specific influence of nickel and cobalt salts proves that the course of the decomposition of ferrates(VI) (like that of permanganates and perrhenates) cannot be explained by any of the mechanisms previously put forward. The reaction mechanism probably involves reduction on the surface of nickel or cobalt micelles and the reduction of their hydroxo-complexes. It is suggested[41] that the use of very pure chemical reagents in the study of oxidation may give qualitatively new results even for simple and familiar reactions.

Ferrates(VI) are powerful oxidising agents, more powerful than permanganates. Even in weakly acidic medium they decompose with the formation of Fe^{III} salts and the liberation of O_2. Mg, Al, P, and S powders react violently with solid K_2FeO_4 on heating. Ammonia is oxidised to nitrite by the action of small quantities of K_2FeO_4, and to nitrate by a large excess. Nitrites are oxidised to nitrates, bivalent manganese to quadrivalent[43], iodates to periodates[44], chromite to chromate[45], arsenite to arsenate[46], etc. Hydrogen peroxide in strongly alkaline medium reduces FeO_4^{2-} to $Fe(OH)_3$. The addition of H_2O_2 in the presence of Trilon B to a suspension of $Fe(OH)_3$ in alkali solution, however, gives ferrate(VI) solution[47,48]. The addition of Trilon B to a prepared alkaline solution of ferrate(VI) increases its rate of decomposition. The reason for the accelerating action of Trilon B on the formation of FeO_4^{2-} by the reaction with H_2O_2 has not been determined.

Organic substances, for example paper, wood, etc., are slowly oxidised by dilute ferrate(VI) solutions; sugar and egg albumin decolorise ferrate(VI) solutions rapidly[30]. Ferrates(VI) are insoluble in alcohols (except Li_2FeO_4 and Na_2FeO_4) and gradually oxidise them to aldehydes.

Ferrates(VI) are isomorphous with chromates and sulphates, and form solid solutions with them[16,49,50]. The infrared (IR) spectra of the isomorphous compounds K_2XO_4 and $BaXO_4$ (X^{VI} = S, Se, Cr, or Fe) are similar, particularly in the high-frequency range. The spectra of the solid solutions of these compounds are also similar[51].

Spectroscopic studies of ferrates(VI) have been shown that the following vibrational frequencies are characteristic of the FeO_4^{2-} ion. The infrared range (220–2000 cm^{-1}) shows an absorption band at about 800 cm^{-1}, with triplet splitting which is distinct for K_2FeO_4 and $BaFeO_4$ but much less distinct for $SrFeO_4$.[29] The visible spectra show a sharp maximum at 505 μm and two minima at 390 μm and 675 μm.[52,53] The high-frequency visible and ultra-violet spectra show a large absorption peak at 19 600 cm^{-1}, asymmetric with a shoulder at 17 800 cm^{-1}, and a small

peak at 12700 cm^{-1}. [54,55] This spectrum is similar to the spectrum of the isoelectronic ion MnO_4^{3-}. The interpretation of the electronic spectra of FeO_4^{2-} and MnO_4^{3-} on the basis of the MO method previously developed for the CrO_4^{2-} and MnO_4^{2-} ions [56] led to the conclusion that the unpaired electrons must occupy a triply degenerate orbital. The earliest measurements of the electron paramagnetic resonance (EPR) of FeO_4^{2-} and MnO_4^{3-} in alkali solutions confirmed this suggestion [57], but later measurements with single crystals of these salts led to the conclusion that the unpaired electrons occupy a doubly degenerate orbital [58].

K and Cs ferrates(VI) are paramagnetic [8]; the effective magnetic moments amount to 2.8–2.9 μ_B, corresponding to two unpaired electrons. The formation of regular tetrahedra is possible only for sp^3- or d^3s-hybridisation. According to Klemm [8], ferrates(VI) show sp^3- and not d^3s-hybridisation. This conclusion was reached by analogy with the FeO_4^{3-} ion, for which magnetic studies showed three unpaired electrons, so that d^3s-hybridisation is impossible. The interpretation of the isomeric shift in the Mössbauer spectrum of K_2FeO_4 shows, however, that the covalent contribution from the oxygen ligands is made to hybridised d^3s-orbitals of the iron [59,60].

Analyses. The familiar methods for the analysis of ferrates(VI) are based on their oxidising properties (arsenite and chromite methods) or on the instability of ferric acid H_2FeO_4 (gas-volumetric method).

The arsenite method is based on the reduction of the ferrate(VI) ion in strongly alkaline arsenite solution [46]:

$$2FeO_4^{2-} + 3AsO_3^{3-} + 11H_2O \rightarrow 2Fe(OH)_3(H_2O)_3 + 3AsO_4^{3-} + 4OH^-$$

The back titration of the excess of arsenite can be carried out with standard solutions of bromate (Methyl Orange indicator, 70–80°), cerate (phenanthroline indicator, in the cold), or permanganate (with the addition of KI). The arsenite method is recommended for the analysis of pure ferrate(VI) specimens which have not undergone decomposition and which do not contain impurities capable of oxidising arsenite.

The chromite method [45] is based on the oxidation of chromite by the ferrate(VI) ion in strongly alkaline solution according to the equation:

$$Cr(OH)_4^- + FeO_4^{2-} + 3H_2O \rightarrow Fe(OH)_3(H_2O)_3 + CrO_4^{2-} + OH^-$$

The chromate ion is titrated with a standard solution of Fe^{2+} and Na diphenylaminesulphonate indicator. The chromate method is particularly suitable for the analysis of dilute ferrate solutions. It can also be modified for insoluble ferrates(VI), with which reaction takes place only on prolonged heating (95–100°, 1 h). [24]

The gas-volumetric method [17,61] is recommended for ferrates(VI) with different degrees of purity; this method involves the decomposition of the ferrates by dilute acids, for example

$$2K_2FeO_4 + 5H_2SO_4 \rightarrow 5H_2O + 2K_2SO_4 + Fe_2(SO_4)_3 + \frac{3}{2}O_2$$

CO_2 impurity in the oxygen liberated in the analysis of specimens contaminated with carbonates is removed by absorption in KOH solution.

The reduction of ferrates(VI) by iodide ions in acid medium according to the equation $FeO_4^{2-} + 4I^- + 8H^+ \rightarrow Fe^{2+} + 4H_2O + 2I_2$ cannot give quantitative results, because of the expected reduction of Fe^{III} impurities usually present in the specimens. The iodometric method is sometimes used, however, for the determination of active oxygen (equivalent to the iodine liberated) together with the determination of the total iron in the specimen [16,17]. The degree of oxidation of the iron is readily calculated from the observed molar ratio Fe : O_{act}. The reaction of KI with ferrate(VI) solutions takes place smoothly, without spontaneous decomposition, but in the reaction of the insoluble $BaFeO_4$ and $SrFeO_4$ with KI in acid solution, which requires longer treatment and increased temperature, a small quantity of O_2 is volatilised, so that the analysis gives low results [17]. Thus for insoluble ferrates(VI), accurate values for O_{act} are obtained only by the gas-volumetric determination.

Uses of ferrates(VI) and their role in various industrial processes. In recent years there has been an increase in interest not only in the theoretical aspects of ferrates(VI) but also in their applied chemistry, chiefly in relation to their oxidising function.

Vil'nyanskii and Pudovkin [62] concluded that the production of sodium chromate from a mixture of natural chrome ironstone, sodium carbonate, and other additives involves the formation of sodium ferrate(VI), which is soluble in the liquid melt formed by the reaction mass at high temperatures (1150°). The ferrate(VI) acts as a carrier of oxygen from the furnace gas to the surface of the chromite granules. It is suggested that the existence of Na_2FeO_4 at such high temperatures is due to an increase in its thermal stability on dissolution in the molten chromate.

Studies of the passivation of iron in concentrated nitric acid have given interesting results [63]. It has been shown that the passivity of iron is due to the formation of a film of ferric acid H_2FeO_4 or a related compound of iron, and not a layer of iron oxide, as assumed by other workers. The sexavalent iron compound is formed in the anodic region as a consequence of the intense local action of galvanic currents when iron reacts with concentrated HNO_3. The formation of this compound is accompanied by its chemisorption on the iron surface, and it has a higher chemical stability in this state than in the free state (analogous to the stability of the passive chromate films chemisorbed on iron). It is unaffected by a large number of reagents with which it reacts, with rapid decomposition, in the free state. On reaction with solutions of ferrates(VI) (or chromates) iron was covered with a passive film which was the same as that formed in the reaction of the acid with iron. When the passivated iron was immersed in NaOH solution, the red-violet colour typical of the ferrate ion was produced, by the replacement of this ion on the iron surface by the preferentially adsorbed OH^- ion. This solution exhibited oxidising properties typical of ferrate(VI). The metastable ferrate film is decomposed by cathodic reduction, mechanical shock, and heating, and in the presence of halide ions.

The production of a corrosion-resistant layer on metallic surfaces by ferrate(VI) solutions has been used to develop a method for protecting iron and steel castings from corrosion [64]. The method is based on the rapid formation of Fe_2O_3 by the decomposition of the thin film of ferrate(VI) on the metal and ferrate(VI) solution. It involves bringing the metal successively into contact with an alkali solution containing a reducing agent (12.5% NaOH + 0.4% 8-quinolinol) and a solution containing an alkali metal ferrate (1%).

Alkali metal ferrates(VI) have found application for decolorising coloured impurities in the caustic solutions obtained in electrolyte baths [65]. The addition of a small quantity of ferrate(VI) (for example 0.5 g Na_2FeO_4) to a very large quantity of a solution containing coloured

impurities (for example 100 g of blue NaOH solution) leads to decolorisation on gentle heating. The resulting solution, purified from chlorine and iron, satisfies industrial standards.

Na_2FeO_4 has proved useful for the purification of hemicellulose by precipitation from alkali solutions [66]. Compared with other methods for precipitating hemicellulose by means of $CuSO_4$, $Pb(CH_3COO)_2$, or Na_3AlO_3, the new method not only gives better purification of the alkali solution and an improvement in the quality of the viscose, but also gives a hemicellulose precipitate which can be filtered off rapidly and used for the production of other materials. It is recommended that Na_2FeO_4 be produced in the plant by direct electrolysis in the baths in which the precipitation is carried out.

Solid K_2FeO_4 is used as an activator in the production of catalysts used in the Fischer–Tropsch process [67,68]. The catalyst is prepared by mixing Fe_2O_3 (α- or γ-modification) with potassium ferrate(VI) powder (0.2–20 wt.%) in a small quantity of alcohol. Tablets with this composition are heated for 4 h at 540° in an oxidising atmosphere and then for approximately 24 h in a reducing atmosphere at 370–870°.

II. FERRATES(IV)

The first papers on the preparation and study of properties of compounds of quadrivalent iron were published in the nineteen-forties [69], although the possibility of existence of these compounds was noted as early as 1909, by Moeser and Borck [70]. They were the first to prepare Sr and Ba ferrates(IV), for which they used the formulae $SrO.FeO_2$ and $BaO.FeO_2$, by heating dry $Fe(NO_3)_3 + Sr(NO_3)_2$ and $Fe(OH)_3 + Ba(OH)_2$ mixtures in a stream of O_2 at 600° and 400° respectively. As shown later by Scholder [71], the Sr and Ba ferrates obtained in this way are always extensively contaminated by oxides of iron and the alkaline earth metals.

Four types of compound of quadrivalent iron are now known: 1) metaferrates(IV) $MFeO_3$‡ (alkali metals, Ba, Sr, Ag, and Pb); 2) orthoferrates(IV) M_2FeO_4 (alkali metals, Sr, and Ba); 3) pentaoxoferrates(IV) M_3FeO_5 (Ba only); and 4) ferrates(IV) of the type $M_3Fe_2O_7$ (Ba and Sr only).

Preparation. The simplest and most widely encountered method for preparing ferrates(IV) is by the thermal oxidation of a mechanical mixture of two solid phases with an M:Fe ratio corresponding to that in the ferrate(IV). In a study of the oxidation of mixtures of two solid phases, Wahl [72] established that for complex compounds§ in which the central atom is in a high oxidation state, neglecting the temperature and the pressure of the gas, the following stabilisation methods are possible: 1) selection of complex-forming ligands; 2) selection of cation; 3) change in the ratio of the number of cations to the number of central atoms.

It can readily be appreciated that the choice of ligand has a significant influence on the degree of oxidation. When it is necessary to stabilise a low or intermediate oxidation state, ligands with a low electronegativity are chosen; on the other hand, the formation of complexes in which the central atom is in a high oxidation state requires ligands with a high electronegativity, such as fluorine and oxygen. Oxygen is preferred, however; there are then extensive possibilities for the stabilisation of higher oxidation states, since oxygen can carry a negative charge greater than unity, and can form π-bonds.

A not unimportant factor in the production of highly oxidised complexes is the choice of cation. Chemical experiments have shown that the formation of these complexes is most favoured by large cations.

The influence of change in the ratio of the number of cations to the assumed central atom on the degree of oxidation is small. For example, it is observed for the oxidation of an $Fe_2O_3 + K_2O$ mixture: $KFeO_2$ is formed at K : Fe = 1 : 1, K_2FeO_4 at 2 : 1, and K_3FeO_4 at 3 : 1. It is not observed, however, for an $Fe_2O_3 + BaO$ mixture: $BaFeO_3$ is formed at Ba : Fe = 1 : 1, Ba_2FeO_4 at 2 : 1, and Ba_3FeO_5 at 3 : 1. Here, the iron in all the products is quadrivalent.

In the preparation of ferrates(IV), combinations of iron oxides, hydroxide, or nitrate with the oxide, hydroxide, carbonate, nitrate, or other compound of the alkali, alkaline earth, or other metal can be used in the mixture being oxidised. A large number of experiments on the preparation of ferrates(IV) by the oxidation of mixtures of two solid phases under different conditions (400–1000°, stream of dry or moist O_2) showed that the Fe^{IV} concentration in the products does not exceed 90%. [32,71,74–77] An Fe^{IV} concentration of 100% was observed in only one instance, in the preparation of Na_4FeO_4 by the oxidation of a stoichiometric $Fe_2O_3 + Na_2O$ mixture in a stream of dry O_2 at 450°. [75] The study of the kinetics of the oxidation of a mechanical $Fe_2O_3 + 2BaCO_3$ mixture in a stream of O_2 at 700–900° showed that the reaction between the components is incomplete at the temperatures of the experiment, leading to the presence of Ba and Fe oxides in the reaction products [73]. Similar results can evidently be expected in the oxidation of other mechanical mixtures.

Recent experiments [77–80] have shown that it is more appropriate to prepare ferrates(IV) by the oxidation of a single solid phase, that is ferrate(III), previously prepared by sintering the above mixtures in air or in an atmosphere of an inert gas at high temperatures (1100 to 1400°). Subsequent saturation of ferrates(III) with oxygen under high pressure increases the degree of oxidation of iron, raising the Fe^{IV} concentration to even 100% (see Table). In most instances, however, Fe^{III} cannot be oxidised completely to Fe^{IV} even by carrying out the preparation at super-high O_2 pressures.

Because of the incomplete oxidation of Fe^{III} to Fe^{IV}, which is evidently due to the insufficient thermal stability of ferrates(IV), non-stoichiometric compounds containing oxygen vacancies in the crystal lattice are obtained. The loss of each oxygen anion is compensated by the conversion of two Fe^{IV} ions into two Fe^{III} ions. Thus the empirical formulae of the oxygen-deficient compounds are: for the metaferrates(IV) $M(Fe^{IV}_{1-2x}Fe^{III}_{2x})O_{3-x}$, for the orthoferrates(IV) $M_2(Fe^{IV}_{1-2x}Fe^{III}_{2x})O_{4-x}$, and for ferrates(IV) of the type $M_3Fe_2O_7$ $M_3(Fe^{IV}_{2-4x}Fe^{III}_{4x})O_{7-2x}$, where $0 \leq x \leq 0.5$.

Van Hook [82,83] established that the degree of oxidation of iron in ferrates depends to some extent on the area of the surface being oxidised. In the study of the influence of the surface area, three $BaFeO_{2.5}$ specimens—a fine powder with an average particle size of ~ 5 μm, a ceramic

‡M represents a bivalent metal atom or two univalent metal atoms.

§Metallates formed on the oxidation of mixtures of two solid phases.

tablet with a porosity of ~ 25%, and a piece of a single crystal grown in air by cooling from the melting point 1370°—were oxidised under identical conditions until their weight showed no further change with time. It was found that the degree of oxidation of iron was greater in the first specimen than in the second, and greater in the second than in the third. It was noted that although adsorption of oxygen took place, it was clearly a secondary factor, since only small differences in the degree of oxidation were observed for specimens for which the surface areas differed considerably from one another.

Preparation of ferrates(IV) by the thermal oxidation of ferrates(III) by oxygen under pressure.

No.	Starting materials (ceramic)	t, °C	P_{O_2}, atm.	Time, h	Composition of ferrate obtained	Fe^{IV}/Fe_{total} %	References
1	$BaFeO_{2.5}$	325	18500	184	$BaFeO_{2.95}$	90	78
2	$BaFeO_{2.5}$	400	20500	88	$BaFeO_{2.95}$	90	78
3	$SrFeO_{2.5}$	1000	65	24	$SrFeO_{2.98}$	96	79
4	$SrFeO_{2.5}$	760	337	168	$SrFeO_3$	100	80
5	$Sr_3Fe_2O_6$	400	15000	144	$Sr_3Fe_2O_{6.9}$	90	77
6	$CaFeO_{2.5}$	300	200	24	$CaFeO_{2.5}$	0	81

Sr and Ba ferrates(IV) can be obtained by the decomposition, in an oxidising atmosphere, of complex compounds containing iron and the alkaline earth metal, for example $M_3[Fe(OH)_6]_2.xH_2O$ and $M_2[Fe(C_2O_4)_3]_2.xH_2O$ (M = Sr or Ba). Here, the formation of the ferrates involves the reaction between the decomposition products of the complexes and the subsequent oxidation of Fe^{III} to Fe^{IV}. Thus when the hydroxoferrates(III) $M_3[Fe(OH)_6]_2$ are heated in a stream of O_2 at 300–450°, products with the composition $MFeO_3 + \frac{1}{2}M(OH)_2$, containing only quadrivalent iron, are formed [32,71]. Attempts to remove the component $M(OH)_2$ by extraction with anhydrous methanol led to appreciable decomposition of the metaferrates(IV) (to 56% Fe^{IV}).

Sr_2FeO_4, Ba_2FeO_4, and Ba_3FeO_5 with an Fe^{IV} concentration of 100% are formed when $M_3[Fe(OH)_6]_2 + xM(OH)_2$ mixtures ($x = 1$ for M_2FeO_4, $x = 3$ for M_3FeO_5) are heated in a stream of O_2 at 800°. [75]

In the products obtained by heating tris(oxalato)-ferrates(III) $M_3[Fe(C_2O_4)_3]_2$ in a stream of O_2, the Fe^{IV} concentration does not exceed 75%. [84,85]

For the preparation of Sr and Ba metaferrates(IV) from the corresponding ferrates(VI), the most suitable starting materials are Ba and Sr ferrates(VI). As already noted, when $BaFeO_4.aq$ specimens are kept, their colour changes from cherry-red to dense black, accompanied by the quantitative conversion of barium ferrate(VI) into barium metaferrate(IV). The liberation of oxygen is complete in several weeks (sometimes days) even in a sealed glass vessel; when the latter is opened, the oxygen volatilises with a loud crack. An important feature is that the oxidation coefficient does not fall below 0.97 even when the experiment is continued for a long time (240 days). Strontium ferrates(VI) do not undergo this transformation.

The conversion of $BaFeO_4$ into $BaFeO_3$ takes place much more rapidly, in 7–20 min, when freshly prepared $BaFeO_4$ is heated to 90–100° in 50% KOH or NaOH solution [32,38]. In concentrated alkali solutions, $SrFeO_4$ decomposes immediately to $Fe_2O_3.aq$, $Sr(OH)_2$, and O_2, and in hot saturated $Sr(OH)_2$ solution it is converted into Sr metaferrate(IV), extensively contaminated by Fe^{III}. [32] Ba and Sr metaferrates(IV) containing not more than 85 to 92% Fe^{IV} can be obtained by the thermal decomposition of Ba and Sr ferrates(VI) in a stream of O_2 at 700 to 1000°.

Only lithium and silver ferrates(IV) have been prepared by double decomposition. Li_2FeO_3 (94–98% Fe^{IV}) was obtained by the reaction of solid K_2FeO_4 and LiOH (Li : Fe = 8) at 300° and subsequent removal of the excess of LiOH by extraction with absolute methanol at −30°. Ag_2FeO_3 (100% Fe^{IV}) was obtained by adding $AgNO_3$ to K_2FeO_4 solution at 0° (Ag : Fe = 2) and washing the resulting precipitate with ethanol and ether at 0°. [32]

Analyses. The compositions of ferrates(IV, V, VI) are usually determined by analysis for the component elements, and expressed as atomic ratios M : Fe : O$_{act}$. The concentration of active oxygen is determined iodometrically (Fe^{IV}, V, VI $\xrightarrow{I+H^+}$ Fe^{II}) or gas-volumetrically (Fe^{IV}, V, VI $\xrightarrow{H^+}$ Fe^{III}). The gas-volumetric method can be used as an independent method for the determination of the Fe^{IV} concentration [61]. An original method for the determination of Fe^{IV} was proposed by Mori [86]. The ferrate(IV) specimen is dissolved in hydrochloric acid containing an excess of Fe^{2+} ions, which reduce Fe^{IV} to Fe^{III}. The quantities of Fe^{IV} and Fe^{III} in the specimen are determined from the total quantity of Fe^{3+} ions and the quantity of unreacted Fe^{2+} ions in the solution. The analysis is carried out in a stream of CO_2 to avoid the oxidation of Fe^{2+} by atmospheric oxygen.

Some authors have used the Mössbauer spectra for analytical studies; the ratio of the intensities of the characteristic peaks of Fe^{III} and Fe^{IV} was taken as equal to the ratio of the concentrations of the corresponding ions [85,87]. Chemical analysis confirmed that the results were correct.

Chemical properties. All the alkali metal ferrates(IV) form loose black powders without a definite crystal structure, stable at room temperature in the absence of moisture. In aqueous solutions or dilute alkali solutions they disproportionate with the formation of the corresponding ferrates(VI) and $Fe(OH)_3$. An exception is Li_2FeO_3, which decomposes in water to $Fe(OH)_3$ with the liberation of O_2. [32] The alkali metal ferrates(IV) are used as oxidising agents for organic substances and for water purification [88].

All the alkaline earth metal ferrates(IV) form black or dark-grey powders, stable in air, with the exception of Ba_3FeO_5. In moist air, the latter disproportionates in a few minutes with the formation of chiefly $BaFeO_4$, with a colour change from black to cherry-red. In a stream of O_2, all Sr and Ba ferrates(IV) are stable as far as 700–1000°; they are insoluble in water, but gradually (very slowly for $BaFeO_3$) decompose to alkaline earth metal salts, Fe^{III} salts, and O_2. On treatment with hydrochloric acid, Cl_2 and O_2 are liberated simultaneously.

Ba and Sr metaferrates(IV) begin to decompose in air at 320°. The decomposition has the characteristics of reversible thermal dissociation. With increase in temperature the dissociation pressure, equal to the atmospheric pressure of oxygen, is reached by $M(Fe^{IV}_{1-2x}Fe^{III}_{2x})O_{3-x}$ with increasing oxygen deficiency.

Structure and physical properties. The series of ferrates(IV) $SrFeO_3$, Sr_2FeO_4, and $Sr_3Fe_2O_7$ are the structural analogues of the corresponding titanates $SrTiO_3$, Sr_2TiO_4, and $Sr_3Ti_2O_7$.[77] These three structural types of ferrate(IV) are related to one another: the compounds with higher alkaline earth metal contents are derived from the perovskite structure by the introduction of layers of Sr and O ions between single or double perovskite layers.

Studies by a number of authors[85,86,90-92] has shown that the compounds with the composition $M(Fe^{IV}_{1-2x}Fe^{III}_{2x})O_{3-x}$ and $M_3(Fe^{IV}_{2-4x}Fe^{III}_{4x})O_{7-2x}$ are characterised by a constant crystal structure over a fairly wide range of values of x. Thus according to Brisi[91], compounds with the composition $Sr(Fe^{IV}_{1-2x}Fe^{III}_{2x})O_{3-x}$ crystallise in a single phase with the ideal perovskite structure, like $SrTiO_3$. No significant displacement of the lines in the X-ray diffraction patterns of specimens with different degrees of oxidation (40, 50, or 75% Fe^{IV}) was observed, and the values of the lattice parameter remained almost unchanged at 3.853 Å. In this instance the contraction which it might appear should have taken place with decrease in the quantity of oxygen ions and the formation of vacancies in the lattice is almost completely compensated by the increase in the ionic radius of iron on going from the quadrivalent to the tervalent state. The observed fact that the lattice parameter remains constant suggested that any compound $SrFeO_{3-x}$, including the stoichiometric compound, can be assigned a lattice parameter within the range 3.85 Å. On this basis it is possible to calculate the minimal distance between the ions in the cubic lattice:

O—O 2.70Å, Sr—O 2.73Å, Fe—O 1.93Å

The value 0.58 Å was obtained empirically for the Fe^{IV} radius by subtracting from the last of the above quantities the radius of the oxygen ion (1.35 Å). The value of 0.58 Å is only approximate, however. In fact we have close packing of the Sr and O ions, and the Fe ions merely occupy the free space in the centre of the octahedron formed by the oxygen ions.

The lattice parameter of recently prepared stoichiometric $SrFeO_3$ was in fact found to be equal to 3.850 Å. Detailed X-ray diffraction studies[80], however, established, in contrast to Brisi's results[91], that in the compounds $SrFeO_{3-x}$, increase in the oxygen deficit is accompanied by a gradual, albeit slight, increase in the parameter of the cubic cell. As oxygen is lost, tetragonal distortion of the cubic perovskite cell is observed, beginning at the composition $SrFeO_{2.84}$¶. As the composition approaches $SrFeO_{2.5}$, the tetragonal cell gradually changes into the monoclinic perovskite cell[93]. Thus as Fe^{IV} is reduced to Fe^{III} in the $SrFeO_3$–$SrFeO_{2.5}$ system there is a decrease in the symmetry of the perovskite cell, related to the change in the oxidation state of iron.

The first studies of the structure of the metaferrates $BaFeO_{3-x}$[74,94,95] showed that the cubic (a = 3.995 Å), tetragonal (a = 3.981 Å, c = 4.005 Å), and hexagonal (a = 5.69 Å, c = 13.89 Å) phases formed by these compounds have structures analogous to that of the corresponding phases of the familiar ferroelectric $BaTiO_3$.

¶ The tetragonal distortion is very small ($c : a \simeq 1.005$). The specimens are "almost cubic". It was probably for this reason that the distortion of the cell was not observed for Brisi's specimens[91].

This feature aroused particular interest in the compounds $BaFeO_{3-x}$ and stimulated further study of their structure[78,84-86,91,96-98].

Some workers considered that the structures found for the ferrates $BaFeO_{3-x}$ should also be shown by stoichiometric $BaFeO_3$, and some, without determining the compositions of the specimens, assigned their structure directly to $BaFeO_3$. If $BaFeO_3$ specimens with known compositions, prepared by different methods, are arranged in order of increasing Fe^{IV} concentration, the following change in structure can be observed. Highly oxidised specimens generally have a hexagonal structure[78,86,91], which may be preserved as far as the composition $BaFeO_{2.70}$,[86] and with decrease in the concentration of Fe^{IV} in the specimens the unit cell parameter gradually increases. When oxygen is lost, beginning from the composition $BaFeO_{2.88}$ (76% Fe^{IV}), the products have the cubic perovskite structure and its distorted forms—tetragonal, orthorhombic, monoclinic, and triclinic[84-86,96]. The dynamics of their interconversion is such that with decrease in the Fe^{IV} concentration there is a gradual decrease in the symmetry of the perovskite cell. Thus analysis of published data indicates that the structural changes in $BaFeO_{3-x}$ are related to the change in the oxidation state of the iron present.

The fundamental importance of this conclusion lies in the fact that the barium metaferrate phases, with structures analogous to those of the polymorphic modifications of $BaTiO_3$, correspond not to $BaFeO_3$, but to different compounds in the $BaFeO_3$–$BaFeO_{2.5}$ system.

The conclusion that $BaFeO_3$ is not a complete structural analogue of $BaTiO_3$, since the metaferrate(IV) corresponds to a single hexagonal structure, was confirmed by recent X-ray diffraction studies of $M(Fe^{IV}_{1-2x}Fe^{III}_{2x})O_{3-x}$ with Fe^{IV} concentrations from 0 to 100%, for which the starting material was $BaFeO_4$.[99]

It was established experimentally that the thermal stability of the hexagonal phase $BaFeO_{3-x}$ increases with increase in the oxygen pressure. The compound exists as far as 915° in air and as far as 1250° at 10 atm O_2, and at 50 atm O_2 it melts without decomposition at 1412°.[82]

The existence of Fe^{IV} in ferrates(IV) and the appreciably covalent character of the bond between Fe and the oxygen ions coordinated to it were confirmed by the Mössbauer spectra[77,79,87,96,100]. The nature of the covalent bond is similar to that observed in compounds containing Fe^{VI}. The Mössbauer spectra show isomer shifts due to the quadrivalent state of iron. The theoretically calculated isomer shift for the free Fe^{4+} ion[101], equal to -1.30 mm s^{-1}, is more negative than the experimental values observed for the compounds containing Fe^{IV}. Thus the isomer shift had the values -0.17 mm s^{-1} for $SrFeO_3$ and -0.29 mm s^{-1} for $BaFeO_{2.95}$ at 298°K. These more positive values are interpreted as resulting from a considerable covalent contribution to the 3d orbitals of the Fe^{4+} ion from the oxygen ligands. Comparison of the values of the isomer shifts for $BaFeO_{2.95}$ and $SrFeO_3$ showed that the covalent contribution to the Fe–O bond is smaller for $BaFeO_3$ than for $SrFeO_3$. Comparison of the isomer shifts for $Sr_3Fe_2O_{6.9}$ and $SrFeO_3$ showed that the introduction of the layers of Sr and O ions between the double perovskite layers has little influence on the bonding. The spectra of the ferrates with an oxygen deficit show quadrupole splitting, indicating the presence of Fe^{III} in addition to Fe^{IV}.

It is suggested[78] that $BaFeO_3$ has an interesting future, primarily because of its unusual magnetic properties.

When $BaFeO_{2.95}$ is cooled, a sharp change from ferrimagnetism to antiferromagnetism is observed at 164°K. The maximal value of the specific magnetisation $\sigma g = 13.8$ electromagnetic units at 164°K. The change in the magnetic ordering is accompanied by a sudden change in the temperature dependence of the conductance. The plot of $\lg\rho$ against $1/T$ shows a peak at the temperature of the transition. No departure from hexagonal symmetry was observed below the temperature of the transition.

Stoichiometric $SrFeO_3$ is antiferromagnetic with a Neel temperature of 130°K. It exhibits anomalous electrical properties. Ceramic discs of this material are good conductors ($\rho \simeq 10^{-3}\ \Omega\,cm^{-1}$) with the same temperature coefficient as metallic conductors [80].

$SrFeO_3$ forms unrestricted solid solutions with $SrTiO_3$, [102] with a linear increase in the lattice parameter a as Fe^{IV} is replaced by Ti^{IV}.

Perovskite series of solid solutions $La_{1-x}Sr_xFeO_{3-y}$ were obtained in an atmosphere of oxygen by replacing the tervalent La by the bivalent Sr. [79,103] With increase in the oxygen pressure during preparation, the oxygen deficit in the solid solutions decreases to almost zero. The stoichiometric compositions $La_{1-x}Sr_xFeO_3$ have distorted perovskite structures.

The system of solid solutions $SrFeO_3$–$BiFeO_3$ shows the structural transformation: cubic → tetragonal → cubic, with increase in the degree of replacement of Sr by Bi. [104]

Tauber [105], from a melt with Ba : Bi : Fe = 1 : 2 : 3, obtained dendritic cubic crystals $(Ba_{0.33}Bi_{0.67})(Fe^{III}_{0.67}Fe^{IV}_{0.33})O_3$ with lattice parameters very close to those of cubic $BaFeO_{3-x}$.

$BaFeO_3$ forms solid solutions with $BaTiO_3$. The conclusion [106] that the addition of small quantities of $BaFeO_3$ (3–5%) to the titanate produces a sharp change in its structure from tetragonal to hexagonal cannot be regarded as correct with respect to Fe^{IV}, since the solid solution specimens were prepared by a method which excluded the formation of Fe^{IV} (heating at 1380°). In this instance the observed sharp change in the structure and ferroelectric properties are due to the introduction of Fe^{III} ions into the $BaTiO_3$ lattice.

III. FERRATES(V)

The only known quinquevalent iron compounds are potassium, sodium, and rubidium ferrates(V). K_3FeO_4 was first prepared in 1956, by the oxidation of an $Fe_2O_3 + 6KO_X$ mixture in a stream of O_2 at 400–500°. [7] The K_3FeO_4 obtained in this way always contains small quantities of $KFeO_2$ and KO_X. Potassium ferrate(V) mixed with $KFeO_2$ is also formed by the thermal decomposition of K_2FeO_4 at 700° in a stream of O_2 [17] (see Russian page 1979). Pure K_3FeO_4 is obtained by the reaction of Fe_2O_3, $KFeO_2$, or K_2FeO_4 with anhydrous KOH (Fe : K = 1 : 3) in a stream of O_2 at 600–700°. [107]

The oxidation of mixtures of RbO_X or RbOH with Fe_2O_3 at 600° in a stream of O_2 gives rubidium ferrate(V) with the composition $Rb_3FeO_{4.4-4.7}$, containing peroxide. When heated for a short time at 350° in a stream of N_2, these products are converted into Rb_3FeO_4. [107]

Sodium ferrate(V) could not be obtained by the corresponding reactions. Na_3FeO_3, prepared from Fe_2O_3 and Na_2O_2 in a stream of N_2 at 600°, reacts with O_2 with the formation of Na_3FeO_4, the degree of conversion being proportional to the pressure of oxygen. Thus the product contains 40 mole % Na_3FeO_4 at 20 atm O_2, and 80 mole % Na_3FeO_4 at 120 atm O_2, and the conversion of Na_3FeO_3 into Na_3FeO_4 is probably quantitative at 200 atm O_2. [107]

In dilute H_2SO_4 and HNO_3, ferrates(V) decompose to Fe^{III} with the liberation of O_2, and in the reaction with HCl, Cl_2 and O_2 are liberated simultaneously. In water or dilute alkali solutions, disproportionation takes place:

$$6K_3FeO_4 + 8H_2O = 4K_2FeO_4 + 2Fe(OH)_3 + 10\ KOH$$

The concentration of active oxygen can be determined iodometrically only in very pure ferrates(V); when $MFeO_2$ or MO_X are present, correct results are obtained only in the gas-volumetric method. The quantity of Fe^V in the specimens can be determined by analysis of the products of disproportionation, in which 66.6% of the Fe^V is converted into Fe^{VI}.

K_3FeO_4 begins to decompose in a stream of O_2 above 700° according to the equation $K_3FeO_4 = KFeO_2 + K_2O + \frac{1}{2}O_2$. At 250–500° in a stream of O_2, K_3FeO_4 is slowly converted into $KFeO_2 + 2KO_X$, and in this instance the decomposition products are formed not by the simple decomposition of K_3FeO_4 but by its reaction with molecular oxygen. This was established from comparative experiments in which K_3FeO_4 was heated in a stream of O_2 or N_2. In the latter, potassium ferrate(V) remains unchanged at these temperatures. Analysis of the products of the decomposition of K_3FeO_4 in O_2 at a pressure of 100 atm and temperatures up to 400° indicates that the following reaction takes place: $K_3FeO_4 + 0.75O_2 = KFeO_2 + 2KO_{1.75}$. [107]

Unlike potassium ferrate(V), Na_3FeO_4 in a stream of O_2 at 200–250° gives up active oxygen with the conversion of Fe^V into Fe^{IV}.

The X-ray diffraction patterns of K_3FeO_4 show that it is amorphous towards X-rays. Magnetic measurements gave an effective magnetic moment of 3.6–3.7 μ_B. [7] These values are close to the spin magnetic moment for three unpaired electrons (3.87 μ_B), expected for Fe^V.

Compounds of octavalent iron have not been prepared. The electron affinities calculated by Ionova and Dyatkina [108] for the isoelectronic oxo-anions of the first transition series, of which the last member is the FeO_4 molecule, change in the following order: TiO_4^{4-} 2.4 eV, VO_4^{3-} 3.8 eV, CrO_4^{2-} 5.5 eV, MnO_4^- 7 eV, and FeO_4 10.7 eV. It can be seen that the FeO_4 molecule should have a very high electron affinity, and this explains the difficulty of obtaining iron tetroxide and the perferrate ion.

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Organosilicon Derivatives of Monoazaheterocycles

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The literature data and studies in the field of organosilicon derivatives of heterocycles containing one nitrogen atom in the ring have been reviewed. The methods of preparation, physical, chemical, and biological properties, and practical applications of organosilicon nitrogen-containing heterocycles in which the silicon atom is linked directly to a ring carbon or nitrogen atom and also via an oxygen atom or a carbon chain have been examined.
The bibliography includes 350 references.

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I. INTRODUCTION

During recent years, the organosilicon derivatives of nitrogen-containing heterocycles have gained an important place in the chemistry of both organosilicon and heterocyclic compounds. It is sufficient to mention their successful applications in the chromatographic analysis of natural products, their ever increasing use in the syntheses of pyridine, pyrimidine, pteridine, and purine derivatives otherwise difficult to obtain, and also new methods of synthesis of nucleosides and penicillins developed on their basis to demonstrate the important role which organosilicon derivatives of nitrogen-containing heterocycles play in preparative organic chemistry. On the other hand, the study of reactions of organosilicon derivatives with derivatives of nitrogen-containing heterocycles and of the chemical, physical, and physicochemical properties of the products yields valuable information about the structures and reactivities of these heterocycles.

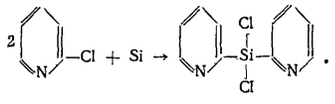
A systematic account of the first data on organosilicon derivatives of nitrogen-containing heterocycles was given in a review[1] which included information about studies published up to 1965. The number of investigations in this field and the wide variety of their subjects have now increased so much that it is desirable to describe them in separate reviews. We felt it necessary to consider in the first place the results of studies on organosilicon derivatives of nitrogen-containing heterocycles with one nitrogen atom in the ring published up to November, 1970.

II. COMPOUNDS CONTAINING THE Si – C_n – HETEROCYCLE GROUP

A. METHODS OF PREPARATION

1. Direct Synthesis

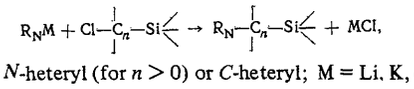
The possibilities of direct synthesis, which is the main industrial method for the preparation of alkyl- and arylchlorosilanes, in the series of nitrogen-containing heterocycles have been hardly investigated. Only two patents indicate that, when 2-chloropyridine is passed over silicon or over a silicon – copper alloy at 350 – 380°C, dichlorobis-(2-pyridyl)silane is formed[2,3]:



2-Bromopyridine reacts similarly. The halogeno-derivatives of other heterocycles have not been used in this reaction.

2. Organometallic Synthesis

The general method for the synthesis of organosilicon derivatives of nitrogen-containing heterocycles in which the silicon atom is linked directly to a ring carbon atom and also to the ring carbon and nitrogen atoms via a carbon chain is based on the interaction of organo-lithium, -potassium, or -magnesium derivatives of heterocycles with R-chlorosilanes ($n = 0$) or R-(chloroalkyl)silanes ($n > 0$)†:



[R_N = *N*-heteryl (for $n > 0$) or *C*-heteryl; M = Li, K, or MgBr]

Using *C*-organolithium derivatives, *N*-methyl-2-pyrrolylsilanes[4], *N*-benzyl-5-indolinylsilanes[5], *N*-alkyl-1-carbazolyl- and *N*-alkyl-3-carbazolylsilanes[6,7], 2-benzothiazolylsilanes[7], 2-pyridylsilanes[8-10], 3-pyridylsilanes[11,12], β-(2-pyridyl)- and β-(4-pyridyl)-ethylsilanes[13,14], 2,3,5,6-tetrachloro-4-pyridylsilanes[15], and 9,10-dihydro-10-methyl-9-acridylsilanes[16] were synthesised in this way. The yields of the trisubstituted pyridylsilanes[8-11] varied from 16 to 50%. (*N*-Alkyl-3-carbazolyl)triphenylsilanes are formed in higher yields than the 1-isomers. For example, whereas 9-ethyl-3-carbazolyl-lithium gives rise to (9-ethyl-3-carbazolyl)triphenylsilane in 64% yield, the yield of the 1-isomer is only 8%. The yield of the latter increases somewhat when bromotriphenylsilane is employed instead

† Unless otherwise stated, R is an organic substituent (Translator).

of the chlorotriphenylsilane[7]. The substitution of the chlorosilane by the bromosilane increases the yield of (2-benzothiazolyl)triphenylsilane from 5 to 19%.[7]

Organic *N*-lithio-derivatives have been used to prepare the piperidides of tri-R-silylacetic acid from their esters[17].

N-Potassio-derivatives of nitrogen-containing heterocycles have been used to synthesise organosilicon phthalimides[18-21] and also tri-R-(*N*-pyrrolylmethyl)silanes[4].

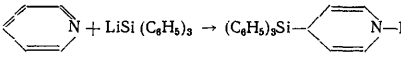
When picolinylpotassium reacts with halogenosilanes, pyridylmethylsilanes are formed[22]. If the initial picolinylpotassium was obtained from potassamide, after its reaction with chlorotrimethylsilane it is possible to isolate from the reaction mixture 2-bis(trimethylsilyl)-methylpyridine in addition to trimethyl-(2-pyridylmethyl)-silane.

Organic *C*-methyl magnesio-derivatives have been used to prepare trialkyl-(2-pyridyl)silanes[11,23], di-R-(2,3,5,6-tetrachloro-4-pyridyl)silanes[15], and tri-R-(8-alkoxy-5-quinolinyl)silanes[24].

Organometallic silyl derivatives, in particular triphenylsilyl-lithium and (tri-R-silyl)-R-lithium, can also be used to prepare *C*-silylated derivatives of nitrogen-containing heterocycles. With halogen-substituted heterocycles, the halogen atom is replaced by the tri-R-silyl-group:

$$R_N{-}Cl + LiSi(C_6H_5)_3 \rightarrow R_N{-}Si(C_6H_5)_3 + LiCl$$

and with unsubstituted heterocycles an addition reaction takes place, for example:



Thus, when triphenylsilyl-lithium reacts with pentachloropyridine in tetrahydrofuran (THF) solution at −70°C, (2,3,5,6-tetrachloro-4-pyridyl)triphenylsilane is formed[25] (together with hexaphenyldisilane and 4,4′-octachlorobipyridyl); (9-alkylcarbazolyl)triphenylsilanes[7,26] and the corresponding (10-ethylphenothiazinyl)triphenylsilane[26] are formed in the reactions with 9-alkyl-2-bromo- and 9-alkyl-3-bromo-carbazoles and with 2-, 3-, and 4-chloro-10-ethylphenothiazines respectively. Triphenylsilyl-lithium cleaves the C–O bond in *N*-alkoxymethylpiperidines with formation of (*N*-piperidinylmethyl)triphenylsilane[27].

Triphenylsilyl-lithium adds to pyridine[28] in the 1,4-positions and to acridine[16,29] in the 9,10-positions. The reaction of acridine with *p*-trimethylsilylphenylmagnesium bromide takes place similarly[30]. On the other hand, in the case of quinoline the addition of *p*-trimethylsilylphenyl-lithium[31] and 2-triphenylsilyl-5-thienyl-lithium[32] takes place in the 1,2-positions.

The addition of trimethylsilylphenyl-lithium to the carbonyl group of phenyl 2-pyridyl ketone leads to the formation of trimethylsilylphenyl-(2-pyridyl)phenylmethanol[33].

3. Amination of Alkenylsilanes

Aziridine[34-42], pyrrolidine[36,37], piperidine[36,37,39,43], and perhydroazepine[44] add to vinylsilanes in the presence of lithium, sodium, potassium, or their amides:

$$\equiv SiCH{=}CH_2 + HN(CH_2)_n \rightarrow \equiv SiCH_2CH_2N(CH_2)_n.$$

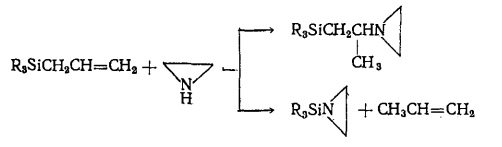
The addition of pyrrolidine and piperidine to triethylvinylsilane in the presence of metallic lithium begins at room temperature and takes place with a spontaneous temperature rise[36,37]. The yields of reaction products after 2 h amount to 70 – 72%. The rate of addition of aziridine is much lower (yield 39%) and pyrrole does not add to triethylvinylsilane under these conditions even after 25 h.[37]

When triethylvinylsilane was heated with aziridine in the presence of sodium for 7 h at 100°C, [2-(*N*-aziridinyl)ethyl]triethylsilane was formed in 90% yield. In the presence of sodamide, the reaction terminates after only 2 h at 50°C. Methyldiphenylvinylsilane readily combines with aziridine even at room temperature.

The rate of addition of piperidine to tri-R-vinylsilanes in the presence of lithium piperidide increases in the following sequence in terms of the organic substituent linked to the silicon atom: ethoxy- < triethyl < trimethyl < dimethylphenyl < methyldiphenyl[39], probably due to the increase in the same sequence of the double bond polarity, which promotes nucleophilic attack. The decrease of the rate of reaction for ethoxy-derivatives can be caused by part of the catalyst being consumed in the cleavage of the $Si-OC_2H_5$ bond[39]. The rate of addition of piperidine to the tri-R-vinylsilanes in THF solution is approximately twice as high as when the reaction is carried out in benzene or heptane[39]. The use of THF also makes it possible sometimes to lower the temperature of the amination reaction and to increase the yield of the reaction products[38].

When R-vinylsilanes with unsubstituted hydrogen atoms react with aziridine in the presence of lithium, dehydrocondensation and addition reactions take place simultaneously, the relative rate of the latter increasing from diethylvinylsilane to diphenylvinylsilane. The introduction of the aziridine group at the silicon atom also increases the rate of the addition reaction[40].

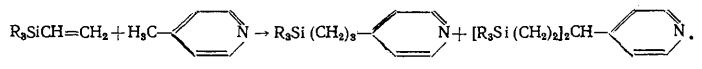
As the double bond is removed further away from the silicon atom in the compounds $R_3Si(CH_2)_nCH{=}CH_2$ (n = 0, 1, or 2), the rate of addition of aziridine decreases. With allylsilanes, addition is frequently accompanied by β-decomposition[34,45]:



(γ-Butenyl)trimethylsilane does not react with aziridine in the presence of $NaNH_2$ even on heating to 100°C. In contrast, *p*-trimethylsilylstyrene readily combines with aziridine[34] even at 50°C.

The addition of piperidine to 1-triethylsilylbuta-1,3-diene in the presence of sodium gives a mixture of 1,4- and 3,4-addition products[46] and the reaction of 1-trimethylsilylbut-3-en-1-yne with piperidyl-lithium gives, apart from the normal product of the addition to the double bond, the corresponding allenic amine[47].

When trimethylvinylsilane is heated with 4-methylpyridine at 55°C in the presence of sodium for 3 – 6 h, mono- (43%) and di-addition (49%) products are formed[48]:

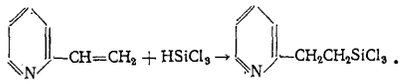


When metallic potassium is employed as a catalyst, the ratio of the products is altered in favour of a higher yield of the disilyl derivative (30 : 60).

4. Hydrosilylation of Heterylalkenes and Heterylalkynes

Trichlorosilane adds to 2-vinylpyridine in the presence of triethylamine and tributylamine giving a high yield

(91% with triethylamine) of trichloro-[β-(2-pyridyl)ethyl]-silane[49]. However, the reaction takes place smoothly also in the presence of other catalysts[49-53]:



High yields of hydrosilylation products are also found in the reaction of trichlorosilane with 4-vinylpyridine and 2,6-dimethyl-4-vinylpyridine[54]. The first stage in this reaction is the formation of a complex $HSiCl_3.nB$ (B = vinylpyridine; n = 3 for 4-vinylpyridine and n = 4 for 2-vinylpyridine)[55]. The complex of trichlorosilane with 2-vinylpyridine decomposes even at room temperature with evolution of heat and a hydrosilylation product is formed[55].

Alkylchlorosilanes and alkylarylchlorosilanes (both with unsubstituted hydrogen atoms) add to 2-vinylpyridine, 4-vinylpyridine, and 2,6-dimethyl-4-vinylpyridine in the presence of a catalyst (*NNNN'*-tetramethylenediamine and Cu_2Cl_2) with formation of β-adducts[56].

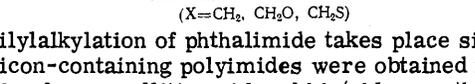
When 2- and 4-vinylpyridines are hydrosilylated with trialkylsilanes in the presence of chloroplatinic acid, a mixture of α- and β- adducts is produced, with the former predominating[51]. Pentamethyldisiloxane[57-59] and *sym*-tetramethyldisiloxane[57] produce α-adducts by this reaction, while heptamethylcyclotetrasiloxane gives a mixture of α- and β-isomers[57].

In the presence of chloroplatinic acid, the hydrosilylation of 2-allyloxypyridine[60,61], *N*-vinyl-lactams[62,63], *N*-vinylsuccinimide[64], and *N*-allyloxymethylphthalimide[65] was achieved.

The hydrosilylation of *N*-propargylpyrrolidine[66], *N*-propargylpiperidine[66,67], and *N*-propargylmorpholine[66] with triethylsilane in the presence of $H_2PtCl_6.6H_2O$ yields γ-adducts with a *trans*-structure. On going from triethylsilane to dibutylmethylsilane and from heptamethyltrisiloxane with three unsubstituted hydrogen atoms to triethoxysilane, there is a gradual increase of the content of the β-adduct in the reaction products and for the last compound the amounts of the γ- and β-adducts are almost equal[67].

5. Amination of Halogenosilanes with Organic Substituents

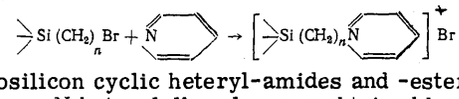
Tri-R-halogenoalkylsilanes silylate the amino-groups of aziridine[42], pyrrolidine[66,68], piperidine[43,68-70], morpholine[44,68,71], thiamorpholine[44], and perhydroazepine[44,72] in the presence of hydrogen halide acceptors (potassium carbonate, triethylamine, excess of heterocyclic base):



(X=CH_2, CH_2O, CH_2S)

N-Silylalkylation of phthalimide takes place similarly[18] and silicon-containing polyimides were obtained from the di-imide of pyromellitic acid and bis(chloromethyl)tetramethyldisiloxane[73].

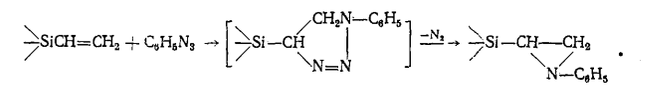
Prolonged heating of halogenoalkylsiloxanes with pyridine gives the corresponding organosilicon pyridinium salts[74-77]:



Organosilicon cyclic heteryl-amides and -esters derived from *N*-heterylalkanols were obtained by the reaction of trimethylsilylbenzoyl and trimethylsilylphenylacetyl chlorides with heterocyclic bases[78,79] and *N*-heterylalkanols[80].

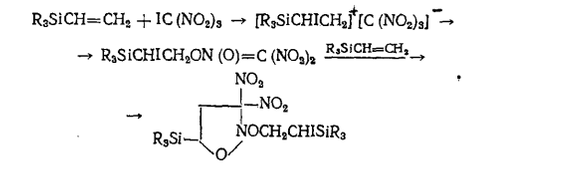
6. Cyclisation Reactions

Organosilicon derivatives of aziridine have been obtained by the reaction of vinylsiloxones with phenyl azide[58,81] at room temperature or with benzyl azide[82] at 60 — 80°C. The first stage of this reaction may be the addition of phenyl azide to the vinyl group with formation of a five-membered ring, which splits off a nitrogen molecule and is converted into an *N*-phenylaziridinyl derivative:



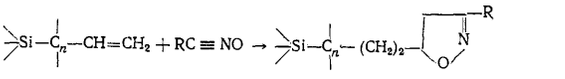
After a 40 day reaction of heptamethylvinylcyclotetrasiloxane and heptamethyl-3-vinyltrisiloxane with phenyl azide, the yields of *C*-aziridinyl derivatives did not exceed 11%. The reaction of allylsiloxanes with phenyl azide is even more difficult[81]. Benzyl azide adds to heptamethyl-3-vinyltrisiloxane somewhat more readily[82]. When the reaction is performed in petroleum ether solution at 30 — 40°C, the yield of product after 10 days was 40.5%.

The addition of iodotrinitromethane to trimethylvinylsilane in carbon tetrachloride solution leads to the formation of an isoxazolidine derivative[83,84]:



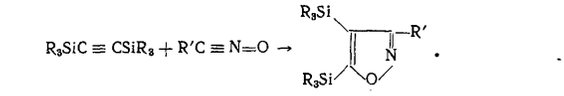
The product of the reaction of allyltrimethylsilane with iodotrinitromethane is *N*-trimethylsiloxy-5-trimethylsilylmethyl-3,3-dinitroisoxazolidine[83].

Organosilicon derivatives of isoxazolidine have been synthesised by the addition of nitrile oxides to vinyl-[85], allyl-[85], and vinylethynyltri-R-silanes[86,87]:

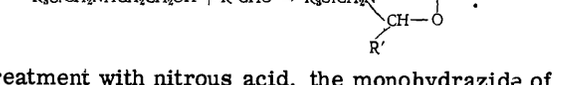


and also by the condensation of vinylsiloxanes with 1,4-dinitrobutane in the presence of phenylene di-isocyanate and triethylamine and by the reaction of alkenylsiloxanes with 1,2-dichloroglyoxime in the presence of triethylamine[88].

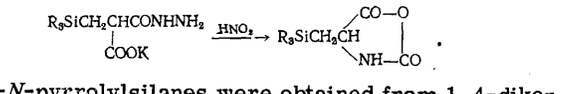
The reaction of ethynylsilanes with nitrile oxides yields isoxazolylsilanes[85]:



Alkyl-*N*-oxazolidinylsilanes were obtained by the condensation of silylaminoalcohols with aldehydes[89]:

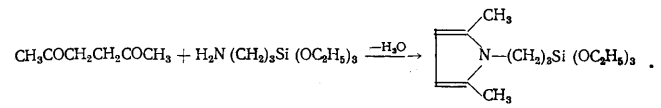


On treatment with nitrous acid, the monohydrazide of trimethylsilylmethylmalonic acid cyclises into an oxazolidinedione derivative[90]:

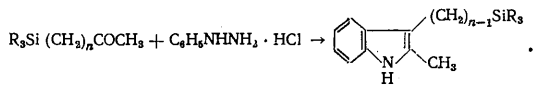


Alkyl-*N*-pyrrolylsilanes were obtained from 1,4-diketones and aminoalkylsilanes[91,92]. Thus triethoxy-γ-(2,5-dimethylpyrrolyl)propylsilane is formed when

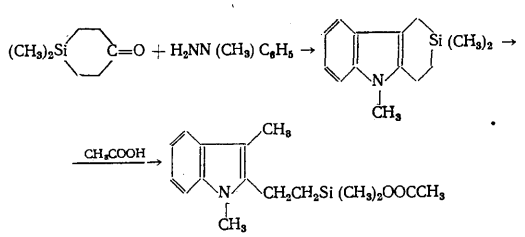
hexane-2,5-dione is heated with γ-aminopropyltriethoxysilane for 1 h at 140—150°C:



The condensation of γ-, δ-, and ε-silylketones with phenylhydrazine hydrochloride at 170—200°C in the presence of copper(I) chloride yielded silyl derivatives of indole[93-95]:

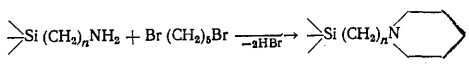


When 4,4-dimethyl-4-silacyclohexanone is refluxed with 1-methyl-1-phenylhydrazine in glacial acetic acid, dimethyltetrahydrosilacarbazole is formed and then converted into indole derivatives[96]:



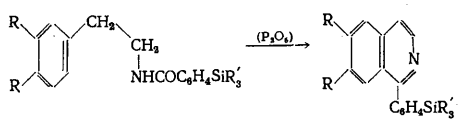
When a solution of *p*-trimethylsilylbenzylamine and itaconic acid is heated to boiling in pyridine, 4-carboxy-*N*-(*p*-trimethylsilylbenzyl)-2-pyrrolidinone is produced[20].

Tri-R-(2-piperidinoethyl)silanes and tri-R-(3-piperidinopropyl)-silanes were synthesised by the reaction of 2- and 3-aminoalkylsilanes with 1,5-dibromopentane[97]:



2,2,4,4-Tetranitropiperidinoalkylsilanes were obtained similarly by the condensation of aminoalkylsilanes with 2,2,4,4-tetranitropentane-1,5-diol[98,99].

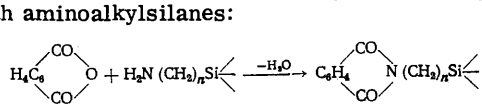
1-Trimethylsilylphenyl- and 1-trimethylsilylbenzyl-derivatives of isoquinoline were synthesised by the cyclisation of β-arylethylamides of the corresponding trimethylsilylarylcarboxylic acids in toluene when acted upon by phosphorus pentoxide or phosphoryl chloride[78]:



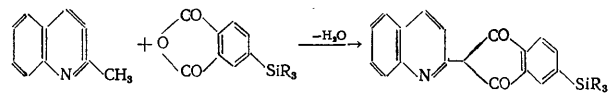
7. Other Methods

The Mannich reaction with piperidine and morpholine has been used for the aminomethylation of tri-R-ethynylsilanes[100] and trimethylsilylmethylacetophenone[101].

Silyl derivatives of succinimide[102,103] and phthalimide[102-105] are formed when dicarboxylic acid anhydrides react with aminoalkylsilanes:

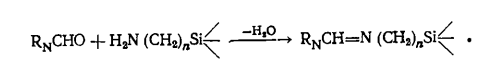


If one employs alkoxyaminoalkylsilanes in this reaction, the hydrolysis of the alkoxy-groups with water liberated on condensation and further polycondensation of phthalimidoalkylsilanols gives rise to polymeric products. Trialkylsilylphthalimides were also obtained by heating the anhydrides of 3- and 4-trimethylsilylphthalic acids with urea at 170°C. The condensation of these anhydrides with quinaldine leads to the formation of the corresponding quinolinophthalones[106]:



N-Heterylsilylalkanols were obtained by the opening of the oxiran ring of alkyloxiranylsilanes with aziridine[107] or phthalimide[104].

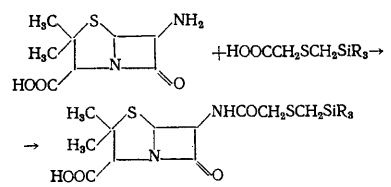
Silylaldimines were obtained by the reaction of heterocyclic aldehydes with aminoalkylsilanes:



The reaction has been used to prepare indole[108], oxazole[108], benzoisoxazole[108,109], thiazole[109], benzoisothiazole[109], pyridine[108], and acridine[108] derivatives.

Organosilicon derivatives of carbazole have been obtained by the reaction of carbazole with trimethylsilylacetyl chloride in the presence of stannic chloride[110]; organosilicon esters of nicotinic acid were obtained by heating alkylchlorosilanes with sodium nicotinate[111]; polymeric alkylsilylpyridylalkylenes were obtained by the copolymerisation of 4-vinylpyridine with methylallylsilacyclobutane[112].

A silicon-containing penicillin was synthesised by the reaction of 6-aminopenicillanic acid with trimethylsilylmethylmercaptoacetic acid in acetone using *NN'*-dicyclohexylcarbodiimide as the condensing agent[113]:



B. PHYSICAL PROPERTIES

Electronic[8,11,114], vibrational[4,15,17,55,66,67,83,86,106,115-118], and ^{1}H NMR[9,10,15,25,46,48,51,57,65,66,86,96,115,119] spectra of organosilicon derivatives of nitrogen-containing heterocycles have been used mainly to confirm the structures of the compounds synthesised.

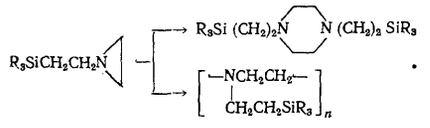
By comparing the calculated and experimental electronic spectra of trimethyl-(2-pyridyl)silane it was suggested that the π electrons of the heterocycle interact with the vacant orbitals of silicon[114]. However, trimethyl-(2-pyridyl)silane is a stronger base than 2-t-butylpyridine (according to potentiometric titration data, the pK_a values are 6.63 and 5.76 respectively). Trimethyl-(4-pyridyl)-silane is a weaker base than 4-t-butylpyridine, the basicity of which is higher than that of the 2-isomer[119].

The changes in the ultraviolet spectra of trialkylpyridylsilanes have been used to investigate the kinetics of their solvolysis[11]. The stereochemistry of this reaction was studied by determining the optical activities of methyl-1-naphthylphenyl-(2-pyridyl)silane and its methanolysis and hydrolysis products[8].

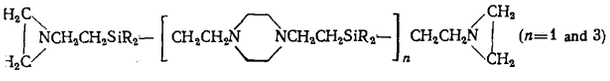
:. CHEMICAL PROPERTIES

. Thermal Reactions

Tri-R-[2-(*N*-aziridinyl)ethyl]silanes remain unchanged fter heating for 5 h at 200°C. An increase of temperaıre to 250 — 300°C leads to the formation of considerable mounts of thermal conversion products among which roducts with a high molecular weight are formed ›gether with products of cyclodimerisation to piperazine ›rivatives owing to the opening of the aziridine ng[117,118,120]:

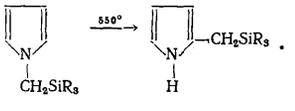


When [2-(*N*-aziridinyl)ethyl]triethylsilane is heated in ə presence of sodium iodide, the only product is the rresponding piperazine derivative, the yield of which ›reases from 22% for a molar reactant ratio of 1 : 0.2 50% for the equimolar ratio[120]. The yield of the poly›r and the degree of polymerisation depend to a conlerable degree on the nature of the groups linked to the icon atom. For example, when R = C_2H_5, heating at ›°C leads to the formation of a tetramer in about 7% ld. On the other hand, dimethylphenyl and ethoxyıethyl derivatives give 70 — 80% of compounds with 5 — 9.[117] Complexes of alkylaziridinylsilanes with c chloride polymerise at a temperature as low as l°C to form polymers with n = 80 — 300°C.[117] Dialkyldi-[2-(*N*-aziridinyl)ethyl]silanes form linear di- tetra-mers on heating to 250 — 300°C:[118]



ırther increase of temperature leads to the formation ross-linked insoluble polymers[118].

When trimethyl-(*N*-pyrrolylmethyl)silane is heated at °C, it isomerises to trimethyl-(2-pyrrolylmethyl)ne[4]:



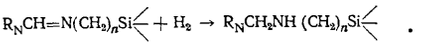
Reduction

he reduction of organosilicon derivatives of nitrogenıining heterocycles has been used to prepare derivawith hydrogenated rings and also to modify the funcl groups in the side chain of the heterocycle or ›s linked to the silicon atom.

ıus pyridylsilanes[33] and alkylpyridylsiloxanes[121] were ›rted by catalytic reduction (H_2/PtO_2) into the correling piperidinylsilanes and alkylpiperidinylsiloxanes)-acridinyl)triphenylsilane (reduction with Zn/HCl) ›onverted into (9,10-dihydro-9-acridinyl)triphenyl›16].

e cyano- and ethoxycarbonyl functional groups of rlsilanes[5], the amide groups of substituted piperi- and morpholinyl-R-silanes[78], and the alkoxy-groups ylalkoxyaziridinylsilanes[38] were reduced with lithium niumhydride.

Aldimines obtained from heterocyclic aldehydes and silylamines were hydrogenated catalytically to amines:

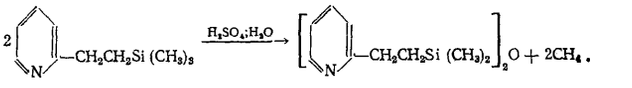


Derivatives of indole[122], oxazole[122], benzoisoxazole[122], pyridine[122], and acridine[122] were obtained in this way.

In the presence of Raney nickel, trimethylsilylmethylphenyl piperidinoalkyl ketones were reduced to the corresponding carbinols[101].

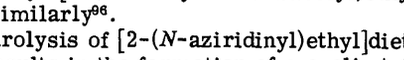
3. The Formation of Siloxanes

When acted upon by concentrated sulphuric acid, trimethyl-[β-(2-pyridyl)ethyl]silane splits off a methyl group. Subsequent hydrolysis yields tetramethyl-1,3-bis-[β-(2-pyridyl)ethyl]disiloxane which forms copolymers with alkyl- and aryl-polysiloxanes in the presence of KOH:[13,14]



Alkylpiperidyl-[97,121] and alkylcarbazolyl-polysiloxanes[110] were obtained similarly.

Alkaline hydrolysis of dialkylethoxy-(*N*-heterylalkyl)-silanes yields 1,3-bis-(*N*-heterylalkyl)tetramethyldisiloxanes:



where R_N = aziridinyl[116], pyrrolidinyl[68], piperidinyl[68], and morpholinyl[68].

Acetoxydimethyl-[β-(3-methyl-2-carbazolyl)ethyl]silane is hydrolysed similarly[96].

Alkaline hydrolysis of [2-(*N*-aziridinyl)ethyl]diethoxymethylsilane results in the formation of a cyclic trimer, while hydrolysis with 95% ethanol leads to a linear trisiloxane with terminal ethoxy-groups. Hydrolysis with an excess of water yields a polysiloxane oil which solidifies on standing[116].

Polysiloxanes were obtained by the hydrolysis of dichloromethyl-(2-succinimidoethyl)silane[64], triethoxy-(3-succinimidopropyl)silane[102,103], triethoxy-(3-phthalimidopropyl)silane[102,103], and diethoxymethyl-[γ-(2-pyridyloxy)propyl]silane[61]. Polysiloxane resins obtained by the hydrolysis of trichloro-[β-(2-pyridyl)ethyl]silane and its 4-analogue do not lose their solubility in inert solvents even after heating to 105°C for 24 h.[49,50,54]

4. Desilylation

The Si — C bond between the silicon atom and the heterocycle in (9-ethyl-3-carbazolyl)triphenylsilane and (9-ethyl-1-carbazolyl)triphenylsilane is readily cleaved by hydrogen chloride in glacial acetic acid[7]. The process also involves a partial cleavage of the Si — C_6H_5 bond.

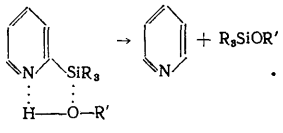
In the combined protonation and desilylation by perchloric acid in aqueous methanol, (9-ethyl-3-carbazolyl)trimethylsilane is more reactive than the corresponding dibenzofuran and dibenzothiophen derivatives[6].

(9-Ethyl-1-carbazolyl)triphenylsilane is cleaved by a solution of alkali in aqueous dioxan or ethanol but with appreciably greater difficulty than the corresponding dibenzofuran and dibenzothiophen derivatives. Under the above conditions, (9-ethyl-3-carbazolyl)triphenylsilane is stable[7].

Trimethyl-(2-pyrrolylmethyl)silane is cleaved by alcoholic alkali with much greater difficulty than benzyltrimethylsilane[4].

The Si — CH_2CO bond in the piperidide of diethylmethylsilylacetic acid[17] is cleaved quantitatively by 5% hydrochloric acid even at 0°C.

In contrast to the 3- and 4-isomers, trimethyl-(2-pyridyl)silane readily reacts with water, methanol, or ethanol to form pyridine and trimethylsilanol or alkoxytrimethylsilane[11,123]. The relative rates of desilylation at 50°C in water, methanol, and ethanol are 740 : 120 : 1. Higher alcohols do not enter into this reaction. The desilylation of trimethyl-(2-pyridyl)silane by water is inhibited by acids, while alkalies do not alter its rate. The reaction is of first order with respect to silane, has a high negative entropy of activation, and does not show an isotope effect. On the basis of these data, one may suppose that the desilylation proceeds via a five-membered cyclic complex[11]:

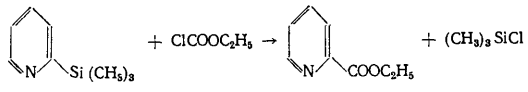


The above mechanism is confirmed by the finding that the hydrolysis and methanolysis of the optically active methyl-1-naphthylphenyl-(2-pyridyl)silane takes place with retention of its configuration[8].

Trimethyl-(2-pyridyl)silane is hydrolysed much faster than trimethyl-(2-pyridyl)germane but more slowly than trimethyl-(2-pyridyl)stannane[124]. The relative rates of hydrolysis of the silicon, germanium, and tin derivatives are $1 : 10^{-4} : 22$.

The rate of methanolysis of trialkyl-(2-pyridyl)silanes as a function of the groups linked to the silicon atom decreases in the following sequence: dimethyl > trimethyl > triphenyl > triethyl[10]. The rate of cleavage of the Si — C bond in methyl-substituted 2-trimethylsilylpyridines, $2\text{-}(CH_3)_3Si(C_5H_3N)R$, by water decreases in the following sequence as a function of the position of the methyl group[9,125] (the positions of the methyl group R and the relative rates of desilylation at 30.2°C are quoted): 4-methyl-(1.70)- > 6-methyl-(1.59) > 3-methyl-(1.58) > H(1) > 5-methyl-(0.71). The same sequence is largely followed also in methanolysis. The only exception is trimethyl-(3-methyl-2-pyridyl)silane which is least reactive in this case[9,125].

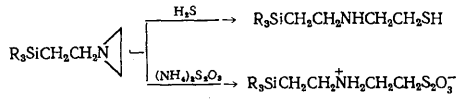
Trimethyl-(2-pyridyl)silane is readily desilylated by carboxylic acid chlorides and chlorocarbonic esters[126]:



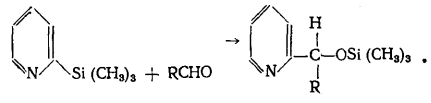
The Si — C bond in trimethyl-(2-pyridylmethyl)silane is cleaved by 95% aqueous ethanol with formation of hexamethyldisiloxane. However, in contrast to trimethyl-(2-pyridyl)silane, this requires prolonged heating and the reaction is catalysed by alkalies and especially by acids[22]. The rate of reaction decreases in the sequence trimethyl-(4-pyridylmethyl)silane > trimethyl-(2-pyridylmethyl)-silane > methyl-2-bis(trimethylsilyl)pyridine. There is a particularly marked difference between the rates of hydrolysis in an acid medium of the last two compounds, probably owing to steric factors which impede the protonation of the nitrogen atom preceding the attack on the silicon atom.

5. Other Reactions

The aziridine ring in [2-(*N*-aziridinyl)ethyl]trimethylsilane and [3-(*N*-aziridinyl)propyl]trimethylsilane is opened by hydrogen sulphide or ammonium thiosulphate with formation of the corresponding silyl derivatives of 2-aminoethanethiol and 2-aminoethanethiosulphuric acid[42]:



Trimethyl-(2-pyridyl)silane adds to aldehydes via the mechanism[127,128]:



A number of the usual reactions involving the functional groups linked to the heterocycle have also been carried out. These include the transformation CN → $CONH_2$ → NH_2 → OH in 2- and 4-substituted trimethyl-(3-pyridyl)-silanes[12], alkylation[96] and vinylation[129,130] of the NH group in trialkylsilylindoles, transamination of 3-dimethylaminomethyl-5-trimethylsilylindole with piperidine[5], the conversion of phthalimidoalkylsilanes into aminoalkylsilanes by treatment with hydrazine hydrate[18,20,21], and the formation of trimethylsilyl-substituted derivatives of indigo[131].

D. BIOLOGICAL PROPERTIES

The toxicity of trialkyl(piperidinylmethyl)silanes to white mice depends little on the nature of the alkyl groups linked to the silicon atom and varies in the range from 45 to 90 mg kg^{-1}.[132,133] Trialkyl-(3-piperidinopropyl)-silanes are somewhat more toxic than 2-piperidinylethyl and piperidinylmethyl derivatives[132-134]. Triethyl-(3-piperidinylpropyn-1-yl)silane (LD_{50} = 195 mg kg^{-1}) is less toxic than the corresponding vinyl and ethyl derivatives[64,132]. The toxicity of diethoxy-[3-(*N*-heteryl)propyl] methylsilanes decreases from the piperidine derivative to morpholine and thiamorpholine derivatives[135,136].

The hydrochlorides of diethylmethyl-(2-piperidinylethyl)silane and triethyl-(3-piperidinylpropyl)silane impair the coordination of the movement of white mice when administered in doses smaller by a factor of 8.2 and 7.3 respectively than the median lethal doses[132].

Trialkyl-(3-piperidinylpropyl)silanes exhibit a fungistatic activity in relation to the pathogenic fungi *Candida albicans*, *Epidermophyton* Kaufmann-Wolf, and *Trychophyton gypseum*. The minimum concentration of the compound inhibiting the growth of *Epidermophyton* Kaufmann-Wolf 41 decreases in the following sequence as a function of the groups linked to the silicon atom: diethylmethyl, methyldipropyl > methyldipentyl > dibutylmethyl, amounting to 12.5 μg ml^{-1} for the last silane.

E. PRACTICAL APPLICATIONS

Alkylpyrrolylsiloxanes and alkylpiperidinylsiloxanes are used as lubricating oils[97,121] and as modifying agents in various oils and resins[121]. Pyridylsiloxanes[121] and (pyridylalkyl)siloxanes[47] are used to synthesise ion-exchange resins.

The products of the joint hydrolysis of diethoxymethyl-[β-(4-pyridyl)ethyl]silane and dichlorodimethylsilane[55] and alkyl-(2-pyridyloxy)polysiloxanes[60] have been used to prepare elastomers. Polysiloxane elastomers based on alkylpyrrolylsiloxanes[92], alkyloxopyrrolidinylsiloxanes[62], and alkylsuccinimidosiloxanes[64] exhibit a high resistance to oils. Alkoxyalkylaziridinylsiloxanes form coatings on the surface of various materials which are resistant to the action of organic solvents[107].

Alkylpyrrolylsilanes have been suggested as antioxidants[137] and the addition of ethoxydimethyl(piperidinylmethyl)silane accelerates the formation of polyurethane foam plastics[68].

Alkylpyridylpolysiloxane salts are used as emulsifying agents[23,76] and also to impart hydrophobic properties to textiles[74,75,79] and to increase their fire resistance[75].

III. COMPOUNDS CONTAINING THE Si—N BOND

A. METHODS OF PREPARATION

1. Reaction of Halogenosilanes with Heterocyclic Bases

A general method for the preparation of organosilicon derivatives of nitrogen-containing heterocycles with an Si—N bond is the reaction of heterocyclic bases with halogenosilanes. Heterocycles with an unsubstituted N—H bond give rise to *N*-silylheterocycles and tertiary heterocyclic bases give rise to complexes or the reaction does not occur at all, depending on the structure of the halogenosilane.

The *N*-silylation of nitrogen-containing heterocycles may be represented by the general mechanism

$$R_NNH + Cl{-}Si\lessgtr \xrightarrow{+B} R_NN{-}Si\lessgtr + B{\cdot}HCl,$$

where R_NNH = aziridine[138-142], pyrrolidine[143-147], succinimide[148], the anhydrides of *N*-carboxy-α-aminoacids[149], phthalimide[65,150], piperidine[43,143,146,151-155], morpholine[152,155-159], perhydroazepine[156], and ε-caprolactam[160,161].

Ammonia[138], triethylamine[138,140,143,149,150,156,160,161], pyridine[65,138], or an excess of the heterocyclic base itself[139,141,146,147,153,154,159] are used as the acceptors (B) of the hydrogen halide liberated. The reaction can be achieved without a solvent[153] or in solution in ethyl ether[151,161], pentane[140,144], benzene[138,139,142,143,154,159], THF,[149] or dimethylformamide (DMF).[150] *N*-Silylpyrrolidine and *N*-silylpiperidine were obtained from iodosilane and the corresponding bases in the gas phase[146].

Tri-R-(*N*-heteryl)silanes and di-R-bis-(*N*-heteryl)-silanes can be obtained in this way readily and rapidly.

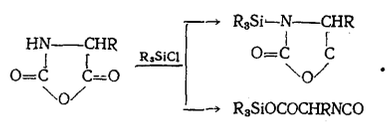
The rate of reaction of di-R-dichlorosilanes with ε-caprolactam decreases in the following sequence as a function of the organic substituent linked to the silicon atom[161]:

$$(CH_3)_2SiCl_2 > CH_3C_2H_5SiCl_2 > CH_3(i\text{—}C_4H_9)SiCl_2 > CH_3C_6H_5SiCl_2 > (C_6H_5)_2SiCl_2.$$

To obtain a high yield of R-tris-(*N*-heteryl)silanes, prolonged heating of the reactants is often necessary[154,156]. Tetrapyrrolidinylsilane was obtained in 50% yield by heating silicon tetrachloride with an excess of pyrrolidine[147]. A similar reaction with piperidine in ethereal solution yielded a mixture of trichloropiperidinylsilane, dichloropiperidinylsilane, and chlorotripiperidinylsilane[151]. To obtain tetrapiperidinylsilane, chlorotripiperidinylsilane must be heated with piperidine for 12 h at 250—270°C.[151] The reaction of morpholine with silicon tetrachloride yielded only chlorotrimorpholinylsilane[159].

A study of the stereochemistry of the reaction of chloromethyl-1-naphthylphenylsilane with pyrrolidine showed that it proceeds with inversion of configuration[144].

In certain cases, when *N*-heterylsilanes are synthesised from chlorosilanes, side reactions reduce their yield. For example, in the reaction of chlorosilanes with aziridine, silylation is accompanied also by the opening of the aziridine ring, which in the absence of hydrogen chloride acceptors becomes the main process[139,146]. Two products are formed in the silylation of the anhydrides of *N*-carboxy-α-aminoacids with chlorotrimethylsilane at 0°C in the presence of triethylamine[149]:



An increase of reaction temperature promotes the formation of an acyclic product polymerisation[149].

Depending on their structure, halogenosilanes react with pyridine to form both ionic and molecular complexes. Bromosilane[162,163], iodosilane[162-164], dibromosilane[162,163], di-iodosilane[162,163], and silicon tetraiodide[163,165,166] form complexes with pyridine which conduct electricity in acetone solutions and to which the following structures have been attributed: $[2C_5H_5N.SiH_3]^+X^-$, $[4C_5H_5N.SiH_2]^{2+}2X^-$, and $[4C_5H_5N.SiI_2]^{2+}2I^-$. In the presence of pyridine, dichlorosilane and chlorosilane form a current-conducting complex $H_2SiCl_2.2C_5H_5N$.[162,163] Fluorosilane and difluorosilane are decomposed by pyridine[163]. Silicon tetrafluoride[162,167-172], silicon tetrachloride[162,165,167,170,172-178], and silicon tetrabromide[162,165,167,170,179] form with pyridine, quinoline, and isoquinoline complexes of the type $SiX_4.2L$ (X = F, Cl, or Br; L = pyridine, quinoline, or isoquinoline). Data concerning the formation of complexes with a different structure[166,177,180-182] were not confirmed[162,168,170,178,183].

The acceptor capacity of tetrahalogenosilanes in relation to pyridine decreases in the sequence $SiCl_4 \sim SiBr_4 > SiF_4$, since the heats of formation $-\Delta H$ of complexes of the type $SiX_4.2C_5H_5N$ also decrease on passing from the chloro- (27.7 kcal mole^{-1}) and bromo- derivatives (26.8 kcal mole^{-1}) to the fluoro-derivative (17.9 kcal mole^{-1})[167,184,185]. The values of $-\Delta H$ quoted in other studies[170,186] are clearly too high.

When mixed silicon tetrahalides were allowed to react with pyridine, the complexes $SiCl_3Br_3.2C_5H_5N$, $SiCl_3Br.2C_5H_5N$, $SiCl_3I.3C_5H_5N$, and $SiCl_2I_2.4C_5H_5N$ were formed[187]. Ionic structures were attributed to the last two compounds[187,188]: $[3C_5H_5N.SiCl_3]^+I^-$ and $[4C_5H_5N.SiCl_2]^{2+}2I^-$.

Trichlorosilane forms a 1 : 2 complex with pyridine[162,167,168], a 1 : 3 complex with 4-vinylpyridine[55], and a 1 : 4 complex with 2-vinylpyridine[55]. Trifluorosilane and tribromosilane form 1 : 4 complexes with pyridine[163]. When bromomethylsilane and iodomethylsilane react with pyridine, 1 : 2 complexes are formed, while chloromethylsilane undergoes quantitative disproportionation under these conditions to methylsilane and dichloromethylsilane[189]. The latter forms with pyridine an extremely unstable complex of unknown composition. The greatest influence of halogenosilanes on the stoichiometry of pyridine complex has been observed with iodosilanes. Thus, whereas iodomethylsilane forms with pyridine a 1 : 2 complex, di-iodomethylsilane forms a 1 : 4 complex and di-iododimethylsilane and iodotrimethylsilane give rise to 1 : 1 complexes[163,189]. Bromotrimethylsilane forms with pyridine an unstable product of unknown

composition[163]. Fluorotrimethylsilane, chlorotrimethylsilane, dichlorodimethylsilane, and trichloromethylsilane do not interact with pyridine[163,167,173,189]. The claims of successful reactions of this type[190,191] were not confirmed in this respect.

Complexes of halogenosilanes with pyridine *N*-oxide[192], picoline[167,168], 2-hexylpyridine[164], 2,4-dimethylpyridine[166], 2,2-bipyridyl[164,165,182,193-204], and phenanthroline[187,196,204] have also been obtained.

Iodotriphenylsilane combines with 2,2′-bipyridyl to form a complex which dissociates in dichloromethane solution into an iodide anion and a triphenyl(bipyridylyl)-siliconium cation in which both nitrogen atoms form coordinate bonds with the silicon atom[193]. The reaction is more difficult with bromotriphenylsilane and does not occur at all with chlorotriphenylsilane.

The reactions of hexachlorodisilane and hexabromodisilane with pyridine involve the cleavage of the Si — Si bond[187]:

$$Cl_3SiSiCl_3 + 3C_5H_5N \rightarrow 2C_5H_5N \cdot SiCl_4 + 1/n\,(C_5H_5N \cdot SiCl_2)_n .$$

Tetrapropylammonium pentafluorosilicate forms an unstable complex with pyridine[205].

Pyridine complexes, similar to those of halogenosilanes, are formed also by a series of other organosilicon compounds: silicon tetraisothiocyanate[206], tetranitrate[207], and oxalate[208], silyltetracarbonylcobalt, and silylpentacarbonylmanganese[209-211]. Poly-(2-vinylpyridine *N*-oxide) (PVPO) forms a complex with silicic acid[212]. Possibly such complex formation is in fact responsible for the increase of the resistance of macrophages to the action of quartz dust under the influence of PVPO.[213,214]

2. Organometallic Synthesis

In the synthesis of Si — N derivatives, *N*-organometallic derivatives of the heterocyclic base are allowed to react with chlorosilanes instead of the base itself:

$$R_NNM + ClSi\lessgtr \rightarrow R_NN{-}Si\lessgtr + MCl$$

M=Li, Na, K, MgBr

Using *N*-lithium-substituted heterocycles, *N*-R-silyl derivatives of pyrrole[215,216] and pyrrolidine[144] were obtained in this way. The reaction of chloromethyl-1-naphthylphenylsilanes with pyrrolidinyl-lithium takes place with inversion of configuration[144].

The reaction of 9-carbazolylsodium with silicon tetrachloride in benzene solution yielded di-(9-carbazolyl)dichlorosilane[217].

N-Pyrrolylsilanes[143,218-220] (and not *C*-pyrrolylsilanes as believed previously), succinimidosilanes[221], phthalimidosilanes[63,221], and *N*-indolylsilanes[143] have been synthesised on the basis of *N*-potassium-substituted heterocycles. The reaction of indolylpotassium with chlorotrimethylsilane is more difficult than the reaction of pyrrolylpotassium[143].

N-Pyrrolylsilanes were also obtained from pyrrolylmagnesium bromide and R-chlorosilanes[215,216,218,222,223]. Pyrrolidinyl-, piperidinyl-, and morpholinyl-silanes were obtained similarly via organomagnesium derivatives[224].

Triphenylsilyl-lithium silylates piperidine with formation of triphenylpiperidinylsilane[225]:

$$(C_6H_5)_3SiLi + HN\bigcirc \rightarrow (C_6H_5)_3SiN\bigcirc + LiH .$$

The reaction of bis(trimethylsilyl)mercury with pyridine leads to the formation of 1,1′-bis(trimethylsilyl)-1,1′,4,4′-tetrahydro-4,4′-bipyridyl[226]:

$$R_3SiHgSiR_3 + 2N\bigcirc \rightarrow R_3SiN\bigcirc\!\!-\!\!\bigcirc NSiR_3 + Hg .$$

2-Methylpyridine and 4-methylpyridine react similarly.

1,4-Bis(trimethylsilyl)-1,4-dihydropyridine was obtained by the reaction of pyridine with chlorotrimethylsilane in the presence of alkali metals[227]:

$$N\bigcirc + 2M + 2ClSiR_3 \xrightarrow{-2MCl} R_3Si{-}\bigcirc NSiR_3 .$$

3. Silylation with Aminosilanes and Silazanes

When aminotriethylsilane is heated to boiling with pyrrolidine over a period of 6 h, triethylpyrrolidinylsilane is formed in 95% yield[143]:

$$(C_2H_5)_3SiNH_2 + HN\square \rightarrow (C_2H_5)_3SiN\square + NH_3 .$$

Piperidine enters into this reaction with somewhat greater difficulty. The yield of triethylpiperidinylsilane reaches 89% only after refluxing the reaction mixture for 10 h.[143] 2-Aminothiazole reacts similarly[228].

Dialkylaminotrimethylsilanes were used instead of aminotrialkylsilanes for the *N*-trimethylsilylation of piperidine[42], perhydroazepine[156], morpholine[156], 2-aminothiazole and 2-aminobenzothiazole[229], δ- and ϵ-caprolactams[160], and also proline and tryptophan esters[230].

Hexamethyldisilazane silylates the NH group of heterocycles with much greater difficulty than do aminotrialkylsilanes. Frequently catalytic amounts of ammonium sulphate[218,231] or chloride[231] are essential for the occurrence of this reaction. Thus after pyrrole has been refluxed for 12 h with hexamethyldisilazane, no reaction was observed. On the other hand, in the presence of ammonium sulphate the yield of trimethyl-(*N*-pyrrolyl)silane reached 50% after only 2 h.[231] Indole was found to be somewhat more reactive than pyrrole[231].

After refluxing for 3 h a mixture of piperidine and hexamethyldisilazane without a catalyst, the yield of trimethylpiperidinosilane reached only 16%, but in the presence of chlorotrimethylsilane it increased to 35%. The addition of ammonium chloride or sulphate increased the yield further to 52 — 55%.[230] The yield of the silylation product depends also on the nature of the solvent and is a maximum when the reaction is carried out in quinoline (61%). Toluene (54%) and decalin (54%) are also satisfactory solvents. In ethyl ether, trimethylpiperidinosilane is not formed at all[230].

The reaction of nitrogen-containing heterocycles with hexamethyldisilazane has also been used to synthesise *N*-trimethylsilylpyrrolidinone[232], *N*-trimethylsilylsuccinimide[221], and *N*-trimethylsilylindoline[231].

4. Silylation with Silanes containing Unsubstituted Hydrogen Atoms

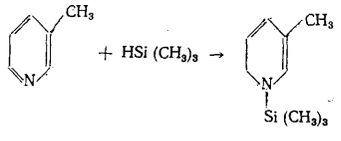
In the presence of alkali metals or Pd/C, silanes with unsubstituted hydrogen atoms enter into dehydrocondensation reactions with heterocyclic compounds containing the N — H bond:

$$R_NNH + H{-}Si\lessgtr \rightarrow R_NN{-}Si\lessgtr + H_2 .$$

Aziridine[35,39,233,234], 2-substituted aziridines[235], pyrrolidine[236], and piperidine[237] were silylated in this way. The reaction with aziridine proceeds more readily than with secondary aliphatic amines and piperidine and may be catalysed by potassium, sodium, and lithium. Aziridine is silylated at the maximum rate by tri-R-silanes containing phenyl and benzyl groups. Trialkylsilanes react more slowly and with alkoxysilanes the rate of dehydrocondensation is lowest. When aziridine reacts with vinylsilanes, the dehydrocondensation process competes with the addition of aziridine to the vinyl group[39]. 2,2-Dimethylaziridine reacts with greater difficulty than 2-methyl- and 2-phenyl-aziridines[235].

The dehydrocondensation of optically active methyl-1-naphthylphenylsilane with pyrrolidine in the presence of palladium and charcoal takes place with inversion of configuration[236].

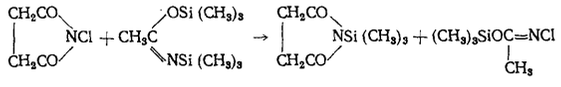
Trimethylsilane reacts with pyrridine in the presence of palladium on charcoal to form *N*-trimethylsilyl-1,2-dihydropyridine (yield about 25% after 25 h at 30°C), *N*-trimethylsilyl-1,4-dihydropyridine (35%), *NN'*-bis(trimethylsilyl)-1,1'-dihydro-4,4'-bipyridyl (25%), *N*-trimethylsilyl-1,2,3,6-tetrahydropyridine (12%), and many other trimethylsilylhydropyridines[238-240]. Pd/C is a more active catalyst than Rd/C, palladium(II) chloride, platinum, and Ru/C. However, Rd/C is more selective, driving the process mainly towards the formation of *N*-trimethylsilyl-1,4-dihydropyridine[239]. With 3-methylpyridine, trimethylsilane adds quantitatively to the 1,4-positions in the presence of Pd/C:[239]



4-Methylpyridine reacts four times as slowly as pyridine and it proved altogether impossible to add trimethylsilane to 2-methylpyridine[239].

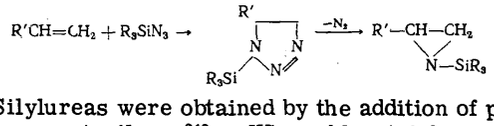
5. Other Methods

N-Trimethylsilylsuccinimide was obtained by the reaction of *N*-chlorosuccinimide with bis(trimethylsilyl)-acetamide[241,242]:



The same compound is formed when *N*-bromosuccinimide reacts with ethyl trimethylsilylacetate[242], bromotrimethylsilane in the presence of styrene[243], and hexa-alkyldisilanes[244,245]. Phthalimide and homodihydrocarbostyril are silylated by bis(trimethylsilyl)acetamide like succinimide[246,247].

Trimethyl-(2-R-*N*-aziridinyl)silanes were obtained by the thermal decomposition of *N*-trimethylsilyl derivatives of dihydro-1,2,3-triazole, which is formed as an intermediate when azidotrimethylsilane adds to alkenes[248]:



N-R-Silylureas were obtained by the addition of piperidine to isocyanatosilanes[249]. When chlorotriphenoxysilane was allowed to react with hexamethylenediamine, the formation of triphenoxy-(*N*-perhydroazepinyl)silane was observed, probably as a result of the cyclisation of (6-aminohexylamino)triphenoxysilane formed initially[250].

B. PHYSICAL PROPERTIES

Electronic[198,222,239], vibration[55,146,147,156,159,161,168,188,196,205,206,209,210,218,234,239,243,251-254], and ^{1}H NMR [140,147,156,239,243,247,255] spectra of *N*-heterylsilanes were not investigated systematically. In both cases spectroscopic data were used only to confirm the structures of the compounds synthesised.

In a number of instances, an attempt was made to assign the bands in the infrared absorption spectra to the corresponding Si — N stretching vibrations. The absorption bands at 695 cm^{-1} for pyrrolidinylsilane[146,253], at 705 cm^{-1} for piperidinylsilane[146], at 910 cm^{-1} for iodopiperidinylsilane[254], at 932 cm^{-1} for chloropiperidinylsilane[254], at 945 — 950 cm^{-1} for R-piperidinylsilanes[156], at 960 cm^{-1} for R-morpholinylsilanes[156], at 975 cm^{-1} for chlorotrimorpholinylsilane[159], and at about 1057 cm^{-1} for trimethyl-(*N*-pyrrolyl)silane[218] were assigned to ν_{as}(S — N).

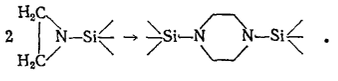
Quantum-chemical calculations have been made for (*N*-pyrrolyl)silanes on the basis of spectroscopic data and it has been concluded that $p_\pi - d_\pi$ interaction takes place in their molecules[222,223]. ^{1}H NMR spectra confirmed the occurrence of such interaction also in the (*N*-aziridinyl)-trimethylsilane molecule[255].

X-Ray diffraction analysis[256] established that the complex $2C_5H_5N.SiF_4$ has a centrosymmetric *trans*-configuration with an Si — N distance of 1.93 Å.

C. CHEMICAL PROPERTIES

1. Thermal Reactions

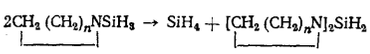
On heating to 250°C, tri-R-(*N*-aziridinyl)silanes are converted into piperazine derivatives[257]:



When platinised charcoal is introduced into the reaction mixture, the yields of products are unaffected. The addition of azobisisobutyronitrile makes it possible to obtain higher yields even when the reaction temperature is reduced to 200°C.

The nature of the organic groups linked to the silicon atom in the tri-R-(*N*-aziridinyl)silane molecule has a considerable influence on its reactivity. Thus, whereas the yield of *NN'*-bis(trimethylsilane)piperazine is only 25% after heating (*N*-aziridinyl)triethylsilane for 5 h at 250°C, in the case of the diethylphenyl derivative the yield of the piperazine derivative reaches 40%, while (*N*-aziridinyl)-diethoxyethylsilane does not undergo any changes under these conditions[257].

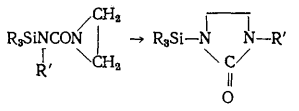
On heating in a sealed tube at 260°C, *N*-silylpyrrolidine and *N*-silylpiperidine disproportionate[146]:



In contrast, trialkyl-(*N*-pyrrolyl)silanes remain unchanged on heating to 260°C for 12 h.[218]

Urea derivatives obtained by the reaction of R-(*N*-aziridinyl)silanes with isocyanates rearrange to

2-imidazolidinone derivatives at a temperature as low as 140°C:[140]



2. Desilylation

The Si — N bond in *N*-heterylsilanes dissociates with elimination of the silyl group under the influence of various reagents: hydrogen chloride[144,146,258], sulphur halides[143], phosphorus[229,259], boron[270], acyl halides[155], carboxylic acid *N*-halogenoamides[242], water[144,155,156,159,168,174,216,218], alcohols[168,218,238-240,261], hydrogen sulphide[258], oxygen compounds of sulphur[258], ammonia[218,230,258], *NN'*-dialkylureas[247,262,263], and lithium aluminiumhydride[144,145].

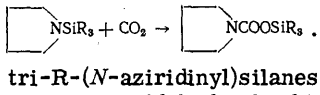
This reaction has been used both for the synthesis of heterocyclic compounds (for example, 1,4-dihydropyridine[238-240]) and their derivatives (for example, *N*-pyrrolylphosphines[259] and di-*N*-piperidinyl sulphide[143]) and for the silylation of compounds containing an active hydrogen atom (for example, *N*-hydroxymethyl-*N*-methylformamide[261] and *NN'*-dialkylureas[247,262,263]).

A study of the stereochemistry of the hydrolysis[144] and cleavage of optically active methyl-(1-naphthyl)phenylpyrrolidinylsilane with boron trifluoride[260] established that these reactions take place with inversion of configuration, while in the cleavage by hydrogen chloride and in the reduction by lithium aluminium hydride the configuration is retained[144].

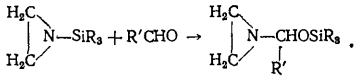
Many reactions which involve the dissociation of the Si — N bond at room temperature can lead to the formation of adducts with retention of this bond at a lower temperature. For example, at −88°C pyrrolidinylsilane and piperidinylsilane form hydrogen chloride complexes of the type $C_5H_{10}NSiH_3 \cdot 2HCl$, which decompose with dissociation of the Si — N bond when the temperature is raised[146]. At −46°C piperidinylsilane and pyrrolidinylsilane form 1:1 adducts with iodosilane[146,254].

3. Addition to Carbonyl Compounds

Tri-R-(*N*-heteryl)silanes add to carbon dioxide and also to carbon disulphide according to the mechanism[264]

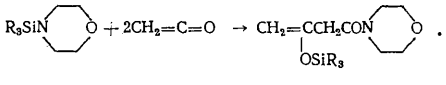


The reactions of tri-R-(*N*-aziridinyl)silanes with aliphatic, aromatic, and heterocyclic aldehydes lead to the formation of tri-R-(*N*-aziridinylalkoxy)silanes[265,266]:

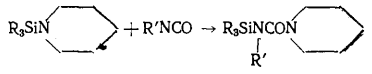


The addition of *N*-trimethylsilylpyrrolidinone[261,267] and *N*-trimethylsilylsuccinimide[261] to benzaldehyde and of trimethylpyrrolidinylsilane and trimethylpiperidinylsilane to chloral[268] takes place similarly.

Trimethylmorpholinylsilane reacts with keten at room temperature to form the morpholide of β-(trimethylsiloxy)vinylacetic acid[269,270]:

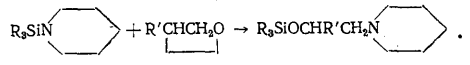


The addition of tri-R-(*N*-aziridinyl)silane[140] and tri-R-piperidinylsilanes[271] to organic isocyanates leads to the formation of *N*-tri-R-silyl-substituted ureas:



4. Reactions with Oxirans and Lactones

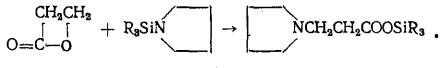
The reaction of trimethylpiperidinylsilane with R'-oxirans at 80°C takes place with the opening of the oxiran ring via the mechanism[272,273]



A necessary condition for the occurrence of this reaction is the presence of powerful electro-accepting substituents in the group R' of the oxiran. For example, when trimethylpiperidinylsilane reacts with trichloromethyloxiran, the yield of (1-trichloromethyl-2-piperidinylethoxy)trimethylsilane is 89% after only 1.3 h, while with chloromethyloxiran the yield of the reaction product does not exceed 45% even after heating for 22 h and methyloxiran and trimethylpiperidinylsilane do not react at all in a sealed tube at 80°C.

The reaction of substituted oxirans with *N*-trimethylsilylpyrrolidinone takes place via a similar mechanism[274,275].

Trimethylpyrrolidinylsilane, trimethylpiperidinylsilane, and trimethylmorpholinylsilane react with β-propiolactone on heating to 80°C with formation of trimethylsilyl esters of β-(*N*-heteryl)propionic acid[224,276,277]:



Trimethylpyrrolidinylsilane reacts faster than the corresponding piperidinyl- and diethylamino-silanes[276].

D. PRACTICAL APPLICATIONS

Trialkylpiperidinylsilanes and trialkylmorpholinylsilanes are used as catalysts for the hydrosilylation of acrylonitrile with trichlorosilane which promote the formation of the β-isomer[152,157,158,278].

Trimethylmorpholinylsilane and methylphenyldipyrrolidinylsilane are used in the preparation of organosilicon polymers[279].

Dihydropyridylsilanes inhibit the oxidation of various polymers and increase their resistance to the action of light[240].

Organosilicon derivatives of aziridine have been used to prepare water- and oil-repellent fabrics[138,142].

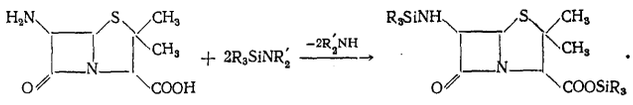
IV. COMPOUNDS CONTAINING THE Si — O BOND

A. METHODS OF PREPARATION

A number of general methods for the silylation of the hydroxy-group have been used to synthesise organosilicon derivatives of nitrogen-containing heterocycles with the Si — O bond. In the presence of tertiary amines, chlorosilanes were used to silylate *N*-hydroxymethylphthalimide[150,280], 2-hydroxypyridine[281-283] (Ismail[283] claims that

the *N*-silylation product was obtained), 2- and 4-pyridylalkanols[284], 4-hydroxy-2,2,6,6-tetramethylpiperidine 1-oxide[285-289], *N*-carboxyanhydrides of hydroxy-α-amino acids[290], proline[291], and picolinic[292], nicotinic[293] and 6-aminopenicillanic[294-296] acids.

The trimethylsilyl ester of 6-trimethylsilylaminopenicillanic acid forms in 29% yield when a suspension of calcium 6-aminopenicillanate is heated with chlorotrimethylsilane in the presence of triethylamine for 3 h to 60°C. When the sodium salt is used instead of the calcium salt, the yield of product falls to 25%.[294] The same compound is formed in 98.5% yield when 6-aminopenicillanic acid reacts with (diethylamino)trimethylsilane at 80 – 150°C with simultaneous distillation of the diethylamine evolved in the process[294]:



The trimethylsilyl ester of 7-trimethylsilylaminocephalosporanic acid is obtained similarly[297].

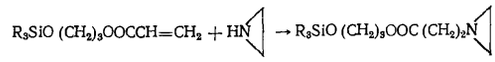
When 6-aminopenicillanic acid is heated with hexamethyldisilazane in nitrogen at 120°C for 3 h, the trimethylsilyl ester of 6-trimethylsilylaminopenicillanic acid is formed in 64.5% yield[294,298].

Silazanes have also been used to silylate penicillins[299-301], lincomycin[302,303], hydroxyproline[304,305], tryptophan[304], pyridylalkanols[306,307], piperidinylalkanols[307,308], morpholinylalkanols[309], and 8-hydroxyquinoline[310].

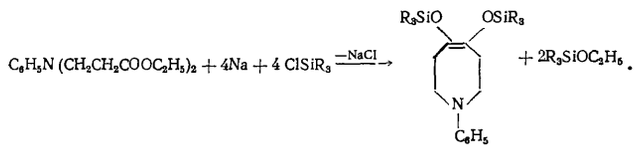
Oxindole and tryptophan have been silylated with bis(trimethylsilyl)acetamide[246,247].

Many reactions leading to the formation of derivatives of nitrogen-containing heterocycles with the Si – O bond were already considered above in the discussion of the chemical properties of compounds with Si – C and Si – N bonds. These include the reactions of trialkyl-(2-pyridyl)silanes with aldehydes[127,128] and the reactions of *N*-heterylsilanes with aldehydes[261,264-268], oxirans[272-275], keten[269,270], and lactones[224,276,277].

Aziridine, azetidine, and pyrrolidine add to the double bonds of trialkylvinyloxysilanes and 3-(trimethylsiloxy)-propyl acrylates with formation of the corresponding 2-(*N*-heteryl)ethoxysilanes and 3-(trimethylsiloxy)propyl β-(*N*-heteryl)propionates[311]:



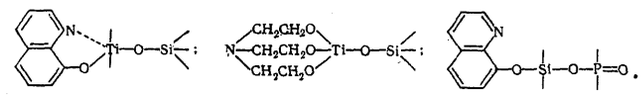
When *NN*-bis-(β-ethoxycarbonylethyl)aniline is heated with sodium and chlorotrimethylsilane in toluene solution, it is cyclised and silylated with formation of 4,5-bis(trimethylsiloxy)-1-phenyl-3,2,6,7-tetrahydroazepine[312]:



Tri-R-silanols[313] and 1,1,3,3-tetra-R-disiloxane-1,3-diols[314-317] form complexes with piperidine, picoline, and quinoline.

When 2-hydroxypyridine *N*-oxide was allowed to react with silicic acid, a complex was formed, which was characterised by conversion into its chloride, hexachlorostannate, and tetrachloroferrate[318] and resolved into optical isomers with the aid of the disodium salt of dibenzoyl-L-tartrate[319].

Oxinatotitanosiloxans[320-341], cyclic nitriloethylene tri-R-siloxytitanates[342], and dioxinatosilicon bisphosphorodichloridate[343] are obtained by the general methods used for the formation of the Ti – O – Si [344] and P – O – Si [345] groups:



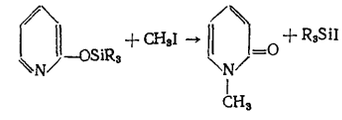
B. PHYSICAL, CHEMICAL, AND BIOLOGICAL PROPERTIES

Studies of the ultraviolet spectra of oxinatosilanes showed that dioxinatodiphenylsilane (λ_{max} = 370 nm) has a chelate structure with a hexacovalent silicon atom, in contrast to trimethyloxinatosilane and dimethyldioxinatosilane[310].

A high inversion frequency of the nitrogen atom in the trialkyl[α-(*N*-aziridinyl)alkoxy]silane molecule was demonstrated by ^{1}H NMR.[346] ^{1}H NMR [272,346,347] and ESR [286,287] spectra were also used to confirm the structures of the compounds synthesised.

The majority of organosilicon derivatives of nitrogen-containing heterocycles with the Si – O bond are readily hydrolysed by water[224,273,283,310,312]. Their Si – O bond is cleaved by methanol[272] and acetic acid[272].

Pyridyloxysilanes readily react with alkyl halides[281,283]. Thus, in contrast to α-pyridone which reacts with methyl iodide only at 100°C under pressure, 2-(trimethylsiloxy)-pyridine reacts with methyl iodide after only brief heating on a water bath with formation of a high yield of *N*-methyl-α-pyridone[281]:



2-(Trimethylsiloxy)pyridine interacts with 2,3,4,6-tetra-acetyl-1-bromoglucose in the presence of $AgClO_4$ even at room temperature, forming *N*-(2,3,4,6-tetra-acetylglucosido)-α-pyridone[281].

Trimethylsilyl esters of 6-trimethylsilylaminopenicillanic acid react with carboxylic acid anhydrides or chlorides and are converted into trimethylsilyl esters of penicillins, which give high yields of the corresponding penicillin on hydrolysis with water[294-296,298,299,348,349]. Cephalosporins are obtained similarly[297].

The complex of benzylpenicillin and potassium methylsiliconate proved to be effective in the treatment of myxomatosis (a virus disease), which is not susceptible to the action of either potassium methylsiliconate or benzylpenicillin separately[350]. Thus it has been shown that the spectrum of the activity of penicillin can be extended by employing its complex with potassium methylsiliconate.

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Modern Ideas on the Biosynthesis of Lignin

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According to modern ideas, the biosynthesis of lignin consists of two main stages, the first of which includes the formation of aromatic monomeric precursors of lignin synthesised in the plant from carbon dioxide via carbohydrates and the second involves the construction of the lignin macromolecule from the monomeric precursors.
The review deals with studies which led to the determination of the individual stages in the biosynthesis of the aromatic precursors of lignin in plants and also with the main features of the formation of polymeric lignin in its synthesis from coniferyl alcohol *in vitro*. Certain aspects of the biosynthesis of lignin *in vivo* have also been considered.
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I. INTRODUCTION

There is no doubt that the study of the formation of lignin in plants is of considerable theoretical and practical interest. As will be shown below, the elucidation of the main aspects of the biosynthesis of lignin yielded much information about its structure. It is also evident that a knowledge of the characteristics of the formation of lignin in plants is necessary for the solution of important problems in the chemistry of lignin such as the relation between various components of plant tissue, the inhomogeneity of lignin, etc. Moreover, information about the formation of lignin in plants may prove valuable also in the development of rational industrial methods for the delignification of vegetable raw materials. Finally, one must emphasise that the study of the biosynthesis of lignin is of interest not only for the chemistry of wood but also for such branches of biology as plant physiology, plant biochemistry, etc.

The problems of the formation of lignin in plants have for a long time attracted the attention of chemists working in the field of the chemistry of lignin but it was not until 1950 to 1960 following the application of new research techniques (the employment of tracer techniques, the method of tissue culture, various biochemical techniques, etc.) that considerable progress has been achieved in this field. The problems of the biosynthesis of lignin in plants have been frequently considered in a number of reviews and monographs [1-13] written mainly by specialists working in this field and therefore dealing primarily with the investigators' own ideas.

The general biosynthesis of lignin in plants can be represented schematically as follows:

$$\text{carbon dioxide} \xrightarrow{\text{photosynthesis}} \text{carbohydrates}$$
$$\xrightarrow{\text{aromatisation}} \text{primary structural elements}$$
$$\xrightarrow{\text{dimerisation}} \text{secondary structural elements}$$
$$\xrightarrow{\text{formation of polymeric molecules}} \text{lignin.}$$

In the biosynthesis of lignin, it is possible to isolate two main stages, the first of which involves the formation of aromatic monomeric precursors of lignin synthesised in the plant from carbon dioxide via carbohydrates and the second involves the formation of lignin macromolecules from the monomeric precursors. Both stages will be examined in detail below.

However, in considering the biosynthesis of lignin in plants one must not forget that the lignification process always takes place in conjunction with other processes involved in the formation of the cell wall. It is known from plant anatomy that wood cells are formed from live cambial tissue which persists throughout the life of dicotyledonous plants and on the activity of which depends the growth of the thickness of the trunk. Owing to the periodic activity of cambium, the wood elements formed from it are deposited during the vegetative period in a certain sequence which results in the formation of annual layers. Secondary wood consists mainly of conducting and mechanical elements which loose their protoplasmic content at an early stage and are converted into physiologically dead tissues. However, wood includes also the live cells of the wood parenchyma and wood rays, the metabolism of these cells characterising the vital properties of secondary wood. On the basis of the foregoing, it is interesting to examine the lignification of plant cell walls within the framework of the metabolism characteristic of cambial and meristematic tissues, since the lignification process is part of the complex biochemical activity of the young cells of the xylem [14-17]. However, examination of this aspect of the biosynthesis of lignin is evidently a task for the future since at present many biochemical processes occurring in the formation of the cell wall have been inadequately investigated. Nevertheless in the discussion below of the chemical aspects of the biosynthesis of lignin, certain problems of the formation of cell walls will be partly elucidated.

Finally the formation of lignin—a phenolic polymer—cannot be treated in isolation from the biosynthesis of many phenolic compounds widely distributed in plants (essential oils, anthocyanins, lignans, tannins, alkaloids, etc.). A definite chemical relation between the elementary structural units of lignin and the above phenolic compounds is evidently a consequence of similar processes involved in the biosynthesis of aromatic substances in plant tissues [18-20]. For a number of reasons, the consideration of these problems is also omitted from this review.

II. FORMATION OF MONOMERIC INTERMEDIATES IN THE BIOSYNTHESIS OF LIGNIN

1. The Role of Carbon Dioxide in the Lignification Process

In 1950 Hartt and Burr [21] reported for the first time that, after sugar cane plants have been exposed to an atmosphere of $^{14}CO_2$ in the dark, the lignin isolated from them is radioactive. Subsequent experiments by Stone, who exposed wheat plants to both prolonged [22] and brief [23] exposure to an atmosphere of $^{14}CO_2$, demonstrated convincingly the involvement of carbon dioxide in the biosynthesis of lignin. After the nitrobenzene oxidation of lignins isolated from the experimental wheat plants, radioactive vanillin, *p*-hydroxybenzaldehyde, and syringaldehyde were obtained. The participation of carbon dioxide in the biosynthesis of lignin was also confirmed by the data of Kreitsberg and coworkers [24,25], who performed experiments with fast growing poplar trees. At the present time the idea that carbon dioxide is the starting material in the biosynthesis of lignin in higher plants is generally accepted.

2. The Role of Carbohydrates in the Lignification Process

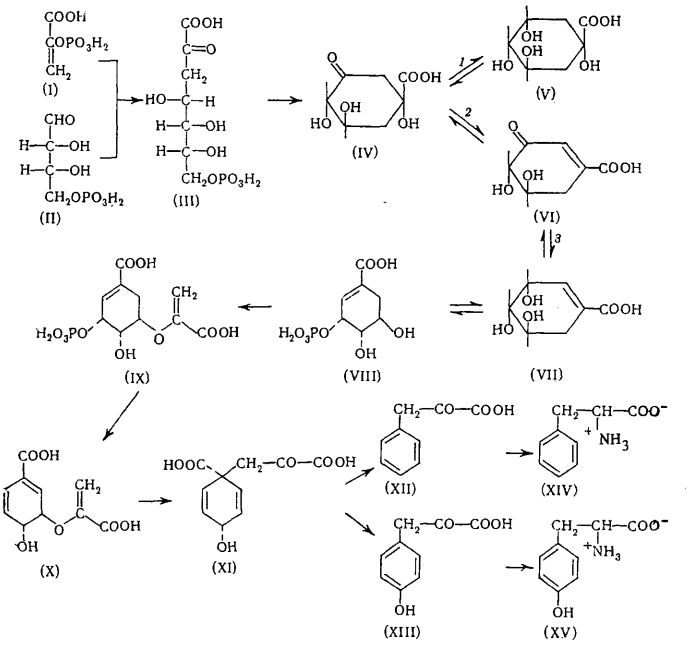
An extensive study on the carbohydrate precursors of lignin was carried out by a group of investigators under the supervision of Nord and Schubert. Schubert and Acerbo [26] demonstrated for the first time an enzymatic mechanism for the conversion of D-glucose into lignin in plants. They introduced labelled D-glucose into the wood of the Norway spruce from the precambial layer of which they isolated radioactive lignin after allowing a period for the metabolism to operate. In a subsequent study by Acerbo et al. [27], a Norway spruce tree was fed [1-^{14}C]-D-glucose and [6-^{14}C]-D-glucose for 28 days, the lignin was oxidised to vanillin, and the latter was decomposed in order to determine the radioactivity of each individual carbon atom. It was shown that in both cases ^{14}C is incorporated preferentially in the 2-, 6-, and 7-positions (carbonyl carbon atoms) and in the 8-position (methyl carbon atom) of the vanillin molecule. These results were confirmed by Kratzl and Faigle [28,29]. Hasegawa and Higuchi also demonstrated the involvement of glucose in the biosynthesis of lignin by introducing labelled glucose into young stems of the eucalyptus [30] and also in tissue culture experiments [31].

However, it has been shown that D-glucose is not the only carbohydrate capable of being converted into lignin. Thus, after injecting radioactive pentoses into the wood of the fast growing poplar, Sergeeva and Kreitsberg [32] isolated radioactive lignin. The involvement of pentoses in the formation of the lignin macromolecule confirmed Klason's hypothesis [33,34] that lignin may be formed from pentosans as a result of intracellular fermentation. Kratzl and Zauner [35] introduced into spruce wood xylitol labelled at all the carbon atoms and observed that the xylitol is incorporated both in polysaccharides and in lignin.

3. The Aromatisation Process

The classical studies by Davis [36-38] and Sprinson [37,39] on mutants of the *Escherichia coli* bacterium established very reliably one of the pathways in the biosynthesis of aromatic aminoacids from carbohydrate precursors. The overall results of these investigations are compiled in Scheme 1.

Scheme 1



According to the sequence presented in Scheme 1, the condensation of phosphoenolpyruvic acid (I), formed in the glycolysis of glucose, and D-erythrose-4-phosphate (II), formed from glucose in the pentose reaction cycle (the "pentose cycle"), leads to the formation of 2-oxo-7-phospho-3-deoxy-D-arabinoheptonic acid (III), which subsequently cyclises into 5-dehydroquinic acid (IV). Subsequent biosynthesis proceeds via the following obligatory intermediates: 5-dehydroshikimic (VI) and shikimic (VII) acids. 5-Phosphoshikimic acid (VIII) combines with a molecule of phosphoenolpyruvic acid (I) to form 3-enol-5-phosphopyruvoylshikimic acid (IX) which is converted into prephenic acid (XI) via the intermediate chorismic acid (X), the presence of which in the reaction cycle was established for the first time by Gibson [40-42]. As shown in Scheme 1, prephenic acid may be decarboxylated with formation of aromatic compounds via two pathways, in only one of which is the ring hydroxyl retained. Thus the first aromatic compounds synthesised by mutants of *E. coli* from carbohydrates are phenylpyruvic acid (XII) and its 4-hydroxy-derivative (XIII), which are converted by transamination into L-phenylalanine (XIV) and L-tyrosine (XV) respectively. Since the above scheme has been considered in detail in all the reviews of the biosynthesis of lignin, we shall not discuss it in depth apart from mentioning that, according to Davis' data [36], shikimic acid (VII) is an obligatory intermediate in the biosynthesis of aromatic compounds in *E. coli*.

At the present time the majority of investigators [3-14] believe that in higher plants the aromatisation of carbohydrate material takes place via shikimic acid (Scheme 1). This hypothesis is based on a number of considerations. Thus Brown and Neish [43] introduced the following ^{14}C-labelled compounds into a solution with wheat and maple cuttings: shikimic acid (VII), L-phenylalanine (XIV), and protocatechuic acid and showed that (VII) and (XIV) were incorporated into the lignin of wheat and maple. Eberhardt

and Schubert[44] converted labelled shikimic acid into the aromatic rings of the lignin macromolecule by implanting the acid in sugar cane plants. The vanillin obtained after the nitrobenzene oxidation of lignin from the experimental plant was decomposed in order to determine the radioactivity of each individual carbon atom. It was found that the vanillin atoms in the 6-, 2-, and 5-positions contained 44, 41, and 0% of the total radioactivity, while the atoms of the initial shikimic acid contained 52, 43, and 0% of the total radioactivity in the same positions. The results of this investigation convincingly demonstrate the conversion of shikimic acid into lignin without any rearrangement of the carbon atoms in its six-membered ring. The studies by Neish and coworkers showed that labelled shikimic acid is incorporated into both phenylalanine (XIV) and tyrosine (XV) by sage[45,46], wheat[47], and buckwheat[47] plants. Since these plants belong to different families, the authors suggested that vascular plants can in general employ shikimic acid for the synthesis of aromatic aminoacids.

Hasegawa and coworkers[48], who studied the distribution of shikimic acid (VII) in plants, established that it is widely distributed in higher plants and particularly in gymnosperms. Among the latter, shikimic acid was detected in greatest amounts in the pine family and the cryptomeria and among angiosperms in the magnolia family. Later the same investigators[49] detected shikimic acid in the leaves of 82 plant species (of the 164 investigated). According to Higuchi's data[50], among 96 woody plant species investigated 70 contained shikimic acid. The wide distribution of shikimic acid in plants is also indicated by Plouvier's results[51-54].

Apart from the data discussed above, the similarity of the biosynthetic pathways to aromatic compounds in micro-organisms and higher plants is also convincingly demonstrated by the observation in plants of enzymes which catalyse some of the reactions shown in Scheme 1. Thus Nandy and Ganguli[55,56] showed that, in the presence of extracts from mung bean seedlings, D-erythrose-4-phosphate (II) and phosphoenolpyruvic acid (I) are converted into 5-dehydroshikimic acid (VI). Mitsuhashi and Davis[57] detected in the pea and in spinach 5-dehydroquinate hydrolyase (5-dehydroquinate dehydratase) (EC 4.2.1.10.)†, which catalyses the (IV) → (VI) conversion (reaction pathway *2*). 5-Dehydroquinate dehydratase was also isolated from the buds of red cabbage[59]. Balinsky and Davis[60,61] isolated shikimate: NADP oxidoreductase‡(shikimate dehydrogenase) (EC 1.1.1.25) from the etiolated epicotyledons of pea seedlings and investigated the effects of various phenolic compounds on them. They found that the enzyme is associated with NADP and does not act on quinic and dehydroquinic acids. Nandy and Ganguli[62] isolated shikimate dehydrogenase from mung bean seedlings and found that in the presence of NADP it determines the position of equilibrium, which is displaced towards the formation of shikimic acid. Higuchi and Shimada[63] investigated the changes in the activity of shikimate: NADP-oxidoreductase in relation to the lignification of bamboo. It is noteworthy that Balinsky and Davis[64] isolated 5-dehydroquinate dehydratase and shikimate dehydrogenase from the extracts of certain higher plants and Gamborg[65] detected these enzymes in suspensions of cell cultures from a number of plants. The above investigators believe that the wide distribution of these enzymes is evidence of their important role in the biosynthesis of aromatic compounds in higher plants.

A few words should be said about the role of quinic acid (V) in the biosynthesis of monomeric lignin precursors. The wide distribution of quinic acid in higher plants[11,48,68,51-54,66-68] evidently indicates that in the biosynthesis of aromatic compounds in plants it can play a more important role than in bacteria. By exposing young rose plants to an atmosphere of $^{14}CO_2$, Weinstein et al.[69] isolated labelled quinic acid, the specific radioactivity of which was higher than that of shikimic acid isolated from the same plants. Subsequent experiments by these investigators[70-72] showed that, when various vascular plants are fed labelled quinic acid, the latter is converted into shikimic acid (VII), phenylalanine (XIV), and tyrosine (XV). Goldschmid and Quimby[73] reported that interconversion of quinic and shikimic acids in hemlock branches. The data obtained by Sergeeva and coworkers[74] in a study of the formation of shikimic and quinic acid in year old poplar shoots fed $^{14}CO_2$ demonstrate that, during the growth of the plant, the acids are genetically related. Gamborg[75] achieved the interconversion of quinic and shikimic acids (reaction pathways *1–3* in Scheme 1) *in vitro* with the aid of three enzymes: 5-dehydroquinate dehydratase, shikimate dehydrogenase, and quinate: NAD oxidoreductase (quinate dehydrogenase) (EC 1.1.1.24) isolated from suspensions of plant cell cultures from mung beans. It is noteworthy that Gamborg was the first to detect quinate dehydrogenase in higher plants[65] and to investigate in detail the properties of this enzyme after isolating it from mung bean cell culture suspension[76].

Among the reactions quoted in Scheme 1, the conversion of shikimic acid (VII) into prephenic acid (XI) has been least thoroughly investigated[77]. So far enzymes catalysing the individual stages of this reaction have not been isolated from micro-organisms in a pure form. In higher plants the enzymes have still not been detected. Therefore there is an evident need for a more detailed study of this reaction at an enzymatic level.

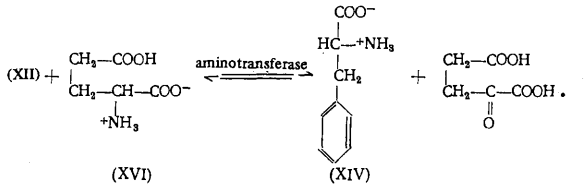
Gamborg and Simpson[78] studied the conversion of prephenic acid (XI) into phenylalanine (XIV) and tyrosine (XV) by enzymes isolated from mung bean plants. They established that mung bean extracts contain aminotransferase (transaminase), prephenate aromatase, and prephenate dehydrogenase, which are responsible for these conversions, and noted that it is impossible to demonstrate the enzymatic formation of phenylpyruvic acid (XII), since it is formed spontaneously when an acid acts upon prephenate. Gamborg and Keeley[79] isolated from the cotyledons of the wax bean prephenate dehydrogenase, which in the presence of NADP catalyses the (XI) → (XIII) conversion. This enzyme was also detected in the cotyledons and shoots of mung bean plants. A study of the changes in the concentration of prephenate dehydrogenase during the development of mung bean plants showed that the maximum concentration is observed in the cotyledons 4–5 days after the start of growth.

The final stage in the formation of phenylalanine and tyrosine, which play significant roles in the biosynthesis not only of lignin but also of other plant phenols[18-20], consists of the transamination of the ketoacids (XII) and (XIII). The transamination reactions were studied in various plants (lupin, maize, barley, pea, oats, and mung beans) by Wilson et al.[80], who detected a number of aminotransferase systems in these plants (α-oxoglutaric

†In these cases where the systematic name of the enzyme is followed by its number (code) in brackets, the name is based on the international nomenclature[58]; in the remaining cases the authors' own designations of the enzymes are retained.

‡ NADP = nicotinamide-adenine dinucleotide phosphate; NAD = nicotinamide-adenine dinucleotide.

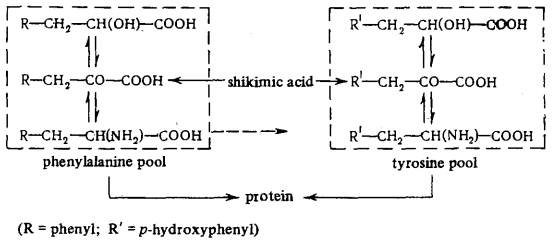
acid–alanine; α-oxoglutaric acid–aspartic acid; α-oxoglutaric acid–glycine; α-oxoglutaric acid–phenylalanine; oxaloacetic acid–alanine; pyruvic acid–methionine). The authors isolated, from etiolated white lupin seedlings and barley seedlings subjected to illumination, aminotransferases which catalyse the transamination of α-oxoglutaric acid with 17 different aminoacids. The authors' experiments with labelled compounds confirmed the presence of aminotransferases in the plants. Kretovich and Uspenskaya [81] investigated the formation of phenylalanine (XIV) as a result of transamination between phenylpyruvic acid (XII) and glutamic (XVI) or aspartic acid in homogenates of pea seedlings:



Gamborg [82,83] isolated from young mung bean plants an aminotransferase catalysing the transamination of a number of cyclic and aromatic aminoacids (including phenylalanine and tyrosine) in the presence of pyruvate or α-oxoglutarate, which behave as amino-acceptors.

In a study of the conversion of labelled shikimic acid into phenylalanine (XIV) and tyrosine (XV) by wheat and buckwheat plants, Gamborg and Neish [47] noted the ease of the interconversion of the α-hydroxy-, α-oxo-, and α-aminophenylpropanoic acids synthesised from shikimic acid and on the basis of their results concluded that there are two different pools of phenyl and *p*-hydroxyphenyl derivatives (the so called "phenylalanine pool" and the "tyrosine pool") (Scheme 2). Within each pool α-hydroxy or α-oxo-acids are readily converted into the corresponding aminoacids. At the same time, no conversion of compounds of the tyrosine pool into those of the phenylalanine pool was observed (the reverse conversion takes place to a significant extent). In addition it was shown that shikimic acid is a better tyrosine precursor than any compound of the phenylalanine pool. The results demonstrate that plants, like bacteria, form tyrosine from prephenic acid as a result of transamination (Scheme 1) but they are also capable of producing it by the hydroxylation of phenylalanine.

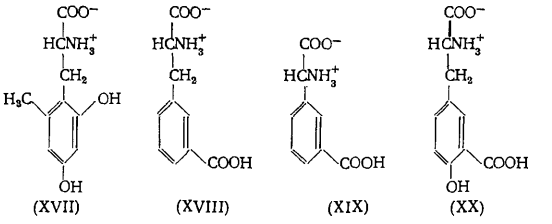
Scheme 2



(R = phenyl; R' = *p*-hydroxyphenyl)

The studies discussed above, which involved both the isolation of plant enzymes and experiments with labelled compounds, suggest that aromatic compounds are formed in plants via a pathway which is identical or very similar to the sequence of reactions presented in Scheme 1. At the same time one should note that many results support the hypothesis that in higher plants there are other synthetic pathways to aromatic lignin precursors than those already discussed. In particular Nandy and Ganguli [55,56] observed that the cell-free extract from mung bean converts glucose-6-phosphate and glucose-1-phosphate into dehydroshikimic acid. Higuchi and Shimada [84] isolated from bamboo shoots D-glucose-6-phosphate: NADP oxidoreductase (EC 1.1.1.49) and 6-phospho-D-gluconate: NADP oxidoreductase (EC 1.1.1.44) and investigated the activities of these enzymes in relation to lignification.

In addition, it is interesting to note that, apart from phenylalanine and tyrosine, certain other aromatic acids have been detected in certain plants. Thus Schneider [85] isolated orcinylalanine (XVII) from the seeds of *Agrostemma githago*. Thompson et al. isolated *m*-carboxy-L-phenylalanine (XVIII) [86] and *m*-carboxy-L-phenylglycine (XIX) [87] from the bulbs of *Iris tingitana*. Larsen and Kjaer [88] detected *m*-carboxy-L-tyrosine (XX) in the seeds of *Reseda odorata*. Unfortunately experiments on the biosynthesis of these aminoacids were not made and it is difficult to say whether they are formed via shikimic acid or in some other way:



According to modern ideas [18–20,89], there exist two main biosynthetic pathways to phenolic compounds: (1) the shikimate pathway, and (2) the acetate–malonate pathway. Studies with labelled compounds, discussed in detail by Neish [90], showed convincingly that the biosynthesis from acetate does not play an appreciable role in the formation of lignin, which is produced from carbohydrates via shikimic acid. It is quite likely that future studies will make it possible to refine and supplement the sequence involved in the formation of aromatic lignin precursors presented in Scheme 1 but there is already no doubt that the scheme correctly reflects the main processes occurring in the biosynthesis of aromatic compounds in plants.

4. Conversion of Aromatic Aminoacids into Monomeric Lignin Precursors

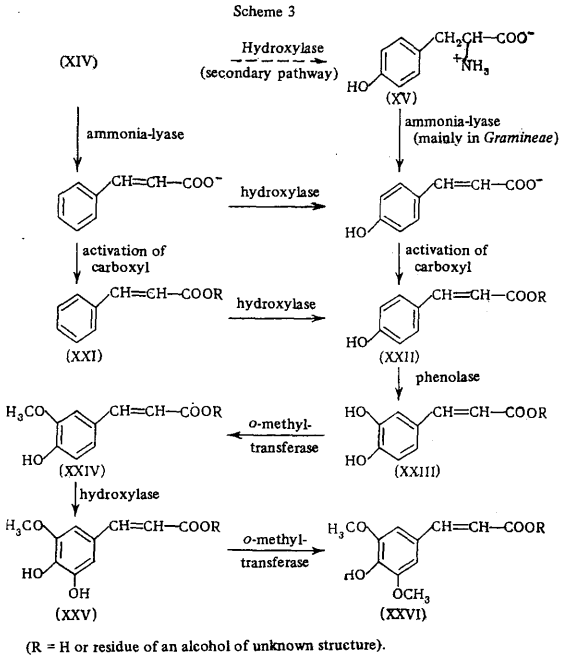
Brown and Neish [91,92] carried out an extensive study on the formation of lignin by introducing into plants labelled phenolic compounds (C_6-C_1 and C_6-C_3), which were regarded as potential intermediates in the biosynthesis of lignin. The results demonstrated that phenylalanine (XIV) is an effective precursor of lignin in many plants, while tyrosine (XV) is used for the biosynthesis of lignin only in a limited number of species. Subsequent studies by Neish [93] and Brown [94], who investigated the formation of lignin from [^{14}C]phenylalanine and [^{14}C]tyrosine in a number of plant species, showed that only species of *Gramineae* employed with equal efficiency both phenylalanine and tyrosine. Although these plant species can incorporate *p*-coumaric acid (XXII, R = H) in lignin, *Gramineae* are distinguished by their capacity to convert tyrosine directly into *p*-coumaric acid, while all other plants form this acid from phenylalanine via cinnamic acid (XXI, R = H).

The above conclusion was confirmed by studies at the enzymatic level. Koukol and Conn [95] demonstrated the presence in six plant species of an enzyme which catalyses the deamination of phenylalanine to cinnamic acid and which was subsequently called phenylalanine ammonia-lyase. At the same time Neish [96] detected in seven grass species an analogous enzyme, tyrosine ammonia-lyase, which deaminates tyrosine to *p*-coumaric acid. Later Young and Neish [97] studied the properties of the above ammonia-lyases which they isolated from wheat plants (*Triticum aestivum*) and bracken (*Pteridium aquilinum*). In addition, Neish and coworkers [98] studied a number of plants belonging to different species and showed that, although tyrosine ammonia-lyase can be detected in other families, only *Gramineae* contain the maximum concentrations of this enzyme.

Thus the results of the above investigations indicate two possible pathways to the formation of *p*-coumaric acid: by direct action of ammonia-lyase on tyrosine, mainly in *Gramineae*, or by the hydroxylation of cinnamic acid formed as a result of the deamination of phenylalanine.

McCalla and Neish [46] studied the sequence of conversions from cinnamic acid (XXI, R = H) to sinapic acid (XXVI, R = H) by feeding labelled phenylalanine to sage cuttings (Scheme 3). They extracted labelled *p*-coumaric (XXII, R = H), caffeic (XXIII, R = H), ferulic (XXIV, R = H), and sinapic (XXVI, R = H) acids, the different rates of incorporation of ^{14}C in each acid agreeing with the sequence shown in Scheme 3. Moreover, the above sequence is confirmed by experiments in which labelled cinnamic and other acids were introduced separately, which led to the observation of rapid conversion of the additive into the final compounds of the sequence and relatively slow conversion into the initial compounds§.

Scheme 3



(R = H or residue of an alcohol of unknown structure).

§ There is convincing evidence for the demethylation of sinapic [99-101] and ferulic [102,103] acids in plants, but the mechanism of this process has not yet been established.

Since it is difficult to suppose that the reactions considered occurred in plants with acids in a free form, the authors suggested that the cinnamic acid derivatives indicated in Scheme 3 are present mainly in alkali-labile bound forms, which are evidently esters. Later El-Basyouni and Neish [104,105], obtained more convincing evidence for the involvement of these bound forms, which they thought to be soluble and insoluble esters, in the formation of lignin. The nature of the bound forms is not entirely clear, but it is believed that they can be bound either to protein fractions [13] or they may be esters of glucose [106-109] or quinic acid [110].

The individual stages of the sequence presented in Scheme 3 have been confirmed by studies at an enzymatic level. Thus Nair and Vining [111] isolated from spinach leaves a phenylalanine hydroxylase, which catalyses the hydroxylation of L-β-phenylalanine to tyrosine at pH 4.2. The same investigators [112] demonstrated the presence in spinach leaves of cinnamic acid 4-hydroxylase, which characterises the hydrolysis of *trans*-cinnamic acid to *p*-coumaric acid. An analogous enzyme was isolated by Russell and Conn [113] from the terminal buds of the pea and Higuchi and coworkers [114] obtained it from bamboo, asparagus, and *Ginkgo biloba* shoots and from Japanese cedar seedlings.

Byerrum et al. [115] showed that in the metabolism of barley and tobacco plants the methyl group of methionine is involved in the formation of the methoxy-groups of lignin. With the aid of labelled compounds, they demonstrated that the reaction consists of the transfer of the methyl group from the sulphur atom of methionine to an oxygen atom in lignin and therefore it can be regarded as an example of transmethylation in higher plants. Later it was shown that in tobacco plants the donors of the methyl group in the formation of methoxy-groups of lignin may be glycine, serine, and formaldehyde [116] and in the poplar glycine may serve this purpose [117]. A number of investigators [118-120] established the presence in grasses and in woody shrubs of enzymes capable of methylating caffeic acid in the presence of *S*-adenosylmethionine. Hess [121,122] detected in petunias and certain other plants an analogous enzyme which methylates 5-hydroxyferulic acid to sinapic acid in the presence of adenosine triphosphate, methionine, or *S*-adenosylmethionine, confirming thereby data obtained earlier with the aid of labelled compounds [101]. Higuchi et al. [123] reported the isolation from bamboo shoots of an *o*-methyltransferase which catalyses the formation of ferulic and sinapic acids. They demonstrated that the activity of the enzyme gradually increases as the bamboo shoots are lignified. Higuchi and coworkers [124] compared the specificities of the *o*-methyltransferases extracted from the bamboo and the poplar (angiosperms) and from *Ginkgo biloba* (gymnosperms). They showed that the methyltransferase from the bamboo and the poplar is *meta*-specific for caffeic, 3,4,5-trihydroxycinnamic, and 5-hydroxyferulic acids. The rate of formation of sinapic acid (XXVI, R = H) from 5-hydroxyferulic acid (XXV, R = H) in the reaction *in vitro* is higher than the rate of formation of ferulic acid (XXIV, R = H) from caffeic acid (XXIII, R = H). On the other hand, the methyltransferase from *Ginkgo biloba* methylates only caffeic acid and not 3,4,5-trihydroxycinnamic and 5-hydroxyferulic acids. The authors suggest that the observed difference between the specificities of the *o*-methyltransferases from gymnosperms and angiosperms is one of the factors responsible for the differences between the metabolism of lignin in these groups of plants. It is noteworthy that, according to the data of Kratzl and Puschmann [125], the methoxylation

of the aromatic ring can occur also in the stage involving the oxidation of coniferyl alcohol.

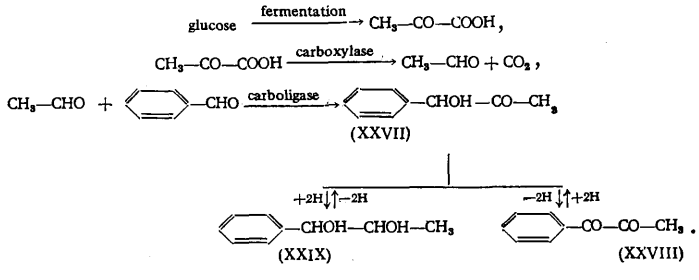
Vaughan and Butt[126-128] isolated from spinach leaves a copper-containing preparation of phenolase which catalysed the hydroxylation of *p*-coumaric acid to caffeic acid. The authors showed that this enzyme behaves like an oxidase with a mixed function (both molecular oxygen and an electron donor, for example ascorbate, NAD.H_2, or 6,7-dimethyl-5,6,7,8-tetrahydropteridine, are essential for the completion of the hydroxylation reaction).

The concluding stage of the biosynthesis of the monomeric precursors of lignin is enzymatic reduction of ring-substituted derivatives of cinnamic acids to the corresponding derivatives of cinnamyl alcohols. A similar conversion of ferulic acid was investigated by Higuchi and Brown[129], who employed a ^{14}C-labelled substrate and showed that ferulic acid is reduced by wheat plants to coniferyl alcohol via the formation of an aldehyde as an intermediate. Gross and Zenk[130-132] confirmed these reactions by studies at an enzymatic level, having isolated the corresponding enzymes from the mycelium of the fungus *Neurospora crassa*. The previously unknown arylaldehyde: NADP oxidoreductase (EC 1.2.1) catalyses the reduction of the carboxy-groups of aromatic acids to the corresponding aldehydes. The second enzyme aryl carbinol: NADP oxidoreductase (EC 1.1.1.2), which catalyses the reversible reduction of aromatic aldehydes to aromatic alcohols, differs from the familiar alcohol dehydrogenases, acting preferentially on primary aromatic alcohols. The authors noted a broad substrate specificity of the enzymes isolated and investigated their properties. Similar enzymes have not so far been isolated from higher plants.

5. The Possibility of Other Biosynthetic Pathways to Monomeric Lignin Precursors

Higuchi[50,133,134] suggested that compounds with the phenylpropane structure, which are monomeric precursors of lignin, may be synthesised in plants via pathways other than those discussed above, namely as a result of a $C_6-C_1 + C_2$ condensation, i.e. by the addition of C_2 compounds to derivatives of phenylmethane formed from 5-dehydroshikimic or shikimic acid.

As early as 1921 Neuberg and Hirsch[135] observed that, in the fermentations of sucrose or pyruvic acid in the presence of benzaldehyde, acetylphenylmethanol (XXVII) is formed. Part of the ketol produced was oxidised to benzoyl methyl ketone (XXVIII), while the remainder was reduced to methylphenylethylene glycol (XXIX). The authors suggested the following sequence of reactions:



The enzyme which catalysed the last reaction was called carboligase. Later Neuberg and coworkers[136,137] reported that, when yeast carboligase acts on aromatic aldehydes (*o*-chlorobenzaldehyde, anisaldehyde, and *o*-toluic aldehyde), the corresponding ketols are formed. Recently the formation of acetylphenylmethanol (XXVII) catalysed by yeast carboligase was noted also by other investigators[138-140].

Since the structures of the side chains of the ketols and diketones thus produced are identical with the products of the ethanolysis of lignin (the so called "Hibbert's ketones"), Higuchi[133,134,141] investigated the possibility of the formation of phenylpropane precursors of lignin as a result of a reaction catalysed by carboligase.

Vanillin, syringaldehyde, and *p*-hydroxybenzaldehyde were separately subjected to fermentation by brewer's yeast in sucrose solution. After fermentation, the resulting solutions were found to contain methyl vanilloyl ketone, methyl syringoyl ketone, and *p*-hydroxybenzoyl methyl ketone, part of these compounds being reduced to the corresponding alcohols and the remainder being oxidised to the corresponding acids. The diketones obtained are identical with certain products of the ethanolysis of lignin. The authors suggested a subsequent formation from the diketones of compounds of the type of acetylphenylmethanol and benzoylmethylmethanol, although the existence of these ketones has not been confirmed experimentally.

The results of a number of investigators[134,141-143] indicate the presence of C_6-C_1 aldehydes in the cambial sap of many woody plants, wheat, and bamboo shoots. Stepanov and Kuzin[144] detected carboligase in the leaves of a number of plants. In addition, Brown and Neish[91,145] reported that, when wheat plants are fed labelled preparations of vanillin and *p*-hydroxybenzoic acid, the latter are incorporated into the wheat lignin. Ishikawa and Takaichi[146] observed that, when adult pea plants are incubated with vanillin and *p*-hydroxybenzaldehyde, their lignin content increases relative to control plants. Freudenberg and coworkers[147,148] showed that labelled [^{14}C]glucovanillin is incorporated into the lignin of young pines. Kratzl[149,150] reported the incorporation of labelled *p*-creosol into lignin.

The results of the above investigations enabled Higuchi[50,133,134] to suggest that C_6-C_1 aldehydes, which may be formed in plants via different pathways[151], are converted into phenylpropanols as a result of a reaction catalysed by carboligase. The phenylpropanols are further transformed by rearrangements and dismutations, as in the mechanism proposed by Hibbert[152,153] and discussed in the next section.

In conclusion of the discussion of questions relating to the formation of monomeric lignin precursors as a result of a $C_6-C_1 + C_2$ condensation, we may note that although such processes may occur in plants, they probably play only a secondary role in the biosynthesis of lignin.

6. The Role of Coniferin in the Lignification Process

As early as 1861, Hartig[154] detected coniferin, which is the β-D-glucoside of coniferyl alcohol, in the cambial sap of conifers. It has now been shown[155] that coniferin is encountered mainly in conifers, comprising six families and 15 species (the syringic analogue of coniferin—syringin—has been detected also in certain deciduous trees). As will be shown below, many investigators regarded coniferin as a precursor of lignin in the wood of conifers

owing to its evident biochemical relation to coniferyl alcohol. Freudenberg and Bittner [156] introduced coniferin synthesised from labelled [^{14}C]coniferyl alcohol under the bark of young spruce stems. Two months after injection, more than 90% of ^{14}C was detected in the lignin fraction. Later Freudenberg and Niedercorn [157] showed that labelled phenylalanine may be converted into both coniferin and into lignin by young spruce stems, and therefore they suggested that coniferin is an intermediate in the formation of lignin. The experiments of Freudenberg and coworkers [147], which are discussed in detail below, showed that coniferin is hydrolysed by β-glucosidase to coniferyl alcohol, from which lignin macromolecules are then constructed. Studies on the role of coniferin by the method of tissue culture [158–165] demonstrated stimulation of lignification by both coniferin and syringin. Kratzl and coworkers [166–168] determined quantitatively the coniferin incorporated in spruce lignin. These studies showed that the aglucone of coniferin is incorporated into lignin without a rearrangement of the side chain.

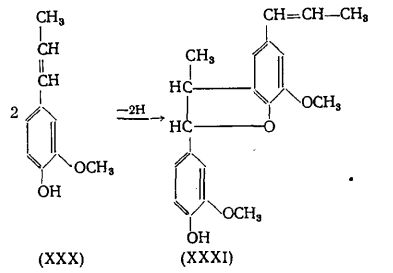
However, despite the above investigations, the question of the role of coniferin in the lignification process still cannot be resolved quite unambiguously. The reason is both the fact that the distribution of coniferin is not universal and the failure to detect β-glucosidase in some lignification processes [150].

III. FORMATION OF LIGNIN FROM MONOMERIC PRECURSORS

The studies discussed in the preceding section concerning the detection in plants of various enzymatic systems catalysing the individual stages of the biosynthesis of monomeric lignin precursors and also experiments with various labelled compounds have been carried mainly *in vivo*, i.e. on plants or tissue cultures. The studies discussed in this section involve mainly experiments *in vitro*. This method has both many advantages and significant disadvantages, which will be discussed below.

1. A Brief Historical Review of Studies on the Biosynthesis of Lignin *in Vitro*

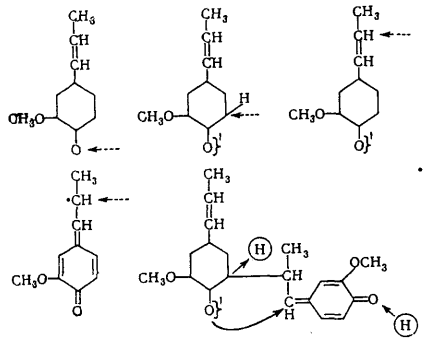
After the determination of the structure of the glucoside coniferin present in the cambial sap of conifers during the vegetative period, Tiemann and Mendelsohn [169] suggested in 1875 that there is a definite genetic relation between coniferin and lignin. In 1897 Klason [170] used this idea in his studies on the chemistry of lignin and suggested that lignin is a product of the condensation polymerisation of coniferyl alcohol formed in the plants on enzymatic hydrolysis of coniferin. Later Klason [171–178] regarded lignin as a condensation product of coniferaldehyde formed by the oxidation of coniferyl alcohol. In 1908 the French chemists Cousin and Hérissey [179,180] observed that, when isoeugenol (XXX) is dehydrogenated, a crystalline product is formed, among others; according to analytical data, it consists of two eugenol molecules. The authors dehydrogenated isoeugenol with an alcoholic solution of $FeCl_3$ or with dehydrogenases from the sap of the fungus *Russula delica* in the presence of oxygen and in both cases obtained the same product. According to the hypothesis of Cousin and Hérissey, the product, which they called dehydrodi-isoeugenol, is a biphenyl derivative. It was not until 1933 that Erdtman [181,182] demonstrated the true structure of dehydrodi-isoeugenol and showed that it is a phenylcoumaran (XXXI):



(XXX) (XXXI)

Erdtman [182] proposed a mechanism for the dehydropolymerisation of isoeugenol to dehydrodi-isoeugenol via the intermediate formation of an oxygen radical¶. The mechanism is presented in Scheme 4 as formulated by the author [182].

Scheme 4



According to Erdtman's hypothesis, the formation of dehydrodi-isoeugenol may be regarded as a model of the biosynthesis of lignin in plants, which is achieved as a result of the dehydropolymerisation of guiacylpropane derivatives containing oxygen in the side chains. Erdtman's hypothesis became the starting point of all subsequent studies on the biosynthesis of lignin, which will be discussed below.

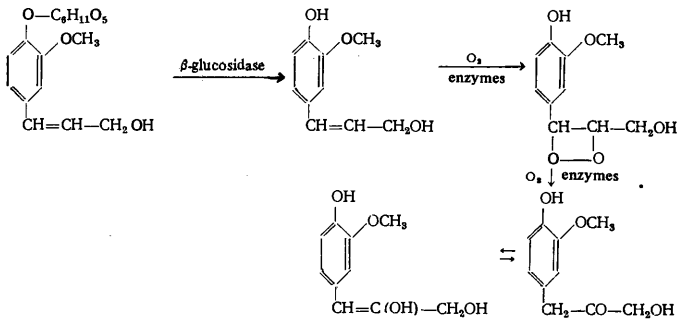
The isolation and identification of various monomeric products of the ethanolysis of wood ("Hibbert ketones") enabled Hibbert to put forward in 1941 the so called dismutation hypothesis [152,153]. According to this hypothesis, the respiration of plant cells is catalysed by substances of the type of coniferyl alcohol, which function as oxygen transferring agents. Hibbert believed that the oxidation-reduction system in plant cells is analogous to the system proposed by Szent-Györgyi [187] for animal cells, which is evident from the Scheme below:

Szent-Györgyi system for animal cells	*Hibert system for plant cells*
HOOC—CO—CH_2—COOH	R—CO—CH_2—CH_2OH
$+2H\downarrow\uparrow-2H$	$+2H\downarrow\uparrow-2H$
HOOC—CH(OH)—CH_2—COOH	R—CH(OH)—CH_2—CH_2OH
$\downarrow-H_2O$	$\downarrow-H_2O$
HOOC—CH=CH—COOH	R—CH=CH—CH_2OH
$+2H\downarrow\uparrow-2H$	$+2H\downarrow\uparrow-2H$
HOOC—CH_2—CH_2—COOH	R—CH_2—CH_2—CH_2OH
	(R = 4-hydroxy-3-methoxyphenyl)

¶ It is noteworthy that the hypothesis of a radical mechanism of the dehydrogenation of phenols, which subsequently became widely accepted in organic chemistry and biochemistry, was first put forward by Pummerer [183–186].

Thus, according to Hibbert's hypothesis, monomeric phenyl compounds are synthesised by plants as respiration catalysts. In higher plants, in the postmortem state of the cells, these compounds are oxidised and readily undergo various reactions (dehydrogenation, condensation, and polymerisation) leading to the formation of lignin. Hibbert's hypothesis was subsequently developed in Manskaya's studies.

In 1947 Manskaya [188,189] investigated the oxidation processes in wood relating to lignin formation. She showed that the cambial tissue and the wood of the new annual layer in the pine contain oxidising enzymes: peroxidase and polyphenol oxidase, whose substrates are coniferin and its derivatives. Manskaya pointed out the equilibrium in the oxidation-reduction processes in the cambial tissue as a result of which phenol oxidation products do not accumulate in the cells. When live cells die during the wood formation process, oxidation processes begin to predominate markedly over reduction processes and polyphenol oxidation products begin to be deposited in the form of lignin. According to Manskaya's hypothesis, the deposition of lignin is related directly to the breakdown of the respiratory apparatus in plant cells. The hypothesis states that the oxidation of coniferyl alcohol in the lignifying cells of the cambium may be represented by the following scheme:



The products obtained as a result of the enzymatic oxidation are converted by further condensation into lignin, which is deposited in the cell walls of the wood. The results of Manskaya's study [190] of the changes in the activity of peroxidase in cambium and the adjacent woody layer and also of the corresponding changes in the coniferin content showed that in the period of maximum enzymatic activity the coniferin content was lowest and conversely. The results of this investigation served as a basis for the conclusion that coniferin is the substrate of the enzymes. Later Manskaya and Bardinskaya [142] oxidised coniferyl alcohol with peroxidase (from the precambial layer of the pine) or by polyphenol oxidase (from the lignified central part of the root of the sugar beet) and obtained polymeric compounds which were close in their elemental composition, the content of functional groups, the molecular weight, and ultraviolet spectroscopic data to Freudenberg's preparations obtained from coniferyl alcohol by the action of enzymes from the field mushroom.

In considering the questions of the biosynthesis of lignin, attention should be concentrated on the work of Freudenberg and his coworkers the aim of which was to prepare and investigate biosynthetic lignin. The studies of these investigators over a period of many years, which involved highly sophisticated experiments, made a considerable contribution to the chemistry of lignin, having provided information not only about the possible pathways of its biosynthesis but also about the structure of this complex polymeric substance.

In 1943 Freudenberg and Richtzenhain [191] and later Richtzenhain alone [192-194] observed the formation of polymeric lignin-like materials when various monomeric phenolic derivatives of the guiacyl and syringyl series were acted upon by the unpurified enzymes of the mushroom *Psalliota campestris*. The results led the authors to the conclusion that lignin is formed by the enzymatic dehydrogenation of substituted phenol derivatives, confirming thereby Erdtman's hypothesis.

In 1949 Freudenberg [195,196] reported the preparation of biosynthetic lignin, which he called dehydropolymer (DHP). The preparation was obtained by the action of enzymes from the sap of the mushroom (*Psalliota campestris*) on coniferyl alcohol at a neutral pH, 20°C and with aeration over a period of three days. The yield of DHP was 93% relative to the initial coniferyl alcohol. The resulting polymer was very close to lignin isolated from spruce wood in terms of important characteristics, such as solubility, elemental composition, the content of functional groups, the yield of formaldehyde on distillation with 28% sulphuric acid, the yield of aromatic acids on methylation, fusion with alkali, remethylation, and oxidation with $KMnO_4$, colour reactions, ultraviolet spectra, etc. This study began a large cycle of investigation on the enzymatic dehydrogenation of coniferyl alcohol. Later Freudenberg and his coworkers studied the principles of the biosynthesis of lignin *in vitro*, investigated the dehydrogenation of coniferyl alcohol by isolating the intermediates, and compared the properties of DHP and spruce wood lignin.

In 1963 Freudenberg and Harkin [197] reported at during the vegetative period the cambial sap contains, together with coniferin, small amount of *p*-glucocoumaryl alcohol and syringin. Accordingly, Freudenberg and coworkers [198-200] dehydrogenated a mixture of *p*-coumaryl, coniferyl, and sinapyl alcohols in molar proportions of 14 : 80 : 6 in order to obtain biosynthetic lignin closest to the lignin from conifers.

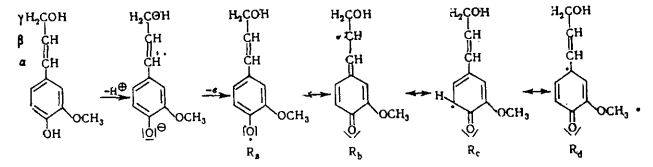
It would hardly be useful to consider the studies of Freudenberg and his coworkers in their historical sequence, which, while giving an idea about the evolution of the authors' views on the structure and biosynthesis of lignin *in vitro*, would make it difficult to describe the present state of this problem. Therefore in subsequent sections we shall consider the main aspects of Freudenbergs investigations and his principal conclusions, which constitute the foundation of present ideas on the biosynthesis of lignin.

2. The Mechanism of the Polymerisation of Coniferyl Alcohol

According to Freudenberg's views [199,201,202]†, coniferyl alcohol is polymerised via a radical mechanism. In the course of the study of the enzymatic dehydrogenation of coniferyl alcohol, Freudenberg and his coworkers [201,203-205] established that, when the action of dehydrogenases from field mushrooms or cambium on an aqueous solution of coniferyl alcohol is terminated as soon as the latter ceases to be detected in the reaction mixture, it is possible to isolate dimeric intermediates in the dehydrogenation reaction. By extracting the reaction mixture with

† Since Freudenberg's studies have served as a basis for his numerous publications dealing with the evolution of his views, in each case the references include both the first publication on the given problem and the latest communications which contain his present views.

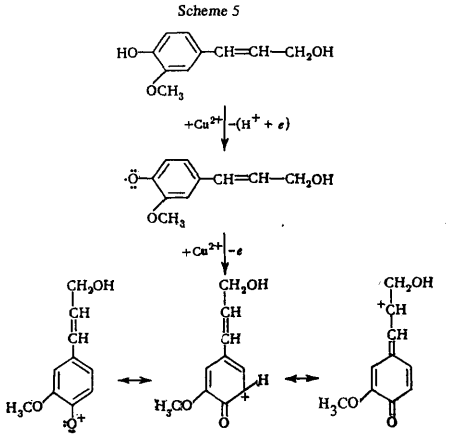
methylene chloride or n-butyl alcohol, dehydrodiconiferyl alcohol [203], DL-pinoresinol [204], and β-coniferyl ether of guiacylglycerol [201] were isolated and then identified. On the basis of these intermediates in the biosynthesis of lignin *in vitro* and also Erdtman's hypothesis that lignin is formed via a radical mechanism, Freudenberg put forward the following scheme for the conversion of coniferyl alcohol in the course of its enzymatic dehydrogenation:



According to this scheme, during enzymatic dehydrogenation, the coniferyl alcohol molecule loses the hydrogen atom from the phenolic hydroxyl to form the aryloxy-radical R_a. This radical can exist in any of the mesomeric forms indicated (R_a–R_d). Freudenberg et al. [206] established that the half-life of these mesomeric forms in a 1 : 1 (by volume) dioxan–water mixture is 45 s. The mesomeric forms of the radical recombine further with one another and undergo various transformations, discussed in detail in the next section, which leads ultimately to the formation of biosynthetic lignin (DHP). One must emphasise that, according to Freudenberg's data [207–209], the dehydrogenation of coniferyl alcohol is not a specific reaction, since it can be initiated by various reactants: laccase isolated from the sap of field mushrooms in the presence of atmospheric oxygen; horseradish peroxidase in the presence of H_2O_2; laccase and peroxidase isolated from the precambial layer of spruce wood; a number of inorganic agents [copper(II) salts, MnO_2, lead peroxide]; radicals such as, for example, 2,4,6-tri-t-butylphenoxyl, etc.

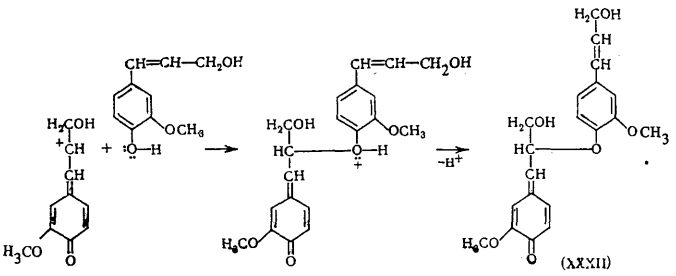
Apart from the radical mechanism of the polymerisation of coniferyl alcohol, discussed above, one should consider the ionic mechanism proposed by Adler [210] (Scheme 5).

Scheme 5



According to Adler's views, the initial reaction has a radical mechanism and takes place without electron transfer. The suggested subsequent "one-electron transfer", as a result of which an unpaired electron is removed from the radicals formed initially, can be achieved either enzymatically or without the involvement of enzymes using Cu^{2+} or Fe^{3+} as catalysts.

The mesomeric cation thus produced can react with coniferyl alcohol which results in the formation of the dimeric quinone methide (XXXII). As will be shown below, the formation of this quinone methide may be represented also as due to the combination of the mesomeric forms R_a and R_b: [201]

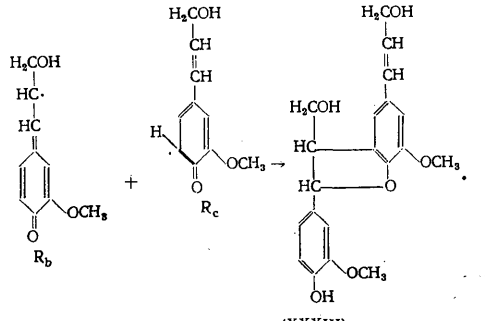


(XXXII)

3. The Principles of the Growth of the DHP Molecule and the Principal Intermediates Isolated in the Course of the Formation of Biosynthetic Lignin

Freudenberg established [211] that the decomposition of the enzymes by NaCN can interrupt the enzymatic dehydrogenation of coniferyl alcohol at any stage with the aim of the subsequent isolation of the intermediate in the biosynthesis of lignin *in vitro*. The best yield of low-molecular-weight intermediates in the dehydrogenation of coniferyl alcohol was obtained after removing approximately one atom of hydrogen from each molecule of the initial carbinol. When large amounts of hydrogen are eliminated, water-insoluble products with a high molecular weight are produced. The intermediates in the biosynthesis of lignin *in vitro* thus produced were separated by paper chromatography. After treating the chromatograms with diazobenzenesulphonic acid, about 40 spots were detected [212]. Freudenberg and coworkers [4,213] succeeded in isolating and then identifying a number of dimeric, trimeric, and oligomeric intermediates. Freudenberg suggested [214] that the intermediates may be referred to as lignols.

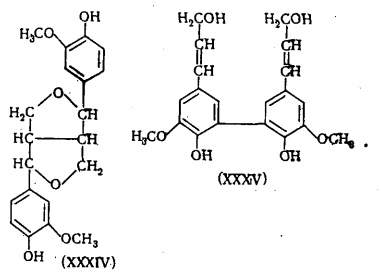
As mentioned in the preceding section, Freudenberg suggested that dilignols are produced as a result of the combination of the mesomeric forms R_a–R_d of the aryloxy-radicals obtained by the enzymatic dehydrogenation of coniferyl alcohol. Thus the combination of the R_b and R_c forms yields dehydrodiconiferyl alcohol (XXXIII): [203]



(XXXIII)

A similar example of the stabilisation of two mesomeric R_b forms owing to dimerisation is provided by the formation of DL-pinoresinol (XXXIV) [204] and also by the formation of dehydrobisconiferyl alcohol (XXXV) [211] as a

result of the combination of two mesomeric forms R_b:

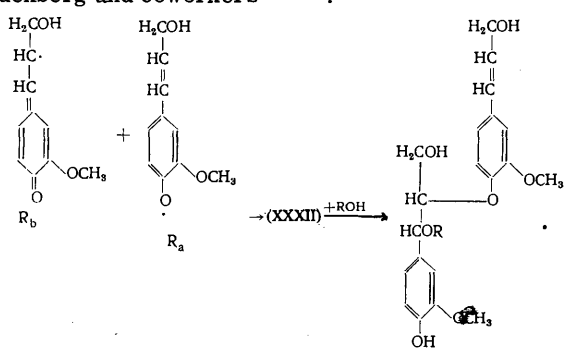


(XXXIV) (XXXV)

According to Freudenberg's views [208,215], the quinone methide (XXXII), formed by the combination of the mesomeric forms R_a and R_b, plays an important role in further biosynthesis of lignin [201]. It is noteworthy that the quinone methide structure proposed initially as hypothetical was subsequently confirmed by ultraviolet spectroscopic measurements [216]. At the same time it was established that the half-life of the quinone methide in a 1 : 1 (by volume) dioxan–water mixture at 20°C is about 60 min. The quinone methide is unstable and cannot be stabilised by an intramolecular rearrangement. Consequently, it is stabilised intramolecularly by combination with the elements of water or other dissociated hydroxyl-containing compounds, provided that steric conditions allow it. The addition of water to quinone methide leads to the formation of the β-coniferyl ether of guiacylglycerol (XXXVI), [201] which constitutes, together with the dilignols (XXXIII) and (XXXIV), the main part of the dimeric intermediates. It is interesting that these three principal dilignols in the biosynthesis of lignin *in vitro* were also detected by Freudenberg and Harkin [197] in the cambial sap of the spruce.

Enzymatic dehydrogenation of coniferyl alcohol in aqueous solution containing 30% of methanol results in the formation of the α-methyl-β-coniferyl ether of guiacylglycerol (XXXVII) [208] and, when the reaction is carried out in an aqueous solution containing 66% of sucrose, the corresponding sugar ester (XXXVIII) is produced [208,217]. Freudenberg regards this benzyl ether linkage as one of the most probable types of lignocarbohydrate linkages in plant tissues.

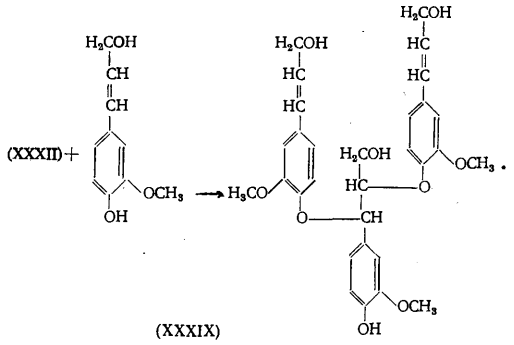
Since the dilignols considered are orthophenols, they can undergo further enzymatic dehydrogenation with reformation of dimeric radicals, which can recombine both with one another and with the mesomeric forms R_a–R_d. Such reactions lead to trilignols, tetralignols, and subsequently oligolignols. A number of the oligomeric compounds were isolated and identified by Freudenberg and coworkers [218–224]:



(XXXVI, R=H)
(XXXVII, R=CH_3)
(XXXVIII, R=$(C_6H_{10}O_5)_nH$)

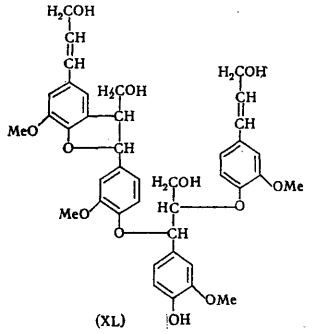
On the basis of the identified intermediates in the biosynthesis of lignin from coniferyl alcohol *in vitro*, Freudenberg [202,212,225,226] formulated the main pathways to the growth of the DHP molecule.

The first pathway consists of continuing dehydrogenation of oligolignols which leads to the formation of new aryloxy-radicals undergoing various recombinations. However, if the growth of the DHP molecule took place exclusively via dehydrogenation, then in this case each structural unit should loose two hydrogen atoms plus a further ~0.4 of a hydrogen atom owing to the formation of the carbonyl groups ($-C\overset{H}{\underset{O}{\diagup\!\diagdown}}$ and $\diagup\!\diagdown C{=}O$), i.e. altogether 2.4 hydrogen atoms. In fact, the maximum loss occurring is approximately two hydrogen atoms [227], which includes the average loss of 1.7–1.8 hydrogen atoms by each DHP structural unit owing to the formation of the bonds and 0.2–0.3 of a hydrogen atom owing to the formation of carbonyl groups. Thus the amount of hydrogen the removal of which leads to condensation corresponds to 1.7–1.8 atoms per structural units, which is insufficient for the formation of large molecules. In other words, a linkage produced as a result of addition or polymerisation and not related to the loss of hydrogen corresponds approximately to each four structural elements associated owing to the loss of hydrogen. This indicates the existence of other pathways to the growth of the lignin macromolecule. In this respect the quinone methide (XXXII), which can combine with phenols without an additional loss of hydrogen, plays a key role. The simplest example of the second pathway to the growth of the DHP macromolecule is the addition of coniferyl alcohol to the dimeric quinone methide (XXXII), which yields a trilignol—the aryl benzyl ether (XXXIX): [218]

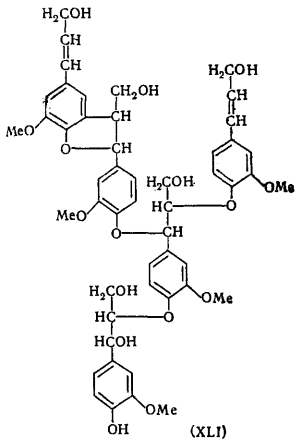


(XXXIX)

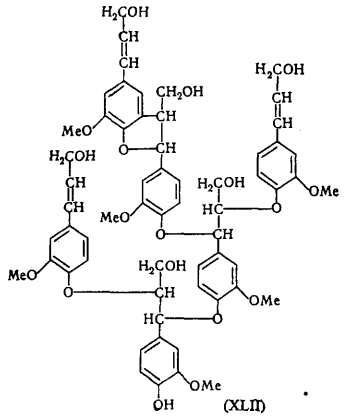
This growth pathway can also be illustrated by the formation of the tetralignol (XL) (the adduct of dehydrodiconiferyl alcohol and the quinone methide [218]), the pentalignol (XLI) (the adduct of the trilignol and the quinomethide) [224], and the hexalignol (XLII) (the adduct of the tetralignol and the quinone methide) [224].



(XL)

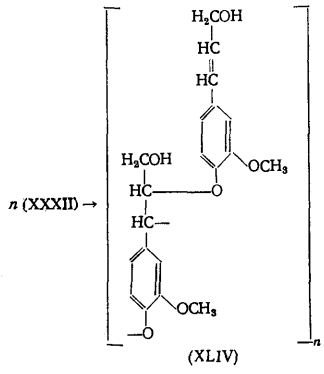


(XLI)



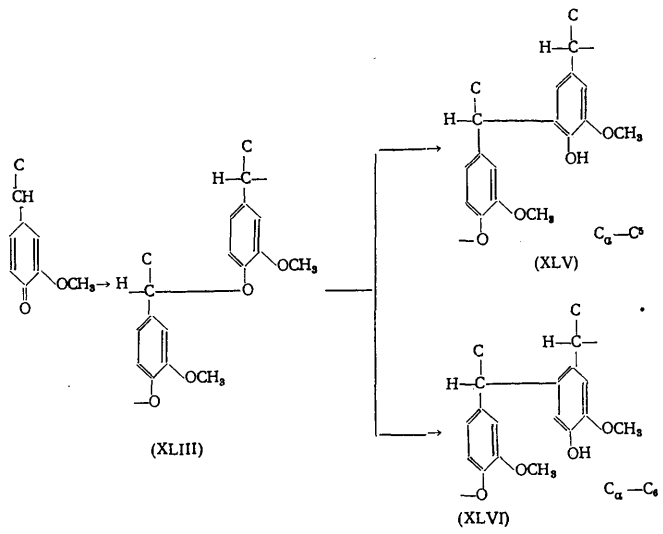
(XLII)

The polymerisation of *p*-quinone methides, leading to the formation of aryl benzyl ethers (XLIII),[228] competes with the addition of phenols to quinone methides. For example, compound (XLIV) is a product of the polymerisation of the quinone methide (XXXII). This process is considered as the third pathway to the growth of the DHP molecule:



(XLIV)

Finally the fourth pathway to the growth to the DHP molecule involves the rearrangement of α-aryl ethers, leading to the formation of diphenylmethane derivatives[222,228]. This process takes place after prolonged treatment with very dilute acids (similar conditions obtain in the cell sap of plants). As a result of the condensation between the α-C atom of the first unit and the fifth carbon atom in the ring of the second unit with simultaneous regeneration of the phenolic hydroxyl of the second unit, the ether (XLIII) is converted into the structure (XLV). A similar condensation of the α-C atom can occur to a lesser extent with the sixth carbon atom of the second unit and even less effectively with the second carbon atom. This rearrangement of α-aryl ethers does not take place solely in polymers but has been observed also with α-aryl guiacylglyceryl ethers (tri- and tetra-lignols)[222,226].



(XLIII)

(XLV)

(XLVI)

The non-enzymatic recombination of various mesomeric forms of the aryloxy-group formed on dehydrogenation of coniferyl alcohol results in a lack of optical activity of the polylignols synthesised both *in vivo* and *in vitro* despite the presence of asymmetric centres[205,215].

4. Chemical and Physical Properties of Dehydropolymers and Their Comparison with Those of Lignin Produced by Mechanical Milling

Table 1 presents semiempirical "formulae" for the $C_{(6)}-C_{(3)}$ structural unit of lignin, various DHP preparations, and lignin produced by mechanical milling [milled-wood lignin (MWL)] and isolated from spruce and beech wood by Björkman's method[229,230]. The data presented are evidence of the similarity of spruce wood MWL and DHP obtained by the enzymatic dehydrogenation of a mixture of coniferyl, *p*-coumaryl, and sinapyl alcohols.

In addition to the data in Table 1, we may mention that, in the MWL from spruce wood and DHP obtained by the enzymatic dehydrogenation of coniferyl alcohol, the total content of hydroxy-groups, determined by Verly's method, is in both cases 1.2–1.4 moles per $C_{(6)}-C_{(3)}$ unit[230,231], of which 0.30–0.35 mole comprises phenolic hydroxyls (determined by potentiometric titration in a non-aqueous medium[227,232]); the content of carbonyl groups, determined by the hydroxylamine method, is 0.20 mole per $C_{(6)}-C_{(3)}$ unit for MWL[230] and 0.15 mole for DHP.[231]

It is interesting to note that the molecular weights of preparations of both biosynthetic lignin and lignin isolated from wood or by mechanical grinding are in the range 6000–10 000.[209,230] The results of spectroscopic studies on these preparations are also similar. The infrared spectra of MWL and DHP are identical except for certain

details due to the fact that the preparations differ somewhat in their contents of carbonyl groups (ν = 1710–1740 cm^{-1}) and ethylene double bonds (ν = 970 cm^{-1}).[233–235] The ultraviolet spectra of both preparations are similar as regards the positions of the maxima and minima. At the same time the extinction coefficient of biosynthetic lignin is higher by a factor of 1.2–1.3%. However, after DHP has been kept in 0.1 *N* inorganic acid at 20°C for one week, the extinction coefficient of biosynthetic lignin becomes the same as that of natural lignin[209,236]. Finally, Freudenberg and Harkin showed[237] that both preparations contain small amounts of free radicals. According to ESR data, their concentration is 2.3×10^{16} spin g^{-1} in MWL from spruce wood and 2.15×10^{16} spin g^{-1} in biosynthetic lignin from coniferyl alcohol.

Table 1. Semiempirical "formulae" of certain preparations of biosynthetic and natural lignins (according to the data of Freudenberg et al.[198]).

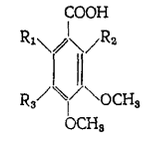
Preparation	Semiempirical "formula"	Loss of hydrogen	Increment of water
DHP from *p*-coumaryl alcohol	$C_9H_{8.75}O_2(H_2O)_{0.30}$	1.25	0.30
DHP from coniferyl alcohol	$C_9H_{7.49}O_2(H_2O)_{0.28}(OCH_3)_{1.01}$	1.51	0.26
DHP from *p*-coumaryl and coniferyl alcohols (1:4)	$C_9H_{7.76}O_2(H_2O)_{0.28}(OCH_3)_{0.83}$	1.44	0.28
DHP from *p*-coumaryl, coniferyl, and sinapyl alcohols (14:80:6)	$C_9H_{7.64}O_2(H_2O)_{0.31}(OCH_3)_{0.92}$	1.44	0.31
MWL from spruce wood	$C_9H_{7.78}O_2(H_2O)_{0.40}(OCH_3)_{0.91}$	1.30	0.40
MWL from beech wood	$C_9H_{6.28}O_2(H_2O)_{0.41}(OCH_3)_{1.36}$	2.36	0.41

*For greater clarity the oxygen content in the "formulae" of the lignins is shown as in the initial alcohol (two atoms per $C_{(6)}$–$C_{(3)}$ unit). The excess oxygen is liberated in the form of water.

The products obtained by the interaction of both DHP and spruce wood lignin with thioglycolic acid had the same elemental composition[196]. This applies also to products of the methylation of DHP and spruce wood lignin with both dimethyl sulphate and alkali and with diazomethane[238], as well as to ammonium lignosulphonates obtained from spruce wood and DHP.[196]

Convincing evidence of the similarity of the compositions of natural and biosynthetic lignins was obtained by cleavage reactions. Thus, when these preparations are treated under identical conditions with hot alkali and then methylated with dimethyl sulphate and the methylated products are oxidised with permanganate. MWL and DHP from a mixture of coniferyl, *p*-coumaryl, and sinapyl alcohols yield more than 20 of the so called degradation acids, mainly methoxybenzoic acids, and the total yield of identified products is about 18% of theoretical[198,214]. The main product of the oxidation of methylated lignins is veratric acid (XLVII), which constitutes about half of the overall yield. The remaining acids were detected in insignificant amounts. Freudenberg and coworkers showed[198,214] that the quantitative ratios and types of acids formed on oxidation of both lignin preparations are identical.

It is interesting to note that in the preparation of biosynthetic lignins from 5-deuterioconiferyl alcohol the loss of deuterium was 45%.[239] On dehydration under the conditions of DHP synthesis, 6-deuterioconiferyl alcohol looses 8–10% of deuterium and 2-deuterioconiferyl alcohol loses 2–4%.[240] These values indicate the relative involvement of various sites in the aromatic ring in the formation of intermolecular C–C bonds of lignin, the reactivity ratios of the 5-, 6-, and 2-positions (45 : 9 : 3) corresponding approximately to the quantitative ratios of the yields of isohemipinic (XLVIII), metahemipinic (XLIX), and hemipinic (L) acids in the products of the oxidative degradation of methylated DHP and MWL:[214]



(XLVII, $R_1=R_2=R_3=H$)
(XLVIII, $R_3=COOH$; $R_1=R_2=H$)
(XLIX, $R_1=COOH$; $R_2=R_3=H$)
(L, $R_2=COOH$; $R_1=R_3=H$)

When biosynthetic lignin obtained from [β-^{14}C]coniferyl alcohol, is cleaved, the isohemipinic acid (XLVIII) formed has 49–52% of the specific radioactivity of the initial alcohol, while metahemipinic acid (XLIX) has 10.5% of the specific radioactivity[241]. The isohemipinic and metahemipinic acids isolated from the oxidative degradation products of lignin, formed in young shoots or after the introduction of similarly labelled phenylalanine[242] or coniferin[206], have the same radioactivities in relation to those of the initial lignins (53 and 12% respectively).

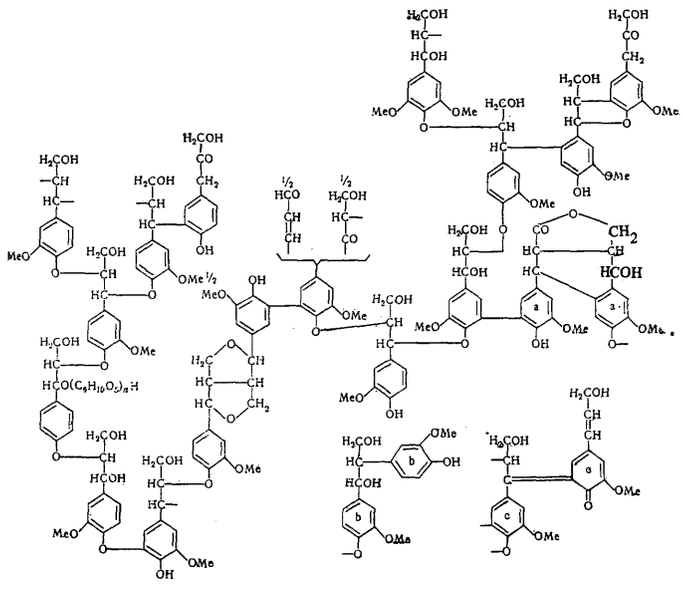
On heating with 28% sulphuric acid, the yield of formaldehyde is 1.1% for MWL and 1.4% for DHP.[209] Finally the yields of vanillin on nitrobenzene oxidation of both preparations are identical and amount to 25% of the initial lignin[209].

Thus the data discussed above demonstrate convincingly the similarity of natural (MWL) and biosynthetic (DHP) lignins as regards many important chemical and physical properties.

5. The Structure of a Lignin Fragment

The data discussed above on the biosynthesis of lignin *in vitro* (intermediates, the ratio of the principal dilignols, the four growth pathways) together with the chemical analyses of spruce wood lignin isolated by Björkman's method (elemental composition, the number and types of hydroxy-groups, the ratio of the three initial monomeric alcohols, the content of carbonyl groups, etc.) and the results of experiments on the polymerisation of labelled [^{14}C]coniferyl alcohol served as a basis of the schematic structural formula of a lignin fragment derived by Freudenberg. The first version[243] proposed in 1961 was subsequently modified several times by the author[220,226,237]. The latest scheme, put forward by Freudenberg at the International Symposium at Grenoble[225], consists of 18 units and corresponds to the composition of the dehydropolymer obtained by the dehydrogenation *in vitro* of a very dilute mixture of 14 moles of *p*-coumaryl alcohol, 80

moles of coniferyl alcohol, and 6 moles of sinapyl alcohol catalysed by laccase.



The detailed characteristics and an assessment of the schematic formula for a lignin molecular fragment as well as its comparison with natural and biosynthetic lignins are given in a number of latest reports by Freudenberg and coworkers [209,215,225,244-247]. In the present review we shall confine ourselves to a Table where certain characteristics of spruce wood lignin are compared with the corresponding data calculated on the basis of the schematic formula of a lignin fragment (Table 2).

Table 2 shows that the characteristics predicted on the basis of Freudenberg's scheme and covering a wide range of the chemical reactions of lignin are satisfactorily consistent with the experimental value. This enabled Freudenberg [225] to assert that at the present time there are no facts in the chemistry of lignin which could not be accounted for by his scheme.

In conclusion of the discussion of Freudenberg's work on the biosynthesis of lignin *in vitro*, we must consider certain methodological questions. Freudenberg [209] correctly suggests that comparison of the biosynthetic and natural lignins is valid only when the following factors are identical in both cases: (1) the initial monomeric products and their ratios; (2) the conditions governing the formation of lignin (enzyme systems, temperature, etc.); (3) the final products.

As shown in the previous sections, in the present stage of the investigation of lignin, all these factors appear to be identical both in the *in vitro* biosynthesis of lignin and in the formation of lignin in the plant. On the basis of the identity of the starting materials and final products in the synthesis of lignin *in vitro* and *in vivo*, Freudenberg [209] concluded that the mechanisms of natural and artificial lignification are the same and that the intermediates formed in both cases are similar. Moreover, Freudenberg [202] postulates that the data obtained in the study of the biosynthesis of DHP from *p*-hydroxycinnamyl alcohols can be used to account for the structure of natural lignin.

The structures of polysaccharides, proteins, and other biopolymers are established by identifying the oligomeric products obtained as a result of their cleavage reactions (mainly by hydrolysis). The determination of the structure of lignin on the basis of those of the oligolignols formed during its biosynthesis *in vitro* constitutes essentially a first attempt to determine by this type of procedure the structure of this complex polymer. One must not forget that the role of lignin in the plant is responsible for a number of the characteristics of its natural synthesis. In contrast to the synthesis of proteins, the molecules of which are constructed with the aid of templets, which ensures their exact reproduction, many stages of the biosynthesis of lignin take place in a random fashion, which is the reason for the wide variety of types of intramolecular bonds in its macromolecule. All this must be taken into account in assessing the structural scheme for a fragment of the lignin molecule devised by Freudenberg.

Table 2. Comparison of certain characteristics of lignin with data calculated on the basis of the schematic representation of a lignin* fragment (according to Freudenberg's data [247]).

Characteristic	Found or calc. for spruce wood lignin	Predicted on the basis of the schematic formula of a lignin fragment
Units capable of reacting with thioglycolic acid (α-ether, α-carbinol, phenylethylene, carbonyl)	0.8	0.8
Formation of lignosulphonic acid**		
Group X } A	0.15	0.17
Group Z } A	0.15	0.20
Group B	0.30	0.28
Total	0.60	0.65
Units capable of splitting off methanol (0.5% HCl, 20°C)	0.62	0.72
Units capable of splitting off methanol after treatment with $NaBH_4$	0.42	0.41
Condensation at 5-C	0.45	0.42
Condensation at 6-C	0.08	0.07
Condensation at 2-C	0.04	
Units capable of involvement in biphenyl linkages	0.25-0.30	0.22
Units capable of forming Hibbert ketones	0.1	0.17
Units capable of forming vanillin and vanillic acid	0.32	0.30-0.35
Aromatic and similar protons } from NMR spectra	2.5	2.4
Aliphatic protons } from NMR spectra	3.8	3.8

*The calculation refers to the average composition of the structural unit.
**Group X = *p*-hydroxybenzyl alcohols and alkyl *p*-hydroxybenzyl ethers; group Z = *p*-alkoxybenzyl alcohol; group B = alkyl *p*-alkoxybenzyl ethers.

On the basis of the foregoing, one must emphasise that the series of Freudenberg's studies on the biosynthesis of lignin has made a major contribution to the chemistry of lignin. Freudenberg's scheme for a lignin macromolecular fragment undoubtedly provides an approximate idea about the structure of lignins. Freudenberg's principal conclusions have been confirmed by the latest studies of Nimz [248-250] on the isolation of dimeric and oligomeric lignin fragments by mild hydrolysis (percolation) of wood. However, Pew's work on the enzymatic dehydrogenation of alkyl-*p*-hydroxyphenylmethanols and *p*-hydroxypropiophenones, discussed in the next section, has revealed a number of new aspects of the biosynthesis of lignin which

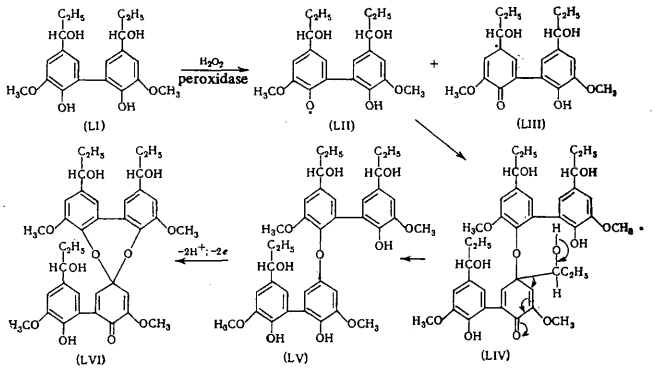
are not accounted for by Freudenberg's theory. Other combinations of groups leading to the formation of hitherto undiscovered structural elements of lignin are quite probable. Thus the question of the formation of lignin in plants and *in vitro* requires further studies.

6. Enzymatic Dehydrogenation of Other Phenylpropane Compounds and "Chemical Synthesis" of Lignin

A considerable number of studies on the preparation of lignin-like polymers by the enzymatic dehydrogenation of phenolic precursors other than coniferyl alcohol have been published. These investigations, which have been quite adequately discussed in the monograph of Brauns and Brauns [2], are of comparatively lesser interest since they deal mainly with the final dehydropolymerisation products. The recently published work of Pew [251-255] on the enzymatic dehydrogenation of a number of phenolic compounds structurally related to lignin is superior in this respect.

The study of the dehydrogenation of model phenols, preferably without C–C bonds in the side chain conjugated with the aromatic ring (eugenol, allylsyringol, isoeugenol, dehydrodieugenol, and others), by the action of peroxidase and hydrogen peroxide, led Pew and coworkers [251] to the conclusion that, apart from the biphenyl linkages, diphenyl ether linkages between monomeric units play a considerable role in the formation of lignin.

In addition, the authors showed that the enzymatic dehydrogenation of the phenols results in the formation of quinone methides of a type different from that described in the literature, which the authors believe can participate in the formation of lignin. Later Pew and Connors [252] published the results of a study of the enzymatic dehydrogenation of a number of alkyl-*p*-hydroxyphenylmethanols. When ethylguiacylmethanol was dehydrogenated in an aqueous solution by peroxidase and hydrogen peroxide, a hitherto unknown dibenzo[*d*,*f*][1,3]dioxepin (LVI) is formed with elimination of the side chain as propionaldehyde:

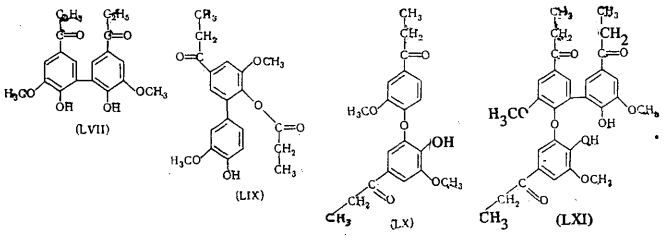


The mechanism of the formation of the dioxepin (VIL) proposed by the authors [252] consists in the initial formation of dehydrobisethylguiacylmethanol (LI) with its subsequent dehydrogenation, which leads to the formation of the biphenylyloxy-radical (LII); this combines with the cyclohexadienone mesomeric form of the same radical (LIII) to yield the dienone tetramer (LIV). The latter is then rearomatised by the elimination of propionaldehyde to form compound (LV), which yields phenoxy- and *p*-cyclohexadienone radicals on further dehydrogenation. The radicals undergo an intramolecular coupling to form the dioxepin (LVI).

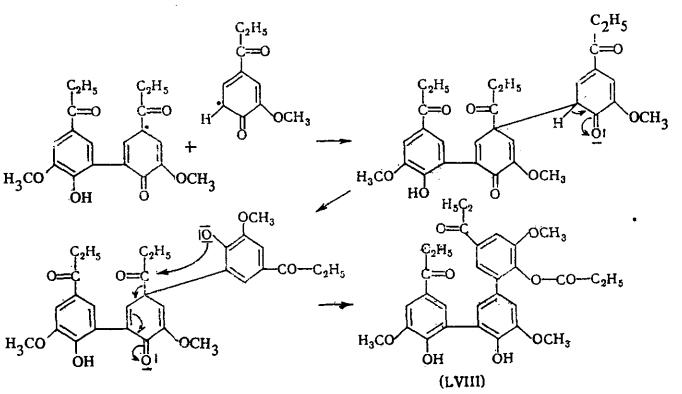
The authors showed [252] that an analogous type of reaction with formation of the corresponding dioxepin is undergone also by β-guaiacyl guaiacylglyceryl ether, the analogue of the extremely important dimeric intermediate in the biosynthesis of lignin *in vitro*. In addition, evidence was obtained showing that other *p*-hydroxybenzyl alcohols and certain ethers reacts similarly.

The results of this investigation enabled Pew and Connors to conclude that cyclohexadienone forms of phenoxy-radicals play an important role in the biosynthesis of lignin. It is particularly true in those cases where the *ortho*-position in relation to the phenolic hydroxyl is blocked, as in the cases where biphenyl and diphenyl ether linkages or a methoxy-group are present in syringic structures. Coupling involving this type of radical is usually accompanied by the removal of the side chain and, when biphenyl groups are present, it leads to the formation of structures of the dioxepin type. The latter can enter into the composition of the lignin macromolecule as such or in the form of quinonoid structures formed by the hydrolysis of the dioxepins.

Pew and Connors [253] also achieved the enzymatic dehydrogenation of a number of *p*-hydroxypropiophenones. When propioguaiacone is dehydrogenated in aqueous solutions by peroxidase and hydrogen peroxide, the product is an *oo'*-dihydroxybiphenyl derivative—dehydrodipropioguaiacone (LVII). In addition to this compound, a triphenyl derivative (LVIII), with an *op'*-biphenyl type of linkage hitherto unknown for lignin and with a propionate ester group, a dimeric ester (LIX), an *o*-diphenyl ether derivative (LX), and a trimer (LXI) containing both the *oo'*-biphenyl and *o*-diphenyl ether linkages were also identified.



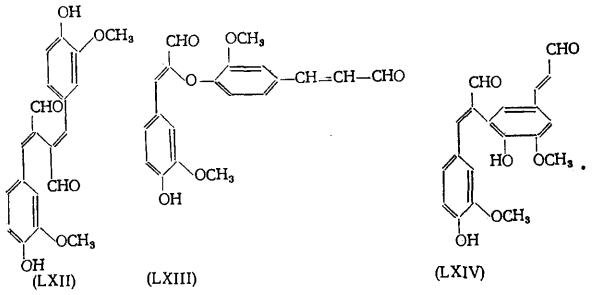
According to Pew and Connors [254], the mechanism of the formation of the trimer (LVIII) consists of the coupling of the cyclohexadienone mesomeric form of the biphenyl radical with the mesomeric *ortho*-radical. The coupling is followed by the rearomatisation of the dienone ring via an intramolecular nucleophilic attack on its carbonyl group in the side chain by the phenoxide ion produced by the deprotonation of the upper unit, which leads to transfer of the side chain and the formation of the ester (LVIII).



The formation of esters via the transfer of the side chain was demonstrated[254] with the aid of spectroscopic methods also on dehydrogenation products of vanillin, acetoguaiacone, and ethyl vanillate and on this basis it was concluded that the reaction is probably general.

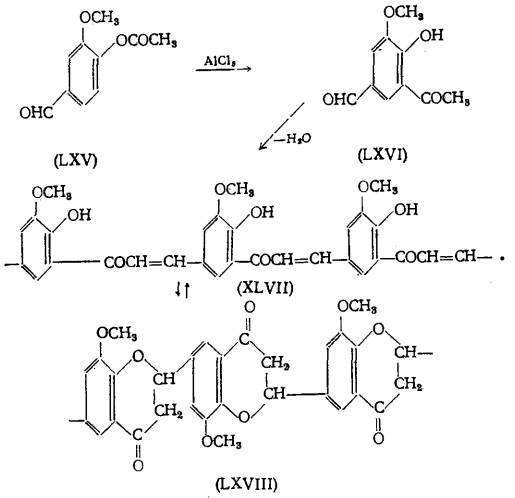
The results led to the hypothesis that lignin contains *op'*-oriented biphenyl linkages—a hitherto unknown type of linkage between monomeric units—and also that aliphatic acid esters are structures characteristic of the lignin macromolecule.

Connors et al.[255] dehydrogenated *trans*-coniferaldehyde in aqueous solution with peroxidase and hydrogen peroxide. They showed that the bulk of the products consists of three hitherto unknown dimers: 2,3-diformyl-1,4-di-(5-guaiacyl)buta-1,3-diene (LXII); α-[4-(β-formylvinyl)-2-methoxyphenoxy]coniferaldehyde (LXIII); α-[5-(β-formylvinyl)-2-hydroxy-3-methoxyphenyl]coniferaldehyde (LXIV):



(LXII) (LXIII) (LXIV)

The results of the above studies on the enzymatic dehydrogenation of various model compounds of lignin, carried out by Pew and coworkers, reveal certain aspects of the biosynthesis of lignin *in vitro* and can be regarded as supplementing Freudenberg's theory. There is no doubt that future studies will broaden current ideas on the biosynthesis of lignin and will lead to the discovery of new structural features of this polymer. Finally, mention should be made of the studies of Russell[256-259] on the chemical synthesis of lignin, which constitutes perhaps the only attempt of this kind. The author employed as the starting material vanillin monoacetate (LXV), which yielded 5-formyl-2-hydroxy-3-methoxyacetophenone (LXVI) as a result of the Fries rearrangement. The acetophenone readily underwent condensation polymerisation to compound (LXVII) which in turn cyclised into poly-8-methoxydihydrobenzopyrone (LXVIII). According to Russell's data, the polymer is in many respects analogous to spruce wood lignin:



(LXV) (LXVI) (XLVII) (LXVIII)

It is noteworthy that, whereas in the biochemical synthesis of lignin the aryloxy-radicals produced react in different forms to yield various recombination products which precludes a strictly defined sequence of linkages between the monomers in the polymer, in the chemical synthesis this type of disorder does not occur. Modern ideas concerning the inhomogeneity of the structure of lignin are inconsistent with Russell's "formula" and therefore his investigations were not continued further and are quoted here only for historical interest.

IV. SOME ASPECTS OF THE BIOSYNTHESIS OF LIGNIN *IN VIVO*

The results of the study of the biosynthesis of lignin *in vitro* led Freudenberg[147,260,261] to a hypothesis concerning the formation of lignin in the plant. During the vegetative period, new cells are actively formed in the cambial layer of wood. Young, still unlignified cells adjoining the cambium are gradually replaced, as they are separated further from the cambial layer, by ripe thick-walled cells, which produce an intense colour on treatment with phloroglucinol and hydrochloric acid. Coniferin has been detected in considerable amounts in the cambial layer and on either side of it. However, the laccase and peroxidase present in the precambial layer are capable of dehydrogenating coniferyl alcohol only. On this basis, one may expect the presence in this part of woody tissue of β-glucosidase which has in fact been detected in cuttings of 2 year old spruce shoots treated with indican (indoxyl glucoside). The β-glucosidase cleaved indican and the free indoxyl formed was rapidly converted in air into indigo, indicating the location of β-glucosidase. It was found that β-glucosidase is absent both from the young cells of the precambial layer and from the ripe lignified cells but is detected in large amounts in an intermediate layer, which is evidently the zone where lignin is formed. On the basis of these results, Freudenberg suggests that the formation of lignin in the plant can be represented as follows. Coniferin diffuses into the tissue where it is cleaved by β-glucosidase to free coniferyl alcohol, which is converted into lignin by the action of peroxidase and laccase. As soon as the tissue, particularly its intracellular parts, is filled by lignin, the cells die and β-glucosidase is no longer detected in them. It is interesting to note that, when the enzyme action continues after the tissue has been filled by lignin, the latter is degraded. Thus, when laccase or peroxidase acts on a suspension of natural or biosynthetic lignin in water, the preparations are degraded in a manner resembling humification and the degradation of phenols in the soil. A similar degradation is observed when wood rot serves as a source of dehydrogenases. Moreover, as mentioned above, the yield of DHP amounts to about 90%, never reaching 100%. According to Freudenberg's views[262], this is because lignin is partly decomposed on dehydrogenation. Thus the same enzymes (laccase and peroxidase) are involved in the formation and degradation of lignin.

As stated in the introduction, the lignification process cannot be regarded in isolation from other processes occurring in the formation of the plant cell. The complete set of these processes includes the biosynthesis of various components of plant tissue, during which different types of chemical linkages may arise between them together with the formation of various morphological components of the cell wall. These problems are undoubtedly of considerable theoretical and practical interest. On the

other hand, the available literature data are very limited, which precludes at the present time the consideration of the problems of the biosynthesis of the complete set of plant cell wall components. Evidently such an attempt is a matter for the future when not only the problems of the biosynthesis of the individual plant components (lignin, celluloses, and hemicelluloses) but also the general relations governing the formation of the plant cells will become adequately elucidated. However, even now many interesting data obtained in the study of the lignification of tissue cultures throw light on certain aspects of the biosynthesis of lignin *in vivo*.

As stated above, the method of tissue culture is widely used [31,99,101,158-165,263-271] in the study of various enzymatic systems involved in the biosynthesis of monomeric precursors of lignin and also in tests on various labelled compounds as lignin precursors. These investigations were considered in individual subsections of section II. Apart from these more of less local problems, experiments on tissue culture permitted an approach to the solution of wider problems of the biochemistry and physiology of plants. These may be formulated as follows: (1) the establishment of the possibility of a local lignification process or of the requirements by this process for compounds entering from the roots or leaves of the plant; (2) the establishment of the identity of the lignin precursors with retention or exclusion of correlations in the plant organism (when the biosynthesis of aromatic lignin precursors is localised, as mentioned above, are obtained); (3) the establishment of the chemical nature of the possible lignin precursors and the discovery on this basis whether the lignification process takes place in isolated tissues via the same pathways as in whole plants; (4) the elucidation of the physiological role of intermediate metabolites of the lignification process in the metabolism of the whole organism.

The studies using the tissue culture method established [264] that the lignin deposited in cell walls of the xylem elements of isolated tissues has a chemical composition similar to that of the lignin of higher plants. Moreover, it has been shown [165] that the biosynthesis of lignin in isolated tissues which have been living for a long time in an *in vitro* culture takes place locally using the carbohydrates of the nutrient medium. Consequently lignification does not require the supply of specific compounds from the roots or plant organs above ground. Since it was observed that inhibition of the growth of tissues does not affect the accumulation of lignin, it has been suggested [162] that the lignification and growth processes are to some extent separate.

The conclusions arrived at as a result of studies on tissue cultures are of great interest and permit an approach to the solution of the problems of the biosynthesis of lignin from a wider standpoint than is allowed by experiments on the biosynthesis of lignin *in vitro*. On the other hand, there is no doubt that these conclusions require certain additions and corrections. Finally a few concluding words may be said concerning the biosynthesis of lignin in connection with the problems of the orthogenesis and phylogenesis of plants.

In 1934 Holmberg [272] studied the lignins isolated from 50 plant species with the aid of thioglycolic acid and observed that the carbon content in the lignins of gymnosperms is higher by 3–4% than in the lignins of angiosperms, while the content of methoxy-groups is higher in the latter than in the former. Later, Hibbert and coworkers [273-275] used Freudenberg's method [276] of nitrobenzene oxidation to investigate plants of different classes and showed that, while the main product of the nitrobenzene oxidation of the lignin of gymnosperms is vanillin, dicotyledonous angiosperms yield a mixture of vanillin and syringaldehyde, while monocotyledonous angiosperms give a mixture of vanillin, syringaldehyde, and *p*-hydroxybenzaldehyde. The results led to the hypothesis that the reaction with alkaline nitrobenzene may be used for a taxonomic classification of plant materials. Subsequent investigations [277,278] by more sophisticated methods for the separation of oxidation products confirmed Hibbert's main conclusion with certain revisions. The results have served as a basis of the concept, generally accepted at the present time, that lignin is made up of phenylpropane derivatives methoxylated to different extents in the aromatic ring. The extensive studies by Manskaya [279-282], Kratzl [283], and others on lignins from different plant groups yielded interesting data concerning the role of lignin in the phylogenesis of plants. Thus Manskaya [279-282] studied living plant forms close to fossil plants in order to establish the formation of lignin in the phylogenesis in various plant groups. The author believes that the distinctive features of the lignins in various plant groups and the nature of the changes in their chemical composition on going from lower to more highly organised plants make it possible to deduce the relative content of lignin and the ratio of its elements methoxylated to different extents in plants existing in the past geological epochs. According to the majority of investigators, lignin which occurred initially in vascular plants of the order *Pteridophyta* (in recent years definite evidence has been obtained for its presence also in mosses [284] and even seaweed [285,286]), probably underwent considerable quantitative as well as qualitative changes during the evolution of plants.

There are many data demonstrating the changes in lignin during the orthogenesis of plants. Thus Stone et al. [287] showed that the ratio of vanillin and syringaldehyde in wheat lignin oxidation products vary with the age of the plants. Higuchi [134] studied the composition of lignin in the upper, middle, and lower parts of the shoots of three bamboo species. He showed [134], that as lignification progresses, there is a considerable increase in the overall content of aldehydes (calculated as the content of Klason's lignin) obtained on nitrobenzene oxidation and also of the ratio of syringaldehyde and vanillin. In the upper part of the bamboo shoots, where the degree of lignification was lowest, the fraction of syringaldehyde in the nitrobenzene oxidation products was also lowest. As lignification proceeded, the fraction of syringaldehyde increased, reaching a maximum in the adult plant. Freudenberg and Torres-Serres [288] showed that the cambial layer of one- and two-year old spruce shoots contains comparatively more *p*-glucocoumaryl alcohol than older spruces. Correspondingly the content of methoxy-groups in LMG from young spruces is 12–13% compared with 15.6% in MWL from the adult spruce [242,288]. These results suggest that the changes in lignin during onthogenesis corresponds to changes which it undergoes during phylogenesis.

The above data are undoubtedly of considerable interest although in the present stage of investigation it is as yet impossible to explain the changes in the degree of methoxylation of lignin during the onthogenesis and phylogenesis of plants.

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Acid-Base Equilibria in Amphiprotic Solvents and Potentiometric Titration

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Modern ideas about acid-base equilibria in amphiprotic solvents (acetonitrile, dimethylformamide, ketones, and others) are discussed. Data are presented for the homoconjugation constants of phenol and benzoic acid derivatives in these solvents and the calculation of acid-base titration curves is described. The question of the solvent acidity scales and their relative positions on a unique acidity scale are discussed. Factors limiting the solvent acidity scale calculated from its autoprotolysis constant are considered. Data are presented for the measured relative (practical) acidity scales for non-aqueous solvents and their mixtures in potentiometric titration. The optimal conditions chosen for acid-base titration are justified. The bibliography includes 180 references.

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1. INTRODUCTION

During recent years considerable advances have been achieved in the physical and analytical chemistry of non-aqueous solutions[1-17]. This has assisted a quantitative assessment of the effect of the properties of the solvent on those of the solute and a further development of the theory of acid — base potentiometric titration in non-aqueous solutions.

The study of acid — base interaction in amphiprotic solvents with weak acid and basic properties showed that the overall scheme of equilibria in electrolyte solutions (acids, bases, and salts) includes a large number of intermediate stages. Therefore a quantitative interpretation of these interactions is very much more complicated than in an aqueous medium or in solvents with properties similar to those of water (lower alcohols, glycols). Progress in this field of science involved measurements by different methods (spectrophotometric, conductimetric, and potentiometric) not only of the dissociation constants of acids and bases in amphiprotic solvents but also of equilibrium constants characterising individual stages of the acid — base interaction. The effect of water and other hydrogen bond donors and acceptors on the conditions governing acid — base interactions in amphiprotic solvents has been characterised quantitatively. The equations derived by Kolthoff make it possible to calculate the pH of buffer solutions and also potentiometric titration curves in solvents such as acetonitrile, dimethylformamide (DMF), and dimethyl sulphoxide.

Since acid — base interaction in any solvent is due primarily to the acid and basic properties of the solvent itself, it is necessary to consider the question of solvent acidity scales. The studies in this field have yielded many new data for autoprotolysis constants and the unique null proton activity coefficients which can be used to construct a unique solvent acidity scale. Factors limiting solvent acidity scales merit special attention, since under real conditions solvents usually contain admixtures of water and other solvents which distort their acid — base properties. This necessitates the study of the physicochemical properties of mixed solvents.

The present review considers the latest data on acid — base interaction in amphiprotic solvents and solvent acidity scales. The large volume of information in this field necessitates continual review and critical assessment of the published work.

In conclusion the choice of the optimal conditions for potentiometric acid — base titration is justified. New studies on the theory and practice of potentiometric acid — base titration have shown that the potentialities of this method are far from being exhausted[18].

2. ACID — BASE EQUILIBRIA AND CALCULATION OF TITRATION CURVES

When an acid HA interacts with a base B in a protolytic solvent SH, a number of reactions take place; the main processes are as follows[8,19-21]:

intrinsic ionisation of the solvent:

$$2SH \rightleftarrows SH_2^+ + S^- ; \quad (1)$$

interaction of the acid with the solvent:

$$HA + SH \rightleftarrows HS \cdots HA \rightleftarrows SH_2^+ \cdot A^- \rightleftarrows SH_2^+ + A^- ; \quad (2)$$

interaction of the base with the solvent:

$$B + SH \rightleftarrows B \cdots SH \rightleftarrows BH^+ \cdot S^- \rightleftarrows BH^+ + S^- ; \quad (3)$$

interaction of the acid with the base:

$$HA + B \rightleftarrows BH^+ \cdot A^- \rightleftarrows BH^+ + A^- . \quad (4)$$

Depending on the properties of the solvent, the acid and the base, a definite relation is established between these equilibria.

When an acid HA is titrated in a solvent SH with a standard solution of a base B, reaction (4) predominates[19]. However, there is the possibility of a simultaneous side reaction (3) in which the solvent interacts as an acid with the titrant. The extent of reaction (4) depends on the relative acid properties of the acid HA and the solvent SH. The stronger the acid HA and the weaker the acid SH, the higher the extent of reaction (4) and the interaction of the HA acid being determined with the titrant B is quantitative. The weaker the acid HA and the stronger the acid SH the less complete is reaction (4).

When a base B is titrated in a solvent SH with a standard solution of an acid HA, the main reaction (4) is accompanied by a side reaction (2). The extent of reaction (4) depends on the relative basic properties of the

base B being determined and the solvent SH. The more basic the properties of the solvent SH and the weaker those of B the less complete is reaction (4) because the side reaction (2) occurs to a considerable degree.

Since in aqueous solutions salts are fully dissociated and strong acid and base solutions may be employed as titrants, for the calculation of titration curves in water it is necessary to know the concentration of the acid HA or the base B being titrated, their dissociation constants K_A or K_B, and the autoprotolysis constant of water K_S.[22,23]

Calculation of acid — base equilibria in water-like solvents such as ethanol and methanol resembles the calculation of titration curves in water, since the formation of ion pairs takes place to only a slight extent and salts behave as strong electrolytes. Compared with water, the activity coefficients in these solvents are appreciably reduced (at the same ionic strength). The Debye — Hückel law may be employed at ionic strengths less than 0.01.[19]

In other alcohols, the dielectric constants of which are less than 24, calculations of titration curves are complicated, since ion pairs are formed. In this case it is also necessary to consider the dissociation constants of the titrant electrolyte and of the salt formed. Such calculations of titration curves have been performed by Kolthoff and Bruckenstein[19] for acetic acid. They studied the acid — base equilibria in acetic acid and measured the dissociation constants of electrolytes and the autoprotolysis constant of the solvent[22]. The titration curves calculated from these data agree satisfactorily with experiment. The lack of data for the dissociation constants of electrolytes and sometimes also the autoprotolysis constants of the solvents precludes the use of the Kolthoff equation for the calculation of titration curves in alcohols with low dielectric constants.

Table 1. The dissociation (K_{HA}) and homoconjugation ($K_{HA_2^-}$) constants of substituted phenols and benzoic acids in acetonitrile.

No.	Compound	pK_{HA}[28,30,32—34]	$\lg K_{HA_2^-}$[27,28,30,32,33]
1	*o*-Nitrophenol	22.0; 22.1; 21.2	2.0; 2.2
2	*p*-Nitrophenol	20.0 20.7; 21.0; 20.9	3.66; 3.15; 3.48; 3.67
3	*m*-Nitrophenol	22.6	3.48
4	2,4-Dinitrophenol	16.0	3.08
5	3,5-Dinitrophenol	20.5; 20.8; 20.9	4.64
6	2,6-Dinitrophenol	16.0; 15.34	2.08
7	4-Chloro-2,6-dinitrophenol	15.0	1.00
8	3-Chloro-4-nitrophenol	19.95	3.62
9	2,4,6-Trinitrophenol	11.0	0.30
10	*p*-Hydroxybenzoic acid	20.8	3.05
11	Benzoic acid	20.7	3.60
12	*m*-Bromobenzoic acid	19.5	3.75
13	3,4-Dichlorobenzoic acid	19.04	—
14	*m*-Nitrobenzoic acid	19.29	4.03
15	*p*-Nitrobenzoic acid	18.7	3.85
16	4-Chloro-3-nitrobenzoic acid	18.55	3.97
17	*o*-Nitrobenzoic acid	18.24	3.98
18	3,5-Dinitrobenzoic acid	16.9	4.0;4.22
19	2,4-Dinitrobenzoic acid	16.19	4.29

Considerable advances have been achieved recently in the study and interpretation of the acid — base interaction in aprotic dipolar solvents (acetonitrile, dimethyl sulphoxide, dimethylformamide, and others). In these solvents, the molecules of which are incapable of forming hydrogen bonds with the acid anions and base molecules, hydrogen-bonded complexes of the type HA_2^- and B_2H^+ are formed.

Much credit is due to Kolthoff, Coetzee, and coworkers[24-26] for their investigation of acid — base interactions in acetonitrile. The formation of complexes via hydrogen bonding between the acid (HA or BH^+) and the conjugate base (A^- or B) was called homoconjugation. Homoconjugation in acetonitrile has been studied comprehensively for the dissociation of phenol and benzoic acid derivatives, amines, and other organic bases[21,24-30].

The existence in solution of species of the type HA_2^- was predicted theoretically[31]. In the first place homoconjugation is determined by the relative basicities of the solvent molecule and the acid anion and the amphoteric properties of the solvent molecule. The capacity of the acid molecule HA for the formation of the complex HA_2^- increases as the proton-donating properties of the acid and the proton-accepting properties of its anions become more pronounced. The possibility of forming an intramolecular hydrogen bond lowers the capacity of the acid for interaction with the anion. Thus *ortho*-substituted phenols and benzoic acids are less involved in the homoconjugation process than the *meta*- and *para*-substituted derivatives. Homoconjugation does not occur when acid anions are additionally stabilised by intramolecular hydrogen bonding or by resonance (the anions of picric acid, 2,4-dinitrophenol, and 2,6-dihydroxybenzoic acid) and also as a result of steric blocking of the ionic group (2,6-di-t-butylphenol)[32,33].

Kolthoff[25] showed that, in the calculation of the concentration of hydrogen ions in a solution of a weak acid, it is necessary to begin with the overall constant $K_{2(HA)}$ which includes the acid dissociation constant K_{HA} and the homoconjugation constant $K_{HA_2^-}$:

$$HA \rightleftarrows H^+ + A^-; \quad K_{HA} = \frac{[H^+][A^-]\, f^2}{[HA]},$$

$$HA + A^- \rightleftarrows HA_2^-; \quad K_{HA_2^-} = \frac{[HA_2^-]}{[HA]\,[A^-]},$$

$$2\,HA \rightleftarrows H^+ + HA_2^-; \quad K_{2(HA)} = \frac{[H^+]\,[HA_2^-]\, f^2}{[HA]^2} = K_{HA}\,K_{HA_2^-},$$

The data in Table 1 show that the homoconjugation constants $K_{HA_2^-}$ for phenol and benzoic acid derivatives are usually fairly high. The acid strength of phenol and benzoic acid derivatives in acetonitrile increases on introduction of electron-accepting substituents. It was found that the relations between pK_{HA} and the σ constants for the substituents in phenols and benzoic acids are linear[32,33]. For benzoic acids, the relations between $\lg K_{HA_2^-}$ and σ are also linear[33]. Fig. 1 shows the variation of pK_{HA} and $\lg K_{HA_2^-}$ with the σ constants of the substituents in benzoic acids (lines I and II respectively). The different forms of these relations are due to the fact that the capacity for homoconjugation is less sensitive to changes in the structure of the compound.

To characterise quantitatively the proton-donating capacity of benzoic acid molecules and the proton-accepting capacity of their anions, Kolthoff and Chantooni[33] measured the heteroconjugation constants of acid molecules in relation to the base Cl^- and of acid anions in relation to the acid *p*-bromophenol (HR):

$$HA + Cl^- \rightleftarrows HACl^-; \quad K_{HACl^-} = \frac{[HACl^-]}{[HA]\,[Cl^-]},$$

$$HR + A^- \rightleftarrows HRA^-; \quad K_{HRA^-} = \frac{[HRA^-]}{[HR]\,[A^-]}.$$

Fig. 1 shows (lines III and IV) that the proton-donating capacity of the molecules increases and the proton-accepting capacity of the corresponding anions falls with increase of the σ constants of the substituents. The overall effect of these changes due to the σ constants is reflected in the relation between $\lg K_{HA_2^-}$ and $\Sigma\sigma$ (line II). Similar relations have been found for phenol derivatives[32].

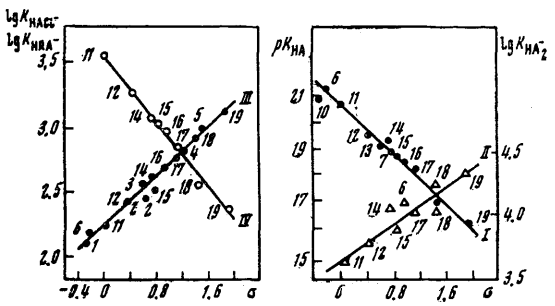

Figure 1. Variation of pK_{HA} (line I), $\lg K_{HA_2^-}$ (line II), $\lg K_{HACl^-}$ (line III), and $\lg K_{HRA^-}$ (line IV) for substituted benzoic acids with the σ constants of the substituents: 1) *p*-methoxy-; 2) *o*-iodo-; 3) *o*-chloro-; 4) 2,6-dichloro-; 5) 5-chloro-2-nitro-; 6) 3,4-dimethyl-; 7) 3,5-dichloro-; numbers 10 — 19 correspond to the ordinal numbers in Table 1.

It has been established that homoconjugation has a significant influence on the shape of the titration curves of acids and bases in acetonitrile. Kolthoff[25] derived an equation relating the activity of hydrogen ions in a solution of a weak acid and its salt, the acid dissociation and homoconjugation constants, and the analytical concentrations of the acid (C_A) and the salt (C_S):

$$a_{H^+}^2 f^2 C_s - a_{H^+} f K_{HA}\{(C_s + C_A) + K_{HA_2^-}(C_s - C_A)^2\} + K_{HA}^2 C_A = 0. \quad (5)$$

In the derivation of Eqn. (5), it was assumed that (1) the salt R_4NA formed in the interaction between the acid HA and the base R_4NOH is fully dissociated, (2) the salt R_4NHA_2 is also a strong electrolyte, and (3) the concentration of hydrogen ions in solution is much lower than the concentration of the salt ($C_{H^+} \ll C_S$). Eqn. (5) is applicable only to a thoroughly purified solvent free from impurities capable of behaving as hydrogen bond donors or acceptors (water, methanol).

Examination of Eqn. (5) shows that, at the instant of half-neutralisation, $a_{H^+} = K_{HA}/f$, i.e. the pH of the solution is determined by the p*K* for the dissociation of the acid. The shape of the titration curve in the buffer region is determined by the product $K_{HA_2^-}(C_S + C_A)$ or $K_{HA_2^-}C_A^0$, where C_A^0 is the initial analytical concentration of the acid titrated. The higher this value the higher the slope of the buffer section of the titration curve, the smaller the pH jump at the end of the titration, and the less satisfactory the conditions for the differential titration of a mixture of acids[35].

Calculation of the pH for the buffer section of the titration curve by Eqn. (5) shows that, when $K_{HA_2^-}C_A^0 \geq 10^2$, an inflection is observed in the titration curve at the half-neutralisation point[25]. Since $K_{HA_2^-}$ for acetonitrile is of the order of $10^3 - 10^4$ (Table 1), the shape of the titration curves is hardly distorted for $C_A^0 \leq 10^{-3}$. In the absence of homoconjugation, the pH in the course of titration from 1% to 99% neutralisation increases by 4 units. In the presence of homoconjugation the pH change is $\Delta pH = -\lg[10^{-4}/(K_{HA_2^-}C_A^0)^2]$. Thus, when $K_{HA_2^-}C_A^0 = 10^3$, ΔpH is as much as 10 units.

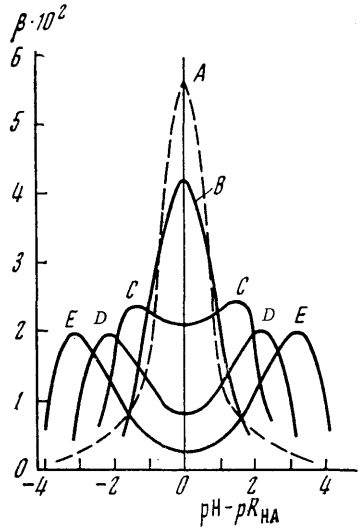

Figure 2. Dependence of the buffer capacity β on the pH of a mixed solution of HA and $(C_2H_5)_4NA$: *A*) dissociation without homoconjugation; *B*) $K_{HA_2^-}C_0 = 1$; *C*) $K_{HA_2^-}C_0 = 10$; *D*) $K_{HA_2^-}C_0 = 100$; *E*) $K_{HA_2^-}C_0 = 1000$.

Kolthoff and Chantooni[25] studied the buffer capacity of solutions of acids and their tetraethylammonium salts as a function of $K_{HA_2^-}C_A^0$. The authors derived from Eqn. (5) an expression for a quantitative characteristic of the buffer capacity of the solution (β):

$$\beta = -2.303\left[\frac{K_{HA}\,K_{HA_2^-}-(C_A^0-2C_s)^2+K_{HA}\,C_A^0-2C_s[H^+]}{[H^+]+4K_{HA}\,K_{HA_2^-}\,(C_A^0-2C_s)-K_{HA}^2/[H^+]}\right], \quad (6)$$

which is applicable to the calculation of β almost over the entire section of the neutralisation curve corresponding to the buffer region. Fig. 2 presents relations between the buffer capacity β and the pH of the solution in mixtures of HA and $(C_2H_5)_4NA$ for different values of $K_{HA_2^-}C_A^0$. Calculation of the buffer capacity by Eqn. (6) at the instant of half-neutralisation when $K_{HA_2^-}C_0 \gg 1$ leads to the expression

$$\beta_{1/2} = -\frac{2.303}{2}\sqrt{\frac{C_0}{2K_{HA_2^-}}},$$

which shows that $\beta_{1/2}$ depends on the ratio $C_0/K_{HA_2^-}$ and is smaller the smaller the value of the ratio.

If homoconjugation takes place to a considerable extent and $K_{HA_2^-}C_0 \geq 10$, the buffer capacity has two maxima which are displaced with increase of $K_{HA_2^-}C_0$ towards more acid and alkaline regions, in accordance with $pH_{1/2}$.

Water and alcohols can behave as hydrogen bond donors and acceptors in aprotic dipolar solvents[32,33,36-41]. Kolthoff and Chantooni[37] made a quantitative study of the effect of these impurities on the acidity of solutions of mixtures of weak acids and their salts in acetonitrile. They showed that, in the presence of a hydrogen bond donor HR, it is necessary to take into account the following equilibria involving the formation of complexes:

$$A^- + HR \rightleftarrows AHR^-; \quad K_{AHR^-} = \frac{[AHR^-]}{[A^-][HR]},$$

$$A^- + 2HR \rightleftarrows A(HR)_2^-; \quad K_{A(HR)_2^-} = \frac{[A(HR)_2^-]}{[A^-][HR]^2}.$$

If the substance is amphoteric, then, owing to its acceptor properties in relation to the hydrogen bond, we have the equilibria (heteroconjugation)

$$HA + B \rightleftarrows AHB; \quad K_{BHA} = \frac{[BHA]}{[B][HA]},$$

$$HA + 2B \rightleftarrows AHB_2; \quad K_{B_2HA} = \frac{[B_2HA]}{[B]^2[HA]}.$$

An equation has been derived for the calculation of a_{H^+} in a buffer solution taking into account heteroconjugation. Apart from the assumptions made in the derivation of Eqn. (5), it was postulated that (1) K_{HA} and $K_{HA_2^-}$ do not change when HR and B are introduced into the solution, (2) HA_2^- is not involved in heteroconjugation, and (3) the $A^-\ldots HR$ and $AH\ldots B$ interactions take place without proton transfer owing to the extremely weak acid and basic properties of HR and B. The equation relating a_{H^+} to the analytical concentrations of the acid and the salt, the equilibrium concentrations of the hydrogen bond donor HR and acceptor B, the acid dissociation constant, and the homoconjugation and heteroconjugation constants is

$$a_{H^+}^2 f^2 W^2 C_s - a_{H^+} f K_{HA} V W \left[(C_s + C_A) + \frac{K_{HA_2^-}}{V W}(C_s - C_A)^2\right] + K_{HA}^2 V^2 C_s = 0, \quad (7)$$

where

$$V = 1 + K_{AHR^-}[HR] + K_{A(HR)_2^-}^2[HR]^2 + \ldots$$
$$W = 1 + K_{BHA}[B] + K_{B_2HA}^2[B]^2 + \ldots$$

The pH values of buffer solutions of methanesulphonic, picric, 3,5-dinitrobenzoic, salicylic, and benzoic acids and their tetraalkylammonium salts in acetonitrile in the presence of added water, calculated by Eqn. (7), agree well with measurements up to a water concentration of 0.7 M. Fig. 3 shows the effect of water and other hydrogen bond donors and acceptors on the pH of a benzoate buffer solution in the presence of an excess of the acid or salt. It demonstrates that, in the presence of excess salt in the buffer solution, the addition of a hydrogen bond acceptor (dimethyl sulphoxide) causes almost no change in the pH of the buffer solution, but the addition of hydrogen bond donors greatly reduces the pH. In the presence of an excess of acid in the buffer solution, water, methanol, and n-butyl alcohol hardly change the pH, while more powerful hydrogen bond donors and acceptors reduce or increase the pH respectively.

It follows from Eqn. (7) that, when the concentrations of the acid and salt are equal, the activity of hydrogen ions is defined by the relation

$$(a_{H^+})_{1/2} = \frac{V}{W} \cdot \frac{K_{HA}}{f}.$$

Consequently $pH_{1/2}$ is in this case smaller by $\lg(V/W)$ than the $pH_{1/2}$ for a buffer solution in which only a homoconjugation process takes place.

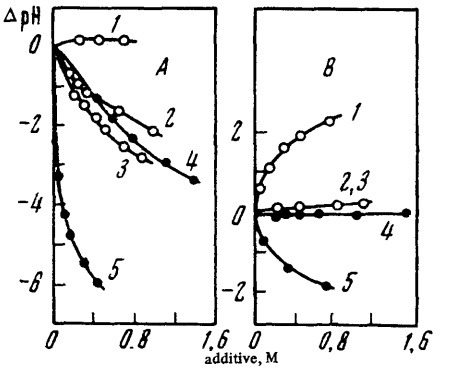

Figure 3. Effect of impurities on the pH of a benzoate buffer solution: *A*) $C_A = 3.6 \times 10^{-3}$ M, $C_S = 3.05 \times 10^{-2}$ M, pH_0 23.40; *B*) $C_A = 6.5 \times 10^{-2}$ M, $C_S = 2.18 \times 10^{-3}$ M, pH_0 16.80; 1) $(CH_3)_2SO$; 2($n\text{-}C_4H_9OH$; 3) CH_3OH; 4) H_2O; 5) $p\text{-}BrC_6H_4OH$;

It follows from the foregoing that heteroconjugation can have a significant influence on the shape of the titration curve in the buffer region[37,42]. According to Eqn. (7) the shape of the curve is determined by the factor[25,37]

$$\frac{C_0 K_{HA_2^-}}{V W}.$$

The study of the effect of methanol added to the solution during the titration is of particular practical interest for acid — base titration in acetonitrile, since standard solutions of quaternary ammonium hydroxides are usually prepared in a benzene — methanol mixture. Fig. 4 presents curves for the potentiometric titration of a 0.02 M solution of 3,5-dinitrobenzoic acid in acetonitrile with tetra-alkyl ammonium hydroxide calculated by Eqns. (5) and (7). The calculations were performed in the range from 0.5% to 99% neutralisation. Fig. 4 shows that methanol has a significant effect only after the point of half-neutralisation. In the presence of *p*-bromophenol, which shows a greater tendency towards heteroconjugation, the titration curve has the shape identical with that for a weak acid in water. The pK_A for 3,5-dinitrobenzoic acid is reduced by 3 units compared with the value in the pure solvent.

Homoconjugation and heteroconjugation in acetonitrile are less characteristic of bases than acids, since acetonitrile has a greater solvating capacity in relation to cations than in relation to anions. These processes have

almost no effect at a base concentration of 10^{-3} M. However, certain hydrogen-bonded complexes B_2H^+ are fairly stable, and their formation must be taken into account in a quantitative interpretation of acid — base equilibria in acetonitrile[12,24,26,29,43]. It has been shown[24] that nitrogenous bases form in acetonitrile not only 1 : 1 hydrogen-bonded complexes B_2H^+ but also more complicated species:

$$B + BH^+ \rightleftarrows BHB^+; \quad K_{BHB^+} = \frac{[BHB^+]}{[B][BH^+]},$$

$$B + BHB^+ \rightleftarrows B_2HB^+; \quad K_{B_2HB^+} = \frac{[B_2HB^+]}{[B][BHB^+]}.$$

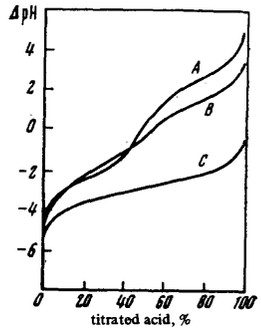

Figure 4. Curves for the potentiometric titration of 0.02 M solution of 3,5-dinitrobenzoic acid calculated by Eqn. (7): *A*) in the absence of impurities; *B*) with 0.1 M R_4NOH solution containing 10% of methanol; *C*) in the presence of 0.5 M solution of *p*-bromophenol.

Table 2. The negative exponents of the dissociation constants (pK_{BH^+}) of the conjugate acids of bases and the logarithms of the homoconjugation constants in acetonitrile[24,29].

Base	pK_{BH^+}	$\lg K_{BHB^+}$	$\lg K_{B_2HB^+}$
Ammonia	16.46	1.04	0.3
Methylamine	18.37	1.54	0.3
Dimethylamine	18.73	1.49	—0.3
Trimethylamine	17.61	0.78	—
Ethylamine	18.40	1.40	0.3
Diethylamine	18.75	0.3	—
Triethylamine	18.46	—	—
n-Propylamine	18.22	1.28	0.3
Tri-n-propylamine	18.10	—	—
n-Butylamine	18.26	1.42	0.4
Di-n-butylamine	18.31	—	—
Tri-n-butylamine	18.09	—	—
t-Butylamine	18.14	1.30	0
Isobutylamine	17.92	—	—
Di-isobutylamine	17.88	—	—
Tri-isobutylamine	18.04	—	—
Piperidine	18.92	1.42	—
Pyrrolidine	19.58	1.51	0.3
Pyridine	12.33	0.6	—
Aniline	10.56	—	—
p-Toluidine	11.25	—	—
Benzylamine	16.76	1.18	—
Monoethanolamine	17.53	1.38	0.18
Morpholine	16.61	1.00	—
1,3-Diphenylguanidine	17.90	—	—

Homoconjugation increases with the strength of the base and the number of hydrogen atoms at the nitrogen atom of the conjugate acid and depends on steric factors (Table 2).

It follows from the pK_{BH^+} data that in acetonitrile all protonated amines are weaker acids than in water owing to the low basicity of acetonitrile[24]. Although on average ΔpK_{BH^+} for bases in acetonitrile and water is 7.6 units, there is a fairly complex quantitative relation between $pK_{BH^+}(CH_3CN)$ and $pK_{BH^+}(H_2O)$. Thus in acetonitrile steric factors play a more important role than in water[29].

Table 2 shows that the formation constants of the complexes BHB^+ in acetonitrile are approximately 100 times smaller than those of the complexes HA_2^-. The tendency of aliphatic amines towards homoconjugation increases in the sequence $R_3N < R_2NH < RNH_2$. Aromatic amines, which are weaker bases, are less capable of homoconjugation than aliphatic amines. For diamines, the formation of BHB^+ decreases with increase of the number of methylene groups owing to the stabilisation of the cation by an intramolecular hydrogen bond[29].

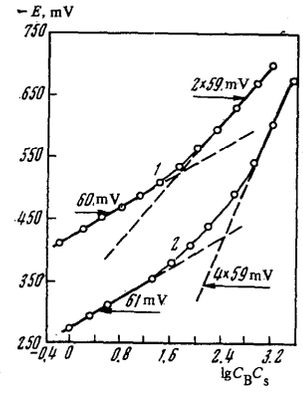

Figure 5. Variation of the glass electrode potential in buffer solutions: 1) piperidine and piperidinium picrate at constant $C_S = 5 \times 10^{-4}$ M; 2) hydrazine and hydrazinium perchlorate at constant $C_S = 5 \times 10^{-4}$ M.

Examination of the effect of homoconjugation on the shape of neutralisation curves for bases showed that, as for acids, the formation of hydrogen-bonded complexes leads to a decrease of the buffer capacity of the solution and a decrease of the pH near the end point of the titration[24]. The main effect of homoconjugation is shown at the beginning of the titration and before the equivalence point where either the base or the salt is present in a large excess. Fig. 5 illustrates the effect of homoconjugation on the change of the glass electrode potential in buffer solutions where the concentration of the salt was kept constant and that of the base was varied. In the absence of homoconjugation, the $E = f(\lg \frac{[B]}{[BH^+]})$ relation is linear with a slope of 59 mV (at 25°C) in accordance with the Nernst equation. When BHB^+ complexes are formed, the equilibrium concentrations [B] and $[BH^+]$ are not equal to the analytical concentrations, because

$$[B] = C_B - [BHB^+] \text{ и } [BH^+] = C_s - [BHB^+]$$

and the relation between E and $\lg(C_B/C_S)$ deviates from linearity. In the presence of a large excess of the base

the relation $E = f(\lg \frac{C_B}{C_{BH^+}})$ is again linear but with a slope of 118 mV (Fig. 5, curve 1). The formation of large complexes leads to a slope $n \times 59$ mV, where n is the number of base molecules bound to the protonated base, i.e. the complex may be represented by B_nHB^+. Fig. 5 (curve 2) illustrates this type of relation for a buffer solution consisting of hydrazine and its perchlorate. It shows that the effect of homoconjugation for bases in acetonitrile occurs for fairly high ratios $C_B/C_{BH^+} \geq 100$.

Table 3. The negative exponents of the dissociation constants (pK_{HA}) and the logarithms of the formation constants ($\lg K_{HA_2^-}$) of the complexes of certain acids in dimethyl sulphoxide[41].

Acid	pK_{HA}	$\lg K_{HA_2^-}$
Picric	—1.0	—
2,6-Dihydroxybenzoic	3.1	—
4-Chloro-2,6-dinitrophenol	3.5	—
2,6-Dinitrophenol	4.9	—
Salicylic	6.8	0.48
3,5-Dinitrobenzoic	7.4	0.36
2,6-Di-t-butyl-4-nitrophenol	7.6	—
3,5-Dinitrophenol	10.6	0.48
p-Nitrophenol	11.0	0.60
o-Nitrophenol	11.0	0.78
Benzoic	11.1	0.78
Acetic	12.6	0.48
5-5-Diethylbarbituric	13.0	—
Phenol	16.4	1.60

In the absence of homoconjugation or when the concentration of the titrated base is less than 10^{-3} M, the neutralisation curves for bases in acetonitrile resemble those in aqueous solution[26].

Table 4. The negative exponents of the acid dissociation constants (pK_{HA}) and the logarithms of the homoconjugation constants ($\lg K_{HA_2^-}$) in dimethylformamide[50].

Acid	pK_{HA}	$\lg K_{HA_2^-}$
Picric	1.4	—
Hydrochloric	3.2	2.2
2,6-Dihydroxybenzoic	3.56	—
4-Chloro-2,6-dinitrophenol	4.7	—
2,6-Dinitrophenol	5.9	—
2,4-Dinitrophenol	6.3	—
Salicylic	8.23	1.7
3,5-Dinitrobenzoic	8.9	3.2
p-Nitrobenzoic	10.6	2.6
3,5-Dinitrophenol	11.3	3.2
p-Nitrophenol	12.5	2.3
Benzoic	12.25	2.4
Acetic	13.4	2.6

Homoconjugation and heteroconjugation phenomena also are observed in other aprotic dipolar solvents such as dimethyl sulphoxide[44,45], dimethylformamide[46-50], sulpholane[51], and acetone[52].

Dimethyl sulphoxide is a more basic solvent than acetonitrile. Therefore dimethyl sulphoxide molecules enter into a reaction with the anion which competes with the homoconjugation process:

$$A^-...HA + SH \rightleftharpoons A^-...HS + HA.$$

As a result, phenols and benzoic acids show a smaller tendency towards the formation of HA complexes in dimethyl sulphoxide (Table 3).

Table 3 shows that the formation constants of the complexes HA_2^- in dimethyl sulphoxide are smaller approximately by a factor of 100 than in acetonitrile (Table 1). In consequence, the potentiometric titration curves in dimethyl sulphoxide have a more pronounced buffer region and a correspondingly sharper change of the pH at the end point of the titration.

Dimethylformamide is somewhat less basic than dimethyl sulphoxide and therefore homoconjugation of acids in this solvent takes place to a greater extent than in dimethyl sulphoxide but to a lesser extent than in acetonitrile[46-50]. The homoconjugation constants in dimethylformamide are approximately ten times smaller than in acetonitrile (Table 4).

The buffer regions on the titration curves of acids and bases in dimethylformamide and dimethyl sulphoxide can be calculated as in acetonitrile. Similar calculations cannot be made for cations because one cannot make the assumptions used in the derivation of Eqn. (5) for the pH in acetonitrile.

3. SOLVENT ACIDITY SCALES

Acid—base equilibria in any solvent are due primarily to the acid—base properties of the solvent itself. Therefore the question of acid—base interaction is closely related to the question of solvent acidity scales. The extent of acidity scale is determined by the autoprotolysis constant of the solvents and their relative positions on the pH scale are determined by the relative trans-solvation energies of the protons in the different solvents (see Izmailov[8], Chapter X, and Bates[53], Chapters VII and VIII).

Izmailov[54,55] proposed unique zero-concentration proton activity coefficients γ_{0H^+} which are determined by the change in the solvation energy of protons when they are transferred from an infinitely dilute non-aqueous solution to an infinitely dilute aqueous solution. The activity coefficient γ_{0H^+} enabled Izmailov[54,56] to establish a unique solvent acidity scale:

$$pA = pH_s - \lg \gamma_{0_{H^+}},$$

where pH_S assumes values ranging from 0 to pK_S for the solvent and $\lg \gamma_{0H^+}$ indicates the shift of the acid limit of the scale in the non-aqueous solvent relative to the acid limit of the scale in water.

A rigorous thermodynamic approach to the determination of the activity coefficients of individual ions is difficult to achieve, since the accuracy of the theoretical calculations of solvation energy is less than that of the differences between the solvation energies in different solvents; experimental methods do not yield an unambiguous answer in those cases where the diffusion potential is high. Therefore several methods have been proposed for the determination of $\lg \gamma_0$ for ions, each of which involves certain non-thermodynamic assumptions[14,53-64]. The problem of the estimation of the γ_0 for ions has engaged the attention of many investigators. They were called "degenerate activity coefficients" by Grunwald,

"medium effects" by Bates, "solvent activity coefficients" by Parker, and "partition coefficients" by Kolthoff.

Izmailov, Aleksandrov, and other investigators of the Kharkov school of physical chemistry have made a major contribution to the theory of unique zero-concentration ionic activity coefficients, in the first place those of hydrogen ions, and their experimental determination in practice[54-56,65-68]. Studies in recent years showed that interest in unique zero-concentration activity coefficients of protons has increased in connection with the further development of methods for the measurements of pH in non-aqueous solutions and the development of the theory of acid – base interaction[69-76]. However, there are few $\lg \gamma_{0H^+}$ data for solvents employed in acid – base titrations and they are contradictory[44,56,73,74].

On the basis of the pK_s and $\lg \gamma_{0H^+}$ data then available, Izmailov[56] included only five solvents in his unique acidity scale (pA). At the present time the unique acidity scale already includes thirteen solvents[77]. The solvent autoprotolysis constants have been determined by various methods[78-89]. A critical assessment of the pK_s values available in the literature for amphiprotic solvents has been made by the authors of the review[77]. Table 5 lists the pK_s and $\lg \gamma_{0H^+}$ values for certain solvents widely employed in analytical practice.

Table 5. The negative exponents of the autoprotolysis constants (pK_s) of certain solvents at 25°C and the values of $\lg \gamma_{0H^+}$.

Solvent	pK_s [77–85]	$\lg \gamma_{0H^+}$ [44,56,67]
Formic acid	6.2	10.0
Acetic acid	14.5	—
Ethylene glycol	15.6	—
Water	14.0	0
Methyl alcohol	16.7	3.1
Ethyl alcohol	19.5	3.9
Isopropyl alcohol	22.0	4.2
t-Butyl alcohol	26.8	—
Acetone	32.5	4.7
Ethyl methyl ketone	31.0	—
Acetonitrile	33.3	7.9
Dimethylformamide	29.4	—
Dimethyl sulphoxide	33.3	—1.5

Acidity in non-aqueous solvents is measured and acidity scales are established also on the basis of the H_0, H_-, and $R(H)$ functions[90-98]. Izmailov (see Ref. 8, Chapter X) showed that the H_0 and H_- functions cannot reflect the activity of hydrogen ions in a non-aqueous solution owing to the different effects of the medium on the activity coefficients of indicator ions and molecules. Other acidity functions (H_R, H_0, H_+, H_{2+}) proposed subsequently suffer from the same disadvantages[99,100].

Cells with transport are mainly used in potentiometric titration in non-aqueous solutions[1,2,4]. The glass electrode, the advantages of which are well known, is employed as the indicator electrode and the reference electrodes are calomel or silver|silver chloride half-cells. The behaviour of the glass electrode in non-aqueous and mixed solvents has been described in a number of studies[101-116]. It has been shown that in many non-aqueous media the glass electrode retains its response to hydrogen ions. However, the applicability of the glass electrode in non-aqueous solutions may be limited in highly acid and highly basic media. The use of reference electrodes in non-aqueous solutions has been described[117-122].

In cells with transport, there is a liquid junction between two solutions where a diffusion potential arises, which leads to an indeterminacy in the measurement of proton activities (see Izmailov[8], Chapter X, and Bates[53], Chapters VII and VIII). However, it has been suggested that the error due to the liquid junction in cells with transport is constant in a given solvent and depends little on the nature of the electrolyte and the activity of protons (see Bates[53], Chapter VIII). Experimental studies have confirmed this hypothesis[67,68,123,124].

A direct measurement of the diffusion potential E_j is impossible and its estimation is extremely difficult. E_j may be determined only when the proton activity coefficients are known (see Bates[53], Chapter VIII). However, since the $\lg \gamma_{0H^+}$ are contradictory, the values of E_j cannot always be estimated unambiguously either[60-62,67,69]. The values of E_j for measurements with an aqueous calomel electrode have been quoted in a number of studies for methyl, ethyl, and isopropyl alcohols, acetonitrile, dimethylformamide, and dimethyl sulphoxide and it has been shown that the E_j can reach several pH units[57,69,125-127]. There are data showing that when the aqueous potassium chloride solutions in the reference electrode is replaced by a methanol solution, E_j decreases[60,112]. When a liquid junction is formed between two aprotic dipolar solvents, E_j does not exceed 20 mV.[60]

The problem of the estimation of the E_j and $\lg \gamma_{0H^+}$ has been recently solved successfully with the aid of the quantity δ proposed by Bates (see Ref. 53, Chapter VIII and Ref. 124), which is defined as the difference

$$\delta = \bar{E}_j - \lg \gamma_{0H^+},$$

where $\bar{E}_j$ is the diffusion potential in pH units.

Measurements of δ in aqueous alcoholic media have shown that in mixed solvents δ is small up to 80 wt.% of the alcohol (see Izmailov[54], Chapter VIII). It is suggested that in this composition range there is a mutual cancellation of E_j and $\lg \gamma_{0H^+}$. A further increase of the content of alcohol in the mixture leads to a sharp increase of δ to 2 – 2.5 pH units. The values of δ have been measured for mixtures of water with alcohols, acetone, dioxan, dimethylformamide, dimethyl sulphoxide, and other solvents[67,68,128-130]. The variation of δ with mixture compositions is explained by changes in the structure and acid – base properties of the mixed solvent.

Together with the question of the extent of solvent acidity scales and their relative positions, the question relating to factors which limit the solvent acidity scale is very important for acid – base titration. The pH range corresponding to the theoretical pK_s solvent acidity scale calculated from the autoprotolysis constant can be by no means always fully employed in acid – base titration in the given solvent. The theoretical solvent acidity scale is limited by the influence of the following factors. In the first place the alkaline titrants employed are usually solutions of bases without the solvent lyate ions, since it is often impossible to obtain the latter. Many solvents have low dielectric constants and therefore acids and bases with strengths equal to those of the lyonium and lyate ions of the solvent cannot exist in them. The concentrations of the compounds titrated and of the titrants are as a rule 0.01 – 0.1 M, which also reduces the pH jump in the titration. Finally the employment of the entire solvent acidity scale in the titration is hindered

also by the loss of sensitivity of the indicator and particularly glass electrodes in highly acid or highly basic regions.

A particularly marked limitation of acidity scales for solvents with weak acid or basic properties is caused by the presence in them of admixtures of water, alcohols, glycols and other solvents with fairly pronounced acid or basic properties[131,132]. The available literature data for the autoprotolysis constants of mixed solvents show that the addition of the first portions of water to isopropyl alcohol, acetone or dimethyl sulphoxide leads to a sharp increase of the autoprotolysis constant and a corresponding contraction of the solvent acidity scale[96,97,114,133–135].

In a mixture of two protolytic solvents SH and MH there are four main inter-related equilibria which determine protolysis in the mixed solvent[132,136–141]:

$$SH + SH \rightleftarrows SH_2^+ + S^-, \quad (I)$$

$$MH + MH \rightleftarrows MH_2^+ + M^-, \quad (II)$$

$$MH + SH \rightleftarrows MH_2^+ + S^-, \quad (III)$$

$$SH + MH \rightleftarrows SH_2^+ + M^-. \quad (IV)$$

To a first approximation, the autoprotolysis constant for the mixed solvent can be regarded as the product of the equilibrium concentrations of the lyonium and lyate ions of the mixed solvent:

$$K_s = (C_{SH_2^+} + C_{MH_2^+})(C_{S^-} + C_{M^-}).$$

Depending on the acid and basic properties of the components of the mixed solvent and its composition, definite relations are established in each specific case between the activities of the individual ions in solution. If the acidities and basicities of the mixture components are similar, then protolysis in the mixed solvent is determined by all four equilibria. Only for mixture compositions close to those of the pure solvents does protolysis correspond mainly to the autoprotolysis of the pure solvents. Examples of mixtures of this kind are those of water and ethylene glycol.

When the acidity and basicity of the solvent MH are higher than those of the solvent SH, the autoprotolysis of SH may be neglected in the mixed solvent (acetone — water mixtures):

$$K_s = C_{MH_2^+} C_{M^-}.$$

For mixtures of two solvents one of which has more pronounced acid properties (SH) and the other more pronounced basic properties (MH), protolysis is determined mainly by equilibrium (III) (mixtures of water and amines):

$$K_s = C_{MH_2^+} C_{S^-}.$$

If the basicities of the solvents constituting the mixture are similar and the acidity of the solvent MH is higher than that of SH (dimethylformamide — water mixtures), the autoprotolysis constant of the mixed solvent may be represented by the following expression [equilibria (II) and (IV)]:

$$K_s = (C_{MH_2^+} + C_{SH_2^+})\, C_{M^-}.$$

If the acid properties of the mixture components are similar and the basic properties of the solvent MH are more pronounced than those of SH (water — methanol mixtures), the expression for the autoprotolysis constant of the mixed solvent is [equilibria (II) and (III)]:

$$K_s = C_{MH_2^+}(C_{M^-} + C_{S^-}).$$

The addition of a solvent MH with a basicity higher than that of the solvent SH leads to a decrease of the acid limit of the acidity scale for the mixed solvent owing to the reaction

$$SH_2^+ + MH \rightleftarrows MH_2^+ + SH.$$

If the acidity of the solvent MH is higher than that of SH, the addition of MH to SH leads to a decrease of the basic limit of the acidity scale for the mixed solvent; this involves the following reaction:

$$S^- + MH \rightleftarrows M^- + SH.$$

Fig. 6 presents as an example three cases of the decrease of the limits of the acidity scales for non-aqueous solvents with weak acid or basic properties in the presence of added water.

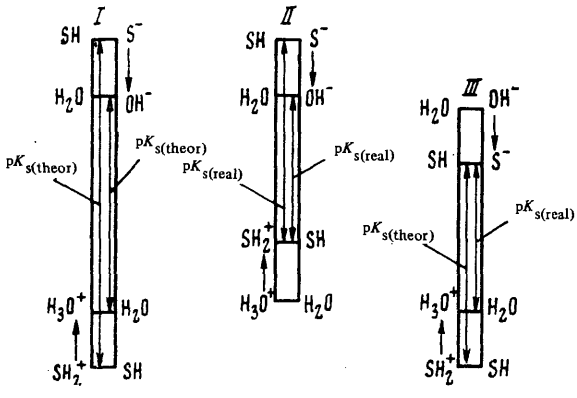

Figure 6. Effect of water on the acidity scales for non-aqueous solvents: I) acidity and basicity of water higher than the corresponding properties of the solvent; II) acidity of water higher and its basicity lower than the corresponding properties of the solvent; III) basicity of water higher and its acidity lower than the corresponding properties of the solvent.

In choosing the conditions for acid — base titration, it is necessary to know the effect of added solvents on each limit of the solvent acidity scale. Since, as stated above, the determination of individual ionic activities involves considerable difficulties, the determination of the variation of the acidity scale limits for mixed solvents on the basis of a rigorous thermodynamic approach is difficult to achieve. There are literature data for $\lg \gamma_{OH^+}$, which determine the variation of the acid limit of the acidity scale for mixtures of water with methyl, ethyl, and isopropyl alcohols and with acetone[57,67,68,74]. These results demonstrate that the addition of water leads to a decrease of the acid limit of the acidity scale for alcohols and acetone since these solvents are less basic than water. The data described above, referring to the acidity scales of non-aqueous solvents and their relative positions on the unique acidity scale, show that at present the physicochemical data necessary for the construction of practical (real) acidity scales for the majority of solvents and their mixtures, which might be used in potentiometric acid — base titration, are not available. It is therefore of interest to obtain practical solvent acidity scales taking into account all the factors which determine the titration conditions.

Real (empirical) solvent acidity scales were first obtained by van der Heijde and Dahmen[142,143]. However, these workers did not give a physicochemical interpretation of their acidity scales. Probably this is why van der Heijde and Dahmen's studies were not developed further in the following decade.

Later a simple and rapid method was proposed for the measurement of real acidity solvent scales, which were called relative acidity scales (E_S).[144] The method of measurement of the relative acidity scales was used successfully to investigate real acid base titration conditions[145-148]. The relative acidity scale is the range of values in millivolts (E_S) or in pH units (E'_S) which may be used in acid — base titration in the given solvent under specified conditions (titrant system, presence of other solvents, etc.). The limits of the E_S scale are measured as the half-neutralisation potentials of $HClO_4$ and R_4NOH solutions which are widely used as the strongest titrants in non-aqueous media[4]. The relation between the negative exponent of the autoprotolysis constant of the solvent and the extent of the relative acidity scale may be represented by the equation

$$pK_s \geqslant E'_s - \lg(a_{H^+}\, a_{OH^-}). \qquad (8)$$

The sign of equality refers to the case where K_S is the autoprotolysis constant of the solvent containing water and the "greater than" sign refers to the case where K_S is the autoprotolysis constant of the pure solvent. It follows from Eqn. (8) that the relative (real or practical) solvent acidity scale in terms of pH units is part of the pK_S acidity scale and depends on the system of titrants employed. Fig. 7 presents the relative acidity scales for water and non-aqueous solvents. Evidently the E_S scales for non-aqueous solvents have different lengths and occupy different positions relative to the acidity scale for water.

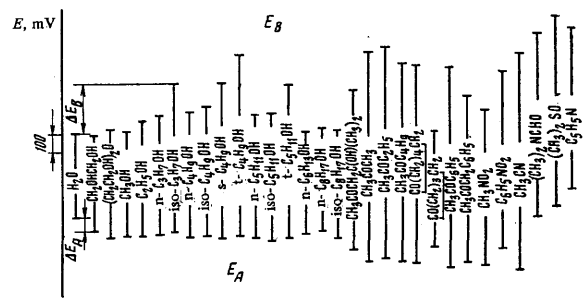

Figure 7. Relative acidity scales for certain solvents.

It has been shown that one of the main factors determining the position of the limits of the relative solvent acidity scale relative to the limits of the scale for water is the acid and basic properties of the solvent[149]. Comparison of the limits of the relative acidity scales with parameters characterising the basic and acid properties of solvents showed that, with decrease of the basic properties of the solvent, the acid limit E_A of the scale shift towards the region of higher proton activities, and with decrease of the acid properties of the solvent, there is a shift of the basic limit E_B of the scale towards the region of lower proton acitivities. Thus, the highest values of the acid limits of relative acidity scales obtain in ketones, acetonitrile, nitrobenzene, and nitromethane, which are least basic; the highest values of the basic limits of relative acidity scales are in ketones, acetonitrile, dimethylformamide, dimethyl sulphoxide, and pyridine, which are characterised by the smallest acidity.

The lengths of the E'_S and pK_S solvent acidity scales are compared in Fig. 8.[83] The values of E'_S and pK_S were taken from the literature[80,81,84,85,88,112,144,150-153]. With the exception of the points referring to acetonitrile and dimethyl sulphoxide, there is a linear relation between E'_S and pK_S. The points lying below the straight line drawn according to the equation

$$E'_s = pK_s + \lg(C_{HClO_4}\, C_{R_4NOH}) \qquad (9)$$

(C_{HClO_4} and C_{R_4NOH} are the $HClO_4$ and R_4NOH concentrations employed in the measurement of the limits of the E'_S scale) are readily explained by the incomplete dissociation of $HClO_4$ and R_4NOH in certain solvents and also by the presence of water and methanol impurities in the solvents, since the R_4NOH solutions were prepared in a benzene — methanol mixture and those of $HClO_4$ were obtained from 70% aqueous solution.

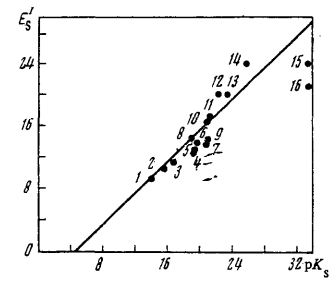

Figure 8. Comparison of the negative exponents of the autoprotolysis constants (pK_S) and the E'_S parameters of relative acidity scales: 1) water; 2) ethylene glycol; 3) methyl alcohol; 4) ethyl alcohol; 5) n-propyl alcohol; 6) n-butyl alcohol; 7) n-pentyl alcohol; 8) isobutyl alcohol; 9) isopentyl alcohol; 10) isopropyl alcohol; 11) s-butyl alcohol; 12) t-butyl alcohol; 13) dimethylformamide; 14) ethyl methyl ketone; 15) acetonitrile; 16) dimethyl sulphoxide.

Since the method of measurement of relative solvent acidity scales and Eqn. (9) yields values of pK_S which are lower than the true values, the points above the straight lines can only be due to incorrect autoprotolysis constants for a number of solvents (t-butyl alcohol, ethyl methyl ketone, dimethylformamide) in the literature. Consequently, comparison of the E'_S and pK_S solvent acidity scales yields information about the reliability of the experimental K_S for solvents, as shown by the authors of the review[83].

The relative positions of the E'_S and pK_S relative solvent acidity scales on Izmailov's pA unique acidity scale are compared in Fig. 9.[83] The filled regions correspond to those parts of the pK_S scale which for one reason or another cannot be used in titration. As already stated, one of such reasons is the incomplete dissociation of $HClO_4$ and R_4NOH in certain solvents. The filled regions can also reflect the

effect of the diffusion potential of the cell used to measure the limits of the E'_S scale.

In the measurement of the limits of the E'_S scale, R_4NOH solutions were prepared in a 1 : 5 benzene — methanol mixture and therefore the solvents investigated contained a certain amount of methanol and benzene and also water. Water and methanol have more pronounced acid or basic properties than many amphiprotic and aprotic dipolar solvents (ketones, acetonitrile, dimethyl sulphoxide, etc.). Therefore one of the factors restricting the limits of the acidity scales for solvents with weak acid or basic properties is of course the presence of water, methanol, and similar solvent impurities.

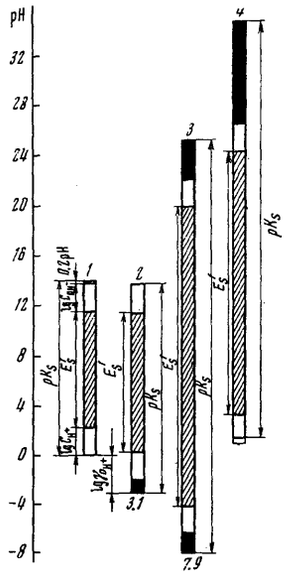

Figure 9. Comparison of the E'_S and pK_S acidity scales in terms of the pA unique acidity scale: 1) water; 2) methyl alcohol; 3) acetonitrile; 4) dimethyl sulphoxide.

The method of measurement of relative acidity scales proved to be effective not only in the study of the chemical-analytical properties of individual solvents but also in the study of the properties of their various mixtures widely used in titration[154-158]. The general laws governing the variation of the limits of the relative acidity scales for mixed solvents have been established. It has been shown that the length and position of the acidity scale for a mixed solvent depend mainly on the lengths and positions of the scales for the mixture components (Fig. 10). If the limits of the acidity scales for the individual solvents differ greatly, the limits of the acidity scale for the mixed solvent vary with composition non-additively. The most marked change in the limits of the acidity scale is observed following the addition of the initial portions of a second solvent with lower values of acidity scale limits. The variation of the limits of the E_S scales for mixed solvents can be explained by the variation of the acid and basic properties of the mixture in relation to those of the individual components, since the acid and basic properties of the mixed solvent vary non-additively with composition (see Izmailov[8], Chapter VII).

Measurements of relative acidity scales for mixtures of protolytic and aprotic solvents showed that the addition of 40 — 50% of the aprotic solvent has almost no influence on the limits of the acidity scale for the protolytic solvent[150]. The variation of the limits of the acidity scales for mixtures is not related to changes in the dielectric constant provided that the latter is not too low ($\epsilon > 10 - 15$).[156]

Comparison of the extents of the E_S scales and solvent polarities on the E_T scale reveals a definite relation between these quantities[151]. For protolytic solvents a decrease of polarity corresponds as a rule to an increase of the extent of the relative acidity scale. If one of the solvents has a higher acid limit and the other a higher basic limit of the E_S scale, then, on passing from solvent to solvent, the change in acid or basic properties may not correspond to the change in the polarity of the mixtures. Under these conditions, the curve relating the limit to mixture composition shows a minimum (mixtures of pyridine with water, methanol, and ethylene glycol and mixtures of nitromethane with alcohols) (Fig. 10).

Comparison of the extents of relative acidity scales for mixed solvents in terms of pH units with published negative exponents of the autoprotolysis constants (pK_S) showed that the variation of these quantities is the same. Consequently the variation of the extents of E'_S scales for mixed solvents reflects correctly the variation of the pK_S for the mixed solvents, as shown for a mixture of water and dimethyl sulphoxide (Fig. 11).

Comparison of the changes in the acid limits ΔE_A of E_S acidity scales for mixture of water with methyl, ethyl, and isopropyl alcohols and actone with the δ values[67,68,128,129] showed that the variation of ΔE_A for the mixtures parallels that of δ (Fig. 12). This confirms the conclusion that the position of the acid limit of the E_S scale on the unique acidity scale is determined mainly by the change in the

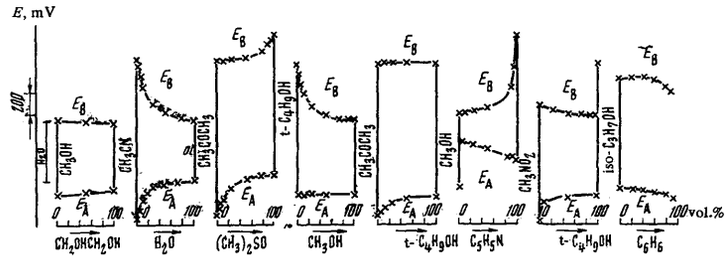

Figure 10. Relative acidity scales for mixed solvents corresponding to different component ratios.

basicity of the solvent and the diffusion potential of the cell used to measure the limits of the E_S scale.

The similarity in the variation of the limits of the E_S scales for mixed solvents made it possible to derive empirical equations for the calculation of the acid and basic limits of the acidity scales for mixtures as a function of mixture composition. With the aid of these equations, the limits and extents of the acidity scales were extrapolated and their values for pure solvents evaluated. This is particularly important for solvents with weak acid and basic properties[159]. On the basis of the E_S scales for pure solvents, it is possible to determine their pK_S values[77].

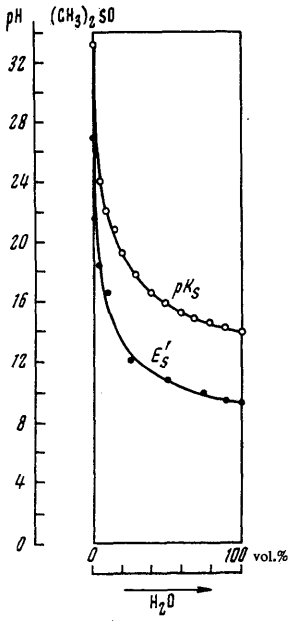

Figure 11. Comparison of the pK_S and E'_S acidity scales for a mixture of dimethyl sulphoxide and water.

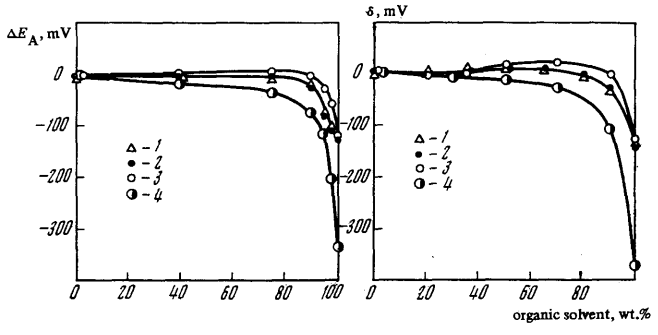

Figure 12. Comparison with δ of the differences ΔE_A between the acid limits of the acidity scales for water and its mixtures with different solvents: 1) methyl alcohol; 2) ethyl alcohol; 3) isopropyl alcohol; 4) actone.

It follows from the foregoing that study of the chemical-analytical properties of mixed solvents by measuring their relative acidity scales has made it possible (a) to establish the main factors determining the practical solvent acidity scale in potentiometric titration, (b) to establish the general characteristics of the variation of the limits of the acidity scales for mixed solvents, (c) to elucidate the role of water and similar added solvents (alcohols, glycols) in acid – base titration, and (d) to propose a simple method for the estimation of the autoprotolysis constants of solvents with insignificant acid or basic properties.

4. CHOICE OF OPTIMAL CONDITIONS FOR POTENTIOMETRIC ACID – BASE TITRATION

In connection with the extensive development of methods for acid – base titration, the problem of a soundly based choice of optimal titration conditions is becoming increasingly urgent. The scientific principles for the employment of non-aqueous solvents in acid – base titration have been developed by Izmailov (see Ref. 8, Chapter XI, and Refs. 160 and 161). Starting with the theory of titration errors developed by Roller, Izmailov specified the principal ways for the improvement of acid – base titration conditions. The choice of conditions for the titration of acids, bases, mixtures of acids, or mixtures of bases is made by comparing the solvent autoprotolysis constants K_S and the acid (K_A) or basic (K_B) dissociation constants. On the assumption of complete dissociation of the titrant and of the salt formed and of the absence of a salt effect, the titration conditions are characterised by the titration constant K_T (C_A and C_B are the concentrations of the acid and base):

$$\text{for acids } K_T = \frac{K_S}{K_A C_A}; \qquad \text{for bases } K_T = \frac{K_S}{K_B C_B},$$

$$\text{for mixtures of bases } K_T = \frac{K_{A_1} C_{A_1}}{K_{A_2} C_{A_2}} (K_{A_1} < K_{A_2}), \text{ and}$$

$$\text{for mixtures of bases } K_T = \frac{K_{B_1} C_{B_1}}{K_{B_2} C_{B_2}} (K_{B_1} < K_{B_2}).$$

On passing from water to non-aqueous solvents, an improvement in the conditions for the titration of weak acids and bases and also of mixtures of acids and mixtures of bases is achieved when the titration constant is appreciably reduced.

When he considered methods for the improvement of titration conditions, Izmailov had at his disposal the autoprotolysis constant of solvents such as alcohols, acetic and formic acids, liquid ammonia and hydrazine. Calculation of the pK_T values for acids and bases from these data led to general agreement between theory and experiment. However, the use of later data for the autoprotolysis constants of acetonitrile, dimethylformamide, and dimethyl sulphoxide to estimate pK_T for phenol and its mononitro-derivatives failed to reflect the improvement in the conditions governing the titration of weak acids which is known to occur on passing from water to these solvents[150]. The apparent conflict between theory and experimental acid – base titration can be resolved if the literature values of the autoprotolysis constants of the solvents are incorrect. The use of the latest K_S data for acetonitrile and dimethyl sulphoxide in the calculation of pK_T indicates a much greater improvement in the conditions for the titration of phenols in these solvents compared with water.

A critical examination of the published data for the solvent autoprotolysis constants and the dissociation constants of the compounds titrated shows that the choice of titration conditions on the basis of the known values of K_S and K_{diss} is impossible for the majority of solvents important in practice. Firstly, few values of K_S for solvents and K_{diss} for electrolytes are available and their reliability is in many cases poor[77]. Secondly, titrations are not usually performed in pure solvents and there are almost no K_S and K_{diss} data for mixed solvents. Thirdly, the choice of titration conditions on the basis of K_S and K_{diss} includes a number of assumptions which are inapplicable to solvents with a low ionising capacity. Fourthly, for aprotic dipolar solvents, where acid — base interaction involves a large number of intermediate stages, the titration conditions cannot be determined by comparing the autoprotolysis constants of the solvents and the dissociation constants of the electrolytes.

In his paper, Charlot[162] states the principles of acid — base titration in non-aqueous media and begins with the same basic postulates as Izmailov. The titration curve is predicted by comparing the pK_S solvent acidity scales with the pH values for various acid — base pairs corresponding to the instant of half neutralisation of the acid (pH = pK). However, the author points out that, owing to the lack of data for the relative positions of the non-aqueous solvent acidity scales, this method is applicable to the assessment of titration conditions in a single solvent only.

The half-neutralisation potential $E_{1/2}$ is frequently used as a chemical-analytical characteristic of the compound determined in a non-aqueous solution[1,2,4,163-179]. Owing to the complete dissociation of the salt formed and its high solubility, the pH of an aqueous solution at the half-neutralisation point is equal to pK_{diss} and therefore the half-neutralisation potential is a function of the dissociation constants only. In most cases $E_{1/2}$ in a non-aqueous solution, employed as a measure of the relative acidity of electrolytes, reflects correctly the variation of their dissociation constants, which is confirmed by the linear relation between $E_{1/2}$ and $pK_{A(ns)}$.[112] Therefore the half-neutralisation potential for the electrolyte in a non-aqueous solvent is largely determined by the same factors as the dissociation constant.

If the electrolyte is a stronger acid than the solvent lyonium ions, the half-neutralisation potential of the electrolyte is reduced to the level of the half-neutralisation potential of SH_2^+; the half-neutralisation potential of a base stronger than the solvent lyate ions is reduced to the level of the half-neutralisation potential of S^-. If the acid or base is a weaker electrolyte than the solvent (considered as an acid or base respectively), its half-neutralisation potential is outside the limits of the acidity scale for the solvent and such electrolytes cannot be titrated as acids or bases in the solvent.

The position of $E_{1/2}$ for the electrolyte on the unique solvent acidity scale depends mainly on the strength of the electrolyte in the given solvent and on the activity of protons in the form of lyonium ions. The half-neutralisation potential for the electrolyte in a non-aqueous solvent depends not only on factors determining the dissociation constant of the electrolyte but also on those which determine the shape of the titration curve in the buffer region. Thus the half-neutralisation potential of the electrolyte has a number of advantages over the dissociation constant in the selection of conditions for potentiometric titration. On the other hand, it is necessary in many cases to know not only the half-neutralisation potential but also the shape of the titration curve for the electrolyte in the buffer region[35].

Van der Heijde and Dahmen[143] attempted to find a theoretical basis for the choice of titration conditions. However, they compared for this purpose the half-neutralisation potentials of acids with the acid limits of empirical solvent acidity scales, which depend on the basicity of the solvents, while the titration conditions for acids are determined by the acid properties of the solvent. This led them to the incorrect conclusion that there is no definite relation between the change in the half-neutralisation potentials of acids on passing from solvent to solvent and the limits of the acidity scales. As a result, the solvent — titrant combinations proposed by van der Heijde for acids and bases of different groups lack a rigorous theoretical basis and the method of selection of titration conditions involving them is complicated and inefficient.

Further studies in this field showed that the basic limit E_B of the relative solvent acidity scale determines the possibility of the titration in the solvent of weak acids and the acid limit E_A determines the possibility of the titration of weak bases, since the half-neutralisation potentials of weak acids are located close to the basic limit and those of weak bases are close to the acid limit of the E_S solvent scale. The higher the basic and acid limits of the E_S scale compared with the limits of the water scale the greater the possibility of titrating in the given solvent weak acids and bases which cannot be titrated in an aqueous solution[144,150,156]. The potential jumps in the titration of electrolytes in the given solvent can be determined approximately as the differences between the basic (for acids) or acid (for bases) limits of the solvent scale on the one hand and the half-neutralisation potential of the electrolyte on the other.

The length of the relative solvent acidity scale characterises the possibility of differential titration of acids or bases in the solvent. A shift of the relative solvent acidity scale to the basic region creates favourable conditions for the differential titration of mixtures of weak and moderately strong acids. A shift of the acidity scale to the acid region improves the conditions for the separate titration of mixtures of strong acids.

In considering the conditions for differential titration of mixtures of bases, one should bear in mind that the position of the acid limit of the scale determines the conditions for the titration of mixtures of weak bases and that of the basic limit determines the conditions for the titration of mixtures of strong bases.

The differentiating effect of solvents is shown to varying extents for acids and bases of different strengths and types. The use of relations between half-neutralisation potentials for acids and bases on the one hand and their pK values in water and Hammett's σ constants on the other makes it possible to predict the half-neutralisation potentials for electrolytes in non-aqueous solvents on the basis of $pK_A(H_2O)$ and σ:[165-179]

$$\Delta E_{1/2} = A\ pK_A\ (H_2O) + B, \qquad (10)$$

$$\Delta E_{1/2} = A'\ \Sigma\sigma + B', \qquad (11)$$

where $\Delta E_{1/2}$ is the half-neutralisation potential of the electrolyte in relation to a standard.

To assess the possibility of the differential titration of a mixture of electrolytes on the basis of $pK_A(H_2O)$ or the σ constants and Eqns. (10) and (11), the values of their half-neutralisation potentials in non-aqueous solutions are found and their differences are determined. For a fairly distinct buffer region on the titration curves for the

individual compounds, a difference between the $E_{1/2}$ for two electrolytes of 150 — 200 mV is usually enough to ensure their separate titration in the mixture[163]. When the potential changes more markedly in the buffer region, the required difference may increase to 300 mV.

On passing from water to non-aqueous solvents, electrolytes belonging to a different reaction series give rise to individual relations between $\Delta E_{1/2}$ on the one hand and $pK_A(H_2O)$ or σ constants on the other[150]. As a result, in some cases there is an improvement in non-aqueous solvents (relative to water) of the conditions for the separate titration of mixtures of electrolytes with similar values of $pK_A(H_2O)$ and in others there is a worsening of the conditions for the separate titration of mixtures of electrolytes with different values of $pK_A(H_2O)$.

Measurements of the relative acidity scales for mixed solvents yield conclusions as to the influence of added solvents on the titration conditions in the given solvent and the use of mixed solvents to improve the conditions for the titration of individual compounds and their mixtures. It was established that the addition of water, methanol, glycols, and similar solvents impairs the titration conditions for weak acids and bases and also for mixtures of electrolytes in solvents with weak acid or basic properties, since it restricts the acidity scales for such solvents[156].

As for individual solvents, the choice of titration conditions in mixed solvents is made by comparing the half-neutralisation potentials of electrolytes with the limits of the acidity scale for the mixtures. If another solvent is added to improve the solvent power of the medium and an attempt is made at the same time to preserve the properties of the main solvent, the permissible content of the added solvent is determined from the dependence of ΔE_A and ΔE_B on mixture composition (Fig. 10). If the second solvent is added to improve the titration conditions, one should bear in mind that a significant improvement of such conditions can be achieved only after adding more than 90 vol. % of the second solvent.

When the use of solvents for acid — base titration is considered, one must take into account the effect of the solvent added together with the titrant to the solution analysed[180]. This applies particularly to R_4NOH solutions, which are usually prepared in alcohol — benzene mixtures. The permissible contents of various alcohols in mixtures used to prepare titrant solutions have been established. However, the choice of the alcohol and its content in the mixture are frequently limited also by the solubility of R_4NOH, the stability of solutions, and the method of their preparation.

The above method of choosing the optimal conditions for acid — base potentiometric titration based on E_S solvent acidity scales and half-neutralisation potentials $E_{1/2}$ of the compounds being titrated has the following advantages. Firstly, account is taken of the effect of many factors determining the titration conditions (the amount and properties of added solvents, the strength and concentration of titrants, the formation of salt precipitates during their titration, etc.) and secondly it is possible to select the conditions for titration in mixed solvents.

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The above discussion of the acid — base equilibria in amphiprotic solvents showed that Izmailov's scheme for acid — base interaction (Ref. 8, Chapter VIII), which includes a number of related processes involving the formation of products of the addition of solvent molecules to those of the electrolyte and the formation of solvated ions and ion pairs, must be supplemented by new equilibria. Kolthoff demonstrated convincingly in the case of acetonitrile, dimethyl sulphoxide, and dimethylformamide that for solvents with weak acid properties these additional equilibria involve homo- and hetero-conjugation processes. Factors determining the degree of homo- and hetero-conjugation have been established and it has been shown that, for a quantitative interpretation of acid — base interaction and the calculation of the pH of electrolyte solutions, it is necessary to take into account the constants characterising these equilibria.

The latest determinations of the autoprotolysis constant of solvents have shown that many amphiprotic solvents (acetonitrile, dimethylformamide, dimethyl sulphoxide, and ketones) have extensive acidity scales. Factors which reduce the limits of solvent acidity scales have been discovered and relations governing the variation of the limits of the acidity scales for mixed protolytic solvents have been established. The importance of water (and similar solvents) for the explanation of protolysis in mixed solvents has been demonstrated.

Studies on acid — base interaction in amphiprotic solvents have promoted the development of the theory of potentiometric acid — base titration. The use of electrolyte dissociation constants and homo- and hetero-conjugation constants permits the calculation of titration curves in the buffer region. The conversion from theoretical solvent acidity scales, calculated from the autoprotolysis constants, into real scales is possible on the basis of the δ values taking into account the overall effect of the zero-concentration proton activity coefficient and the diffusion potential in measurements in cells with transport. The effect of numerous factors which determine the conditions governing acid — base titration is reflected in the extent of the relative (real) E_S solvent acidity scale and the electrolyte half-neutralisation potential $E_{1/2}$. The knowledge of these chemical-analytical characteristics permits a choice of the optimal titration conditions.

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Analytical Chemistry of Metal Complexes with Nitrogen-containing Ligands of the 2,2′-bipyridyl Type

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A brief account is given of the analytical properties of complexes formed by metals with derivatives of 1,10-phenanthroline and 2,2′-bipyridyl, compounds that are widely used in chemical technology, biochemistry, and especially analysis. Detailed consideration is given to the possibilities and limitations of analytical methods based on various properties of these complexes (light absorption, luminescence, solubility, redox properties, etc). A list of 249 references is included.

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I. INTRODUCTION

The ability of the heterocyclic amines—1,10-phenanthroline and 2,2′-bipyridyl—to form complex compounds with various metals is widely used in many branches of chemistry and technology. The employment of these complexes in analysis is governed by their specific analytical properties.

The complexes formed with iron, copper, nickel, cobalt, and other metals tend to have high thermal and thermodynamic stability because of strong ligand fields and the formation of π-back bonding with the metals. The presence of a system of conjugated double bonds in these amines is responsible for the deep colour of the complexes, which enables them to be used in spectrophotometric analysis.

The present Review surveys the principal analytical properties of the metal complexes of 1,10-phenanthroline, 2,2′-bipyridyl, and their derivatives, which are widely used in analysis and several other fields of chemistry.

II. SPECTROPHOTOMETRIC METHODS

1. Effect of Substituents on Complex Formation with 1,10-Phenanthroline, 2,2′-Bipyridyl, and their Derivatives

The well known formation of a triphenanthrolineiron complex has long been used for the spectrophotometric determination of bivalent iron. The great stability of this complex is due to delocalisation of charge from the t_{2g} orbital of iron to the π-orbital of the ligand[1]. Iron(II) is known to form stable complexes with ligands having sufficiently strong fields to produce pairing of electrons in $3d$ orbitals. 1,10-Phenanthroline (phen) and 2,2′-bipyridyl (bipy), which form low-spin complexes with iron(II) contrasting with the high-spin ethylenediamine complexes[2], fall into this category of ligands. The lowest unoccupied levels in $[Fe\,phen_3]^{2+}$ and $[Fe\,bipy_3]^{2+}$ are antibonding molecular orbitals located between the ligands and the e_g orbitals of the metal, which explains the possibility of the formation of dative π-bonds. Oxygen-containing ligands (ethylenediaminetetra-acetic, citric, oxalic, tartaric acids), which form high-spin complexes with iron(II), bind it less firmly, and can therefore be used to mask other elements (aluminium, lead, bismuth, calcium, etc.) in the determination of iron with 1,10-phenanthroline[3,4].

On the other hand, manganese(II), zinc(II), cadmium(II), cobalt(II), nickel(II), and copper(I) form more stable complexes with phenanthroline than do aluminium, thorium, lead, bismuth, and calcium, which are characterised rather by bonding with oxygen- and sulphur-containing ligands. This property is exploited to mask the above metals in the complexonometric determination of aluminium, lead, bismuth, and other ions[5-7].

Complexes formed by metals with phenanthroline are usually more stable and more intensely coloured than are those with bipyridyl. The extension of conjugation by the incorporation of a further aromatic ring in the case of phenanthroline probably creates energetically more favourable orbitals for the establishment of π-back-bonding.

The stabilities of complexes of bivalent metals with phenanthroline and its methylated derivatives show that methyl groups in positions 2 and 5 have different effects on the properties of the ligands. The monocomplexes $[ML]^{2+}$ formed by phenanthroline, bipyridyl, and 5-methylphenanthroline have the stability sequence

$$Mn<Cd<Fe<Zn<Co<Ni$$

but the tricomplexes $[ML_3]^{2+}$ have the different sequence[8,9]

$$Mn<Cd<Zn<Co<Cu<Fe<Ni.$$

The variation in the position of iron in these series is due to the abnormally high stepwise stability constant K_3, which exceeds considerably the preceding two constants and the corresponding constant for nickel (Table 1).

The markedly higher stability of triphenanthrolineiron than of the diligand complex is due to the transition from a high-spin to a low-spin configuration.

A similar effect is not observed with the 2-methylphenanthroline complexes, where di- and tri-ligand complexes have the same stability sequence

$$Mn<Fe<Zn<Cd<Co<Ni<Cu$$

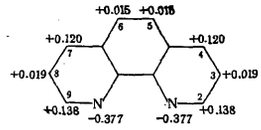
with the exception of univalent copper, which does not form a triligand complex. The position of copper in this

sequence is responsible for the use of 2,9-substituted phenanthroline derivatives for its analytical determination. In some cases the wavelengths and the molar absorption coefficients at band maxima for the iron and copper complexes of methylated phenanthrolines are additive functions [10-12] (see Table 2).

Table 1.

	Ni	Fe
lg K_1	8.6	5.8
lg K_2	8.1	5.2
lg K_3	7.6	10.0

The absorption of light by the iron complexes is most intense with the 4,7-substituted phenanthroline complexes. According to the diagram of the distribution of electron density [13]



(I)

positions 4 and 7, 2 and 9 in the phenanthroline molecule have a high positive charge (I), so that replacing the hydrogen atom at these positions by various donor groups produces a marked change in the properties of the complexes of metals with these ligands. Thus in the case of 4,7-diphenylphenanthroline (bathophenanthroline) the introduction at these positions of phenyl groups, possessing a greater donor power than methyl groups, doubles the sensitivity of the reaction with iron(II) ($\epsilon = 2.22 \times 10^4$) in comparison with phenanthroline. Bathophenanthroline is one of the most sensitive reagents for bivalent iron [14-16] (Table 3).

Table 2. Absorption of light by iron(II) complexes of methylated 1,10-phenanthrolines [10-12].

Positions of CH_3	λ, nm	$10^{-3}\epsilon$	Positions of CH_3	λ, nm	$10^{-3}\epsilon$
—	510	11.1	4,5	516	12.7
3	502	11.5	5,6	520	12.6
4	511	13.5	4,7	512	14.0
5	515	12.2	3,4,7	504	14.0
3,4	505	13.7	4,5,7	517	14.5
3,8	496	11.5	3,4,7,8	500	13.8
3,5	506	12.5	3,4,6,7	510	14.0

In 2,9-substituted phenanthrolines complex formation is influenced mainly by steric factors, owing to the nearness of the substituents to the nitrogen atoms. Thus 2,9-dimethylphenanthroline forms a stable, intensely yellow ($\epsilon = 7950$) dicomplex with copper(I) and the corresponding 2 : 1 iron complex (slightly coloured and unstable), but an iron tricomplex is not formed at all. This enables 2,9-dimethylphenanthroline (neocuproin) to be used as a highly sensitive reagent for copper(I) in the presence of iron(II), [11,17,18] titanium [19], tellurium [20], and plutonium [21].

The phenyl groups in 2,9-diphenylphenanthroline not only prevent the formation of tricomplexes of iron but also probably impede significantly the formation of a tetrahedral dicomplex of copper [13]. This is indicated by the halving of the molar absorption coefficient ($\epsilon = 3620$) in comparison with neocuproin.

Bipyridyl derivatives exhibit similar complexing properties. Positions 3,3′ (or 6,6′) in 2,2′-bipyridyl correspond to positions 2,9 in phenanthroline. Complex formation by bipyridyl with iron or copper leads to stabilisation of the rings in the same plane, and the optical density of such compounds, as a consequence of resonance conjugation, is little inferior to those of the phenanthrolinate complexes [22]. Thus, although 4,4′- and 5,5′-dimethyl derivatives of bipyridyl form tricomplexes with iron having the same absorption intensity [22] ($\epsilon = 8700$) as that of $[Fe\,bipy_3]^{2+}$, the absorption intensity of the iron complex with 3,3′-dimethylbipyridyl is only one-fifth of this value, owing to destruction of the planarity of the structure, which impairs the conditions of conjugation [23]. As in the case of neocuproin, the methyl groups do not prevent formation of a 2 : 1 copper(I) complex, but on the contrary they increase its stability, perhaps owing to enhanced basicity of the nitrogen atoms [22]. Probably for the same reason copper forms complexes [24-26] with bipyridyl-3,3′-diamine and 4,4′,6,6′-tetramethylbipyridyl, whereas iron does not yield complexes with these ligands. These reagents are highly specific for the determination of copper, but are little used owing to the difficulty of preparing them [27].

The presence of aromatic rings fused *ortho* to the nitrogen atoms produces the same effects as do methyl and phenyl groups, without yielding any analytical advantages (Table 3). Somewhat greater selectivity (for copper) in the case of 2-isoquinol-1′-ylquinoline is accompanied by a loss of reagent sensitivity ($\epsilon = 2550$). It is interesting that the introduction of a methyl group at position 3 of the quinoline ring in 2-pyrid-2′-ylquinoline and in 2,2′-biquinolyl diminishes only the sensitivity of the reagent, without affecting the stability or other properties of the complex [27]. Yet the copper complex of 3-phenyl-2,2′-biquinolyl even absorbs rather more strongly than does the corresponding biquinolyl complex, which probably indicates that steric hindrance is balanced by the high donor power of the aromatic ring [13]. In the case of 4,4′-diphenyl-2,2′-biquinolyl the donor properties of the phenyl groups are still more evident ($\epsilon = 9020$ in comparison with 5490 for the biquinolyl complex) [13,26,27]. A highly specific reagent for copper(I) is cuprotest—a derivative of bathophenanthroline containing aromatic groups *ortho* to the nitrogen atoms [28]: no anion (up to 1 M concentration) interferes with the determination of copper(I) with the exception of cyanide, thiosulphate, ethylenediaminetetra-acetate, and sulphide; the determination of microgram quantities of copper is not affected by 10 μg of any other metal. One of the most sensitive and selective reagents for copper(I) is 2,9-dimethyl-4,7-diphenylphenanthroline (bathocuproin), in which the selectivity of neocuproin is combined with the sensitivity of bathophenanthroline [29] and which can be used to determine copper in iron. While about half as sensitive as dithizone, this reagent is far superior in selectivity.

Very little investigation has been made of the effect of various acceptor substituents on the complexing properties

Table 3. Derivatives of 1,10-phenanthroline and 2,2′-bipyridyl in spectrophotometric analysis.

Reagent	Ion to be determined	λ, nm	$10^{-3}\epsilon$	Optimum pH	Solvents and extractants	Foreign ions and possible elimination of their effect	Ref.
1	2	3	4	5	6	7	8
1,10-Phenanthroline	Fe^{2+}	510	11.1 11.4	2—9 —	propylene carbonate —	Cu^+ and ClO_4^- interfere —	47,67,242
	Cu^+	435	7.03		—	—	242
	Ru^{2+}	610 (fluorescence)		6—8	—	platinum metals (50 μg, but 20 μg of osmium) do not interfere	83,248
	Ag^{2+}	420	—	—	—	Ni^{2+}, Co^{2+}, Hg^{2+}, Tl^+ interfere	236
	Mo	508	6.29	—	3 *N* HCl	Co^{2+}, Cu^{2+}, Al^{3+}, Cr^{3+} interfere; 1 mg Fe and 5 M SO_3^{2-}, NO_2^-, Ca^{2+}, Cu^+ do not interfere, but the colour lasts only 30 s	166,167
	Ti^{3+}	410	0.80	1.8—2.8	bis-2-ethylhexyl hydrogen phosphate	Ti^{IV} not extracted by this extractant in presence of oxalic acid	156,216
2,2′-Bipyridyl	Fe^{2+}	552	8.7	3—9	—	—	242
	Cu^+	435	4.55		aqueous-alcoholic medium	—	242
	Ru^{2+}	450	14.5	—	—	—	10
		630 (fluorescence)		7	—	platinum metals (50 μg, but 20 μg of osmium) do not interfere	85—87,248
	Ti^{3+}	340	3.9	3.4	bis-2-ethylhexyl hydrogen phosphate	Ti^{IV} not extracted in presence of excess of reagent	156,216
Phenanthroline-3-sulphonic acid	Fe^{2+}	512	12.24	3—11	—	$HClO_4$ does not interfere	65
Phenanthroline-5-sulphonic acid	Fe^{2+}	517	10.84	—	—	$HClO_4$ does not interfere	65
4,7-Diphenylphenanthroline (bathophenanthroline)	Fe^{2+}	533	22.2	2—9	aqueous-alcoholic medium or extraction with nitrobenzene, propylene carbonate, isopentanol, or alcohol + chloroform	Cu^+ does not interfere at pH ⩽ 4; Fe can be determined in Mo, W, Sn, Nb, and Ta of high purity	14—16, 69—71
	Ru^{2+}	460	27.0	4—5	hexanol	Ru can be determined in U on heating and with excess of the reagent	84
2,9-Dimethylphenanthroline (neocuproin)	Cu^+	454	7.95	3—10	hexanol or isopentanol	Fe does not interfere	11,17—21
Neocuproin + bathophenanthroline mixture	Cu^+	454	7.95	2—3	isopentanol in aqueous phase	Cu determined in organic phase, and Fe in aqueous phase, since Cu^+ at pH < 4 does not form a complex with bathophenanthroline	235
	Fe^{2+}	535	22.0				
2,9-Dimethyl-4,7-diphenylphenanthroline (bathocuproin)	Cu^+	479	14.2	5	hexanol	Cl^-, ClO_4^-, NO_3^-, PO_4^{3-}, SO_4^{2-}, etc. do not interfere with determination of Cu in Fe	29
5,6-Dihydro-4,7-dimethyl-2,3,8,9-dibenzo-1,10-phenanthroline (cuprotest)	Cu^+	554	7.95	3—11	chloroform	hardly any metal (10 μg·ml^{-1}) or anion up to 1 M (except $S_2O_3^{2-}$, CN^-, S^{2-}, edta) interferes	28
5-Nitrophenanthroline	Fe^{2+}	510	11.79	0 (HNO_3)	aqueous medium or extraction with mixture of higher alcohols	—	32,33
2,9-Dimethylnitrophenanthroline (nitroneocuproin)	Cu^+	455	7.92	5—6	aqueous medium or extraction with hexanol and with chloroform	Al^{3+}, Pb^{2+}, Zn^{2+}, Ni^{2+}, F^-, SO_4^{2-} do not interfere with determination in Pu	17
Phenanthroline-4,7-diol	Fe^{2+}	520	15.0 (4 M NaOH)	8—18 M NaOH	—	CN^- interferes	22
3,3′-Dimethyl-2,2′-bipyridyl	Cu^+	455	6.57	7—8	aqueous medium or extraction with isopentanol	Fe does not interfere in determination of Cu^+ in Pu, Te	22
4,4′,6,6′-Tetramethyl-2,2′-bipyridyl	Cu^+	455	7.9	—	isopentanol, chloroform	Fe^{2+}, Co^{2+}, Ni^{2+} do not interfere	25
		454	6.7				
4,4′-Diphenyl-2,2′-bipyridyl	Fe^{2+}	552	21.1	—	—	—	221
	Cu^+	463	9.6				
2-Pyrid-2′-ylquinoline	Cu^+	490	5.78	—	isopentyl and benzyl alcohols, ethyl acetate and chloroform	neither Fe^{2+} nor Fe^{3+} interferes	11,13
2,2′-Biquinolyl (cuproin)	Cu^+	540	5.49	>3	chloroform	Ti(1 mg ml^{-1}) interferes; Fe^{2+}, Co^{2+}, Ni^{2+} do not interfere	11,13,27
		546	6.4		butanol		26
3-Methyl-2,2′-biquinolyl	Cu^+	525	4.12	3	chloroform	neither Fe^{2+} nor Fe^{3+} interferes	11,13,27
4,4′-Diphenyl-2,2′-biquinolyl	Cu^+	554	9.02	—	—	—	11,221
2,2′,2″-Terpyridine	Fe^{2+}	552	12.0	3—10	nitrobenzene used in $HClO_4$ medium	Co^{2+} interferes	45,242

Table 3 (continued).

Reagent	Ion to be determined	λ, nm	$10^{-3}\epsilon$	Optimum pH	Solvents and extractants	Foreign ions and possible elimination of their effect	Ref.
1	2	3	4	5	6	7	8
4,4″-Diethyl-4′-phenyl-2,2′,2″-terpyridine	Fe^{2+}	570	27.1	—	—	—	221
2-Pyrid-2′-ylbenzimidazole	Fe^{2+}	490	3.8	5.7	isopentanol	Ag^+, Hg^{2+}, and tartrates interfere strongly	91
2-Pyrid-2′-ylimidazoline	Fe^{2+}	560	7.8	9	isopentanol	Co^{2+}, Fe^{3+}, Cu^+ form yellowish complexes	91
4,4′,4″-Triphenyl-2,2′,2″-terpyridine (terrosite)	Fe^{2+}	583	30.2	3—8	alcohol–chloroform mixture	—	102
2,4,6-Tripyrid-2′-yl-1,3,5-triazine	Fe^{2+}	593	22.6	3—6	—	Fe can be determined in silicates;	102,103
		595	24.1	3—7	nitrobenzene or propylene carbonate	Cr^{3+}, Bi^{3+}, Hg^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+}, $C_2O_4^{2-}$, NO_2^-, CN^- interfere	
4,6-Dipyrid-2′-yl-1,3,5-triazin-2-amine	Fe^{2+}	497	8.0	—	nitrobenzene	—	104,105
3-4′-Ethylpyrid-2′-yl-1,3,5-triazine	Fe^{2+}	605	24.37	—	aqueous–alcoholic medium	—	104,105
5,6-Diphenyl-3-pyrid-2′-yl-1,2,4-triazine	Cu^+	488	7.99	2—7	isopentanol	Fe determined after Cu, by decomposing complex of latter by means of NaCN;	109
	Fe^{2+}	555	23.5	—	—	Co^{2+}, Ni^{2+}, CN^- interfere, to a less extent also NO_2^-, $C_2O_4^{2-}$	
5,6-Diphenyl-3-4′-phenylpyrid-2′-yl-1,2,4-triazine	Fe^{2+}	561	28.7	4—7	isopentanol or nitrobenzene	Co^{2+}, Ni^{2+}, Cn^- interfere	102,108
1,10-Phenanthroline and Bromophenol Blue	Fe^{2+}	630	59.0	8.7—8.9	chloroform + isopentanol (4:1)	to determine Fe in especially pure hypophosphite it is first concentrated as ferroin iodide (pH 2–10)	117
1,10-Phenanthroline and Rose Bengal (tetrachlorotetraiodofluorescein)	Cu^{2+}	570 (fluorescence)	62.5	7—9	chloroform	Ag^+, Cd^{2+}, Co^{2+}, Mn^{2+}, Ni^{2+}, Pb^{2+}, Zn^{2+}, CN^- interfere;	126,127
		570 (fluorescence)	—	—	ethyl acetate	Cu first extracted with neocuproin to improve selectivity	
1,10-Phenanthroline and Bromopyrogallol Red	Cd^{2+}	620	10.0	7.8—8.1	—	Fe^{3+}, Al, Cr, Pb, Zn, Ni, Mo, Co interfere	128
	Ag^+	635	51.0	7	—	edta, Fe^{2+}, Au^{III}, Nb^V, Th^{IV}, UO_2^{2+}, CN^-, $S_2O_3^{2-}$ interfere	129
Silver(I) complex with Bromopyrogallol Red or Rose Bengal	CN^-	635	51.0	7	—	Fe^{3+}, Co^{2+}, Cu^{2+}, $S_2O_3^{2-}$, SCN^-, I^- interfere	130
		570	40.0	7	—		
1,10-Phenanthroline and sulpharsazen	Ag^+	600	—	5—7.5	—	Ag first extracted with dithizone in order to separate from Hg^{2+}, Cu^{2+}, Pd^{2+}, NO_3^-	131
		630	—	10.8	—		
1,10-Phenanthroline and galloin	Ag^+	630	40.0	—	—	pyridine and ammonia do not form a mixed complex	132
1,10-Phenanthroline and dithizone	Ni^{2+}	520	49.1	6.0	chloroform	—	118
1,10-Phenanthroline and catechol	Nb^V	360	18.0	3.5—4.5	chloroform	—	165
1,10-Phenanthroline and thiocyanate	Nb^V	400	24.0	3—5 *M* HCl	chloroform + tributyl phosphate (10:1)	—	165
Ferroin	CN^-	597	—	9.2—9.7	chloroform	Cu^{2+}, SO_4^{2-}, SCN^-, ClO_4^- do not interfere	79,243
	SCN^-	515	22.5	5—10	nitrobenzene	Co^{2+}, Cu^+, Ni^{2+}, Zn^{2+}, I^-, Br^-, NO_3^- interfere	75,244
	ReO_4^-	528	—	2—8	nitrobenzene	Mo and W (5 mg) do not interfere	241
	CrO_4^{2-}	516	—	3—4	nitrobenzene	Cr^{3+}, Ni, Cu, Zn, Mo, Cl^-, SO_4^{2-}, PO_4^{3-} do not interfere;	76
	HBF_4^-	510	12.0	4—8	dichloromethane	Fe^{3+}, Pb^{2+} interfere	73
	ClO_4^-	510	11.0	5(acetate buffer)	nitrobenzene or n-butyronitrile	can be used to determine Fe^{2+} in $HClO_4$ medium	74,245,247
	$HSal^-$	516	—	5.5—9.5	nitrobenzene	—	72
	PF_6^-	505	—	2.2—10.6	n-butyronitrile	—	246
	$PtCl_6^{2-}$	516	—	2—6	nitrobenzene	—	73
	AsF_6^-	505	—	2.2—10.1	n-butyronitrile	many anions interfere	237

Table 3 (continued).

Reagent	Ion to be determined	λ, nm	$10^{-3}\epsilon$	Optimum pH	Solvents and extractants	Foreign ions and possible elimination of their effect	Ref.
1	2	3	4	5	6	7	8
	$[Sn(C_2O_4)_3]^{2-}$	—	—	—	nitrobenzene	Ag^+, Hg^{2+}, Ti^{IV}, Mo, W interfere	239
	$[AuCl_4]^-$	511	—	—	chloroform	Co, Cu, Ni, Fe, Mn, Pt, Pd, Ir, Os, Hg do not interfere	177
	I^-	500	—	4.5	—	ClO_4^-, SCN^- interfere strongly;	75
		516	—	—	nitrobenzene	Cl^- ions do not interfere even in large excess	
Iron Bathophenanthrolinate	$HSal^-$	536	—	2.5—4.5	butyl acetate	—	73
Tris-2,2′-bipyridyliron(II) complex	SCN^-	518	21.7	—	4-methylpentan-2-one	I^-, Br^-, NO_3^- interfere	75,243,244
	$HgBr_4^{2-}$ (HgI_4^{2-})	526	—	6.5	dichloromethane	Sn^{2+}, Cu^{2+} interfere; they are masked by nitrilotriacetic acid	73
	CCl_3COOH	516	—	4	nitrobenzene	PO_4^{3-}, SO_4^{2-} do not interfere	240
	$TlBr_4^-$	524	—	4.5	dichloromethane	Hg^{2+}, Au^{III}, I^-, edta interfere; Fe^{3+}, Cu^{2+}, Zn^{2+}, Pb^{2+} do not interfere	238

of phenanthroline and bipyridyl. The latter ligand is made unreactive towards iron(II) by carboxyls at positions 3,3′ and 5,5′.[22] Phenanthroline-2-carboxylic acid forms a series of mixed complexes with copper and cadmium as well as dicomplexes with iron, cobalt, nickel, manganese, zinc, and cadmium in which it acts as a terdentate electronegative ligand. Iron forms either a dinuclear complex or a six-coordinate complex, a chloroform solution of the latter exhibiting weak absorption ($\epsilon = 2500$).[30,31]

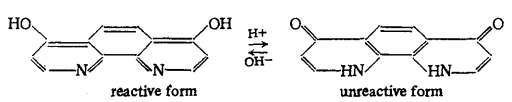
5-Nitrophenanthroline can be used to determine iron at pH 0; the sensitivity of the reaction depends on the nature of the acid, but is unaffected by the nitro-group. Conditions for the determination of iron are best in nitric acid. Phenanthroline behaves as a monobasic acid $phenH^+$ with $K_{diss,25^\circ} = 1.1 \times 10^{-5}$. Because of the high equilibrium constant

$$K_{eq:25^\circ} = \frac{[Fe\ phen_3^{2+}][H^+]^3}{[Fe^{2+}][phen.H^+]^3} = 2{,}5 \cdot 10^6,$$

the phenanthrolinate complex is formed quantitatively at pH 3–9; the complex already begins to be decolorised at pH < 2.[32,33] Probably the nitro-group in nitroferroin, by diminishing the basicity of the nitrogen in phenanthroline, increases the stability of the complex, which makes possible the determination of iron in more acid media.

Similarly, copper(I) can be determined at a lower pH with nitroneocuproin than with neocuproin[17].

In acid and neutral medium phenanthroline-4,7-diol exhibits very little complexing power for iron(II), but in strongly alkaline solutions it becomes an extremely sensitive reagent for iron ($\epsilon = 1.5 \times 10^4$)—as a consequence of the equilibrium



reactive form unreactive form

postulated[22] by analogy with 4-hydroxyquinoline[34].

2. Kinetics of Reactions Involving Metal Complexes of 1,10-Phenanthroline and 2,2′-Bipyridyl

In the analytical application of various phenanthroline derivatives and in the assessment of the stability of complexes formed by various metals, the pH of the medium must be taken into account not only in connection with the acid–base properties of the ligands but also in relation to hydrolysis and aquation, reactions which affect complex formation and the stability of complexes in solution.

Kinetic investigations of the aquation and hydrolysis of various substituted ferroins[35–39] have shown that donor substituents—methyl, phenyl, and amino—in positions 4,7 and 5,6 confer the greatest stability towards these reactions. Acceptor groups—nitro and chloro—in contrast, by diminishing the electron density on iron atoms in tricomplexes, facilitate attack by hydroxide ions on the central atom during hydrolysis, and promote the replacement of ligands by water molecules. Therefore both aquation and hydrolysis occur most rapidly in 5-nitro-, 5-chloro-, and 5-methyl-6-nitro-ferroins, and with greatest difficulty in 4,7- and 5,6-dimethylferroins, as well as in 5-aminoferroin. The kinetic characteristics of ferroin itself are intermediate between those of the two kinds of derivatives. The only exception is the 4,7-dihydroxyphenanthrolinate complex of iron, which readily undergoes aquation in acid medium, while being very stable in alkaline medium.

Solutions in aqueous organic solvents and also various masking ions are very often used in analytical practice to improve the solubility of reagents and enhance the stability of complexes. Therefore planned kinetic investigations of aquation, dissociation, and other reactions involving complex ions will give extremely valuable information on the influence of the ionic strength, the polarising properties of the medium, and the chemical nature of the solvent on the state of these ions in solution.

Thus polarographic studies have revealed a specific effect of methanol on the stability of various bipyridyl complexes of copper[40]. Complex formation between platinum(II) and phenanthroline or bipyridyl is considerably more rapid in the presence of alcohols[41-43]. In this connection it is noteworthy that $\lg(k_w/k_b)$ (where k_w and k_b are the rate constants for the aquation of 5-nitroferroin in aqueous solution and in aqueous butanol respectively) is an extremal function of the mole fraction of the alcohol[44]. This may be due to changes in the structure of the solution, so that structural factors must be considered when organic additives are used.

Study of the racemisation of triphenanthroline-iron and -nickel complexes yields interesting results enabling the stability of complexes to be assessed[45]. Whereas the rates of racemisation and dissociation are the same for $[Ni\,phen_3]^{2+}$ (which is consistent with several known facts), the rate of racemisation of ferroin far exceeds the rate of dissociation, which can be explained by postulating a complicated mechanism of intramolecular rearrangement occurring in a solution of the complex.

The reactivity of such complexes undergoes great changes in the presence of electrolytes[46]. Thus the large cations of strychnine, quinine, and brucine accelerate the dissociation and the racemisation of $[Fe\,phen_3]^{2+}$ and $[Ni\,phen_3]^{2+}$ (probably by diminishing the electron density in the bond between the central metal atom and a ligand nitrogen atom). On the addition of acids, on the other hand, the rate of dissociation decreases, to a far greater extent for $[Fe\,phen_3]^{3+}$ than for ferroin.

Kinetic differences in the rates of formation of complexes with phenanthroline can be used for the simultaneous determination of iron(II) and iron(III).[47] In determinations with phenanthroline iron(III) is usually reduced to the bivalent state by means of ascorbic acid, hydroxylamine, or sodium sulphite[48]. This method can be used to determine iron in vanadium (in weakly acid medium vanadium(IV) gives a colourless complex with phenanthroline[49]).

Tervalent iron gives the most stable complexes with oxygen- and sulphur-containing ligands, in which it is present in a high-spin state owing to the energetic advantage of the d^5 configuration. For this reason the dark blue triphenanthroline complex $[Fe\,phen_3]^{3+}$ is less stable than ferroin, and is obtained by oxidising the latter[13]. Many studies indicate[50-55] that direct reaction between iron(III) and a solution of phenanthroline produces polynuclear complexes of presumed structure[54]

$$[phen_2(X)Fe-O-Fe(X)phen_2]^{2+},\ \text{where } X = Cl^-,\ SCN^-\ \text{etc.}$$

Polynuclear complexes are formed with phenanthroline not only by iron but also by copper[56-60], chromium[61], rhodium[62], molybdenum[63], and palladium[64], but inadequate study has been made of their complicated structure, conditions of formation, and analytical properties.

3. Enhancement of Selectivity of Determination by Extraction

The sensitivity to metals of many phenanthroline reagents, especially those containing phenyl substituents, is limited by the sparing solubility of the reagents themselves in water. The solubility of triphenanthrolineiron in perchlorate media is increased by introducing a sulphogroup at position 3 or 5. The spectral characteristics of the complex remain almost unchanged[65]. The solubility of complexes of copper with bathocuproin has been increased in this way[64].

However, a decrease in the solubility of reagents and complexes in water is usually accompanied by an improvement in their solubility in organic solvents. The application of extraction methods greatly enhances the selectivity and the sensitivity of reactions. Whereas long-chain alkyl sulphates and alkanesulphonates (Teepol) are required for the extraction of ferroin[67], bathophenanthrolineiron is extracted very well by chloroform and by pentanol[16], which enables 0.25 μg of iron to be determined in the presence of $H_2PO_4^-$. However, the kinetic stability of the iron complex in chloroform [with an iron(III) content of 25 mg and above] is debatable[68].

More often a more polar extractant (nitrobenzene[69,70]) or a less toxic one (propylene carbonate[15]) is used. When isopentanol is used to extract the iron complex, the presence of cobalt, whose complex is not extracted at pH 2–9, does not interfere with the determination[11]. Iron has been determined in tin, molybdenum, tungsten, niobium, and tantalum of high purity by an extraction–photometric method using isopentyl alcohol[71]. Such methods for determining anions are based on the ability of ferroin and $[Fe\,bipy_3]^{2+}$ to form insoluble precipitates with many anions. The most stable and insoluble adducts are usually given by large anions—both organic[72,73] (salicylate, picrate, pentachlorophenoxide) and inorganic[74-76] (SCN^-, ClO_4^-, CrO_4^{2-}, $PtCl_6^{2-}$, $HgBr_4^{2-}$, etc.) (Table 3)—which is consistent with the low hydration energies calculated for large ions by means of Born's equation. Thus the use of nitrobenzene to extract adducts of ferroin with chloride, bromide, iodide, thiocyanate, and perchlorate ions showed that the difference ΔH between energies of solvation in water and in the solvent was most negative with the last three anions, zero for bromide, and positive for the chloride ion, which agrees with their stability and extractability[75,77].

Very sensitive methods for determining iron have been based on the formation of adducts of ferroin with dioctyl sulphosuccinate[78] and with cyanides[79]. The latter method enables iron to be determined in the presence of copper, since the colourless copper complex $Cu(CN)_3^{2-}$ is more stable than the corresponding complex with phenanthroline, and on extraction with chloroform in the narrow pH range 9.2–9.7 most anions do not interfere with the determination of iron.

Like ferroin, nickel(II), cobalt(II), zinc(II), copper(I), and cadmium(II) form[80,81] the compounds $M\,phen_3X_2$ ($X = I^-$, SCN^-, ClO_4^-), which can be used for the extractive spectrophotometric determination of the metals, but these methods are insufficiently specific. Several such compounds are suitable for gravimetric determination.

A rapid method for determining nickel in the presence of iron and cobalt is based on formation of the complex of nickel(II) with phenanthroline and trichloroacetic acid, which is extracted with dichloroethane. In the presence of cerium(IV) as oxidant iron and cobalt are not extracted[82].

Ruthenium(II)—an electronic analogue of iron—forms when heated with phenanthroline a yellow tricomplex, which is suitable for its spectrophotometric determination[83]. However, a more sensitive method is to extract tribathophenanthrolineruthenium with hexanol ($\epsilon = 2.7 \times 10^4$), which is inferior in sensitivity only to the 4-phenylthiocarbazide method[84].

4. Luminescent and Catalytic Properties of Metal Complexes of 1,10-Phenanthroline and 2,2′-Bipyridyl

Since preliminary separation of ruthenium from osmium and other platinum metals is required by most—including catalytic—methods, a certain advantage attaches to those based on the specific fluorescence of the bipyridyl [85], 4,4′-dimethylbipyridyl, and 5,6-dimethylphenanthrolinate complexes of ruthenium [86-88]. None of the platinum metals (up to 50 μg—osmium up to 20 μg) interferes with the determination of 0.02–0.07 μg of ruthenium. The strength of emission by the osmium complex is one-sixtieth of that due to the ruthenium complex.

Luminescence has been discovered in triphenanthroline-iridium(III) complexes in dimethylformamide solution [89].

Since transition metals usually quench luminescence by the ease of $d-d$ transitions, ruthenium(II) and iridium(III) are evidently exceptional in having a sufficiently large energy difference between filled and vacant orbitals in their tricomplexes.

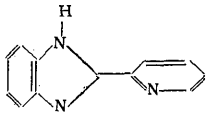
The fluorescent properties of mixed phenanthroline complexes of samarium, europium, terbium, dysprosium, etc. are very important for the development of methods for the analysis of rare-earth metals.

Many complex compounds of transition metals with phenanthroline and bipyridyl exhibit catalytic properties. Thus $[Fe\,bipy_3]^{3+}$ catalyses the chain decomposition of hydrogen peroxide [46]. Bipyridyl complexes of copper(II) actively influence the luminol–hydrogen peroxide system, widely used in luminescent analysis, the catalytic activity increasing in the sequence [90]

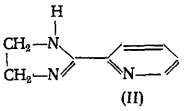
$$Cubipy_3^{2+} < Cubipy_2^{2+} < Cubipy^{2+}.$$

5. Photometric Reactions Involving Ligands Containing One or More N.C:C.N Groups

2-Pyrid-2′-ylbenzimidazole (I) and 2-pyrid-2′-ylimidazoline (II)

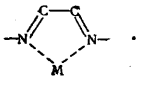


(I)

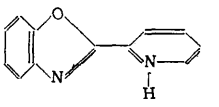


(II)

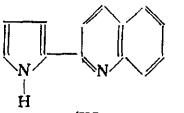
have been used [91] as reagents containing the ferroin grouping N.C:C.N. The tricomplex of iron(II) with (II) absorbs considerably more strongly than does that with (I) (ϵ = 3800 and 7800 respectively), probably owing to the unfavourable steric influence of the aromatic ring in (I), as with reagents of the type 2,2′-biquinolyl and 2-pyrid-2′-ylquinoline [11,92]. Although possessing no advantages over other reagents, (I) and (II) have found wide application in the pharmaceutical industry for the production of various derivatives substituted at the NH group, whose acidic properties are greatly dependent on the nature of the metal—iron, cobalt, nickel, zinc, copper, or manganese—coordinated into the ring



It is interesting that iron(II) does not form complexes with 2-pyrid-2′-ylbenzoxazole (III) and 2-pyrrol-2′-ylquinoline (IV)



(III)



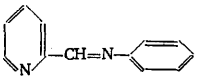
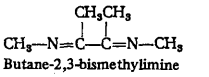
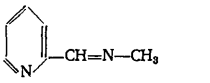
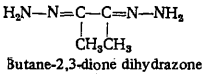
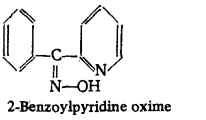
(IV)

perhaps owing to diminished basicity of the nitrogen atom in the five-membered ring [93]. Furthermore, formation of a complex with (IV) is sterically hindered, as with copper and cobalt.

Bipyridyl *NN′*-dioxide forms seven-membered cyclic complexes, resembling complexes of pyridine *N*-oxide in the character of the bond with the metal [94]. However, they are relatively unsuitable for spectrophotometry owing to insufficient intensity of absorption.

Comparison of the structure of reagents for iron and for copper indicates the presence of two specific groups [13]—for iron(II) the N:C.C:N group, and for copper(I) R.CH.N:C.C:N.CH.R, where R = CH_3, C_6H_5, NH_2.

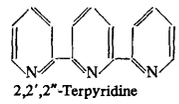
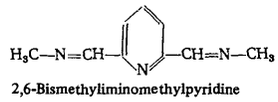
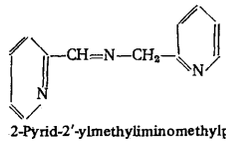
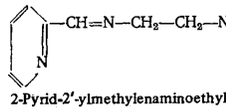
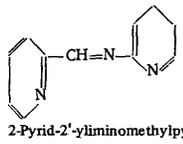
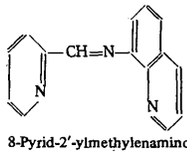
Table 4. Spectral characteristics of complexes of iron(II) with ligands containing a ferroin group [95,96].

No.	Ligand	λ, nm	$10^{-3}\epsilon$
1	 2-Phenyliminoethylpyridine	578	—
2	 Butane-2,3-bismethylimine	568	10.7
3	 2-Methyliminomethylpyridine	551	11.15
4	2,2′-Bipyridyl	522	8.7
5	1,10-Phenanthroline	510	11.5
6	 Butane-2,3-dione dihydrazone	444	7.0
7	 2-Benzoylpyridine oxime	560	15.6

The character of complex formation between the ligand and iron(II) may vary depending on the nature of the groups directly adjacent to the nitrogen atoms of the ferroin grouping. This is evident from the spectral characteristics of complexes of iron with ligands containing different groups directly attached to the nitrogen atoms [95,96] (Table 4). Thus the tricomplex of iron with butane-2,3-dione dihydrazone is sharply distinguished in its visible and ultraviolet spectra from the remaining complexes, which probably indicates that the nature of the ligand changes

under the influence of complex formation. The charcter of complex formation between different metals and 2-benzoylpyridine oxime is determined, as with all oxime and dioxime reagents, by the ability of the hydroxyl hydrogen to be replaced by the metal [97].

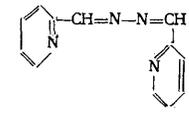
Table 5. Spectral characteristics of dicomplexes of iron(II) with ligands containing a terpyridine grouping N : C.C : N.C.C : N. [98]

No.	Ligand	λ, nm	$10^{-4}\varepsilon$
1	 2,2′,2″-Terpyridine	552	—
2	 2,6-Bismethyliminomethylpyridine	585	—
3	 2-Pyrid-2′-ylmethyliminomethylpyridine	568	1.1—1.2
4	 2-Pyrid-2′-ylmethylenaminoethylamine	592	—
5	 2-Pyrid-2′-yliminomethylpyridine	667	0.75
6	 8-Pyrid-2′-ylmethylenaminoquinoline	659	0.65

The most crucial sites for selectivity towards iron and copper are the 2,9-positions in phenanthroline and the 3,3′-positions in bipyridyl. A 2-carboxyl converts phenanthroline into a terdentate ligand, while bipyridyl and phenanthroline completely lose their ability to form complexes with iron(II) when methyl, phenyl, and amino-substituents are present in these positions. This is explained by steric hindrance to the coordination of iron, which does not develop on complex formation with copper(I); this may be connected with the size of the cations. Replacement of methylimino by ethylimino deprives both substituted phenanthrolines and aliphatic imines (e.g. No. 2 in Table 4) of their ability to yield tricomplexes [96] with iron(II). The appearance of aromatic rings and the increase in their number on passing from butane-2,3-bismethylimine to phenanthroline are accompanied by a shift in the absorption maxima of the iron(II) complexes to shorter wavelengths, but the lengthening of the chain of conjugated double bonds in 2-phenyliminomethylpyridine produces a bathochromic shift owing to the delocalisation of π-bonds. A similar bathochromic displacement is observed in a series of iron(II) dicomplexes with Schiff bases containing a terpyridine grouping N:C.C:N.C.C:N (Table 5). [98] The replacement of aliphatic double bonds (2, 3) by single bonds (4) or double bonds in an aromatic ring (5, 6) leads to a bathochromic shift in the spectrum of the iron(II) complexes, which is especially marked in the last case.

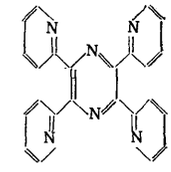
2,2′,2″-Terpyridine, like 2,2′-bipyridyl, is a planar ligand, as is confirmed both by X-ray examination and by the absence of optically active bisterpyridine complexes, e.g. with ruthenium(II) and nickel(II). [46] The formation of octahedral complexes produces some strain in the terpyridine molecule owing to the inevitable distortion of the angles between the pyridine rings. Since such deformation should be still greater with quaterpyridine, four coordination cannot be achieved with this compound. As a reagent, terpyridine has no advantages over bipyridyl, but its derivatives are widely used in analysis, and compounds containing terpyridine and bipyridyl groupings find application in biology. Their complexes with metals—iron, cobalt, nickel, ruthenium, osmium—are intensely coloured and possess biological activity.

Certain difficulties in studying complex formation are created by multidentate ligands [99]. Thus terdentate pyridine-2-carbaldehyde azine forms strongly coloured octahedral complexes with iron(II) and nickel(II). However, dinuclear compounds of the type $[M_2A_3]^{4+}$ are also known, where A represents



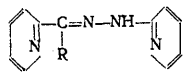
and is a bisbidentate ligand. This reagent forms also the iron complex $[FeA_3]^{2+}$. As with phenanthroline and bipyridyl, the presence of any substituent in position 2 of the pyridine ring strongly affects the coordinating properties of such ligands.

It is interesting that 2,3,5,6-tetrakispyrid-2′-ylpyrazine



is a terdentate ligand like terpyridine, since simultaneous coordination of all six nitrogen atoms is impossible without destroying the planarity of the structure. Furthermore, the coordination of one nitrogen atom of the pyrazine ring causes a marked diminution in the donor properties of the other, which is confirmed by the fact that pyrazine does not form diquaternary ammonium bases. However, unsubstituted pyrazine forms compounds with copper(I), nickel(II), and cobalt(II), in which both nitrogen atoms of the pyrazine ring are coordinated with the metal [100].

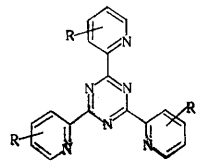
In the terdentate hydrazine derivatives of general formula



either three donor nitrogen atoms may be coordinated depending on the pH (to form the complex cations $[MA_2]^{2+}$) or (in alkaline medium) all four nitrogen atoms may be coordinated to form neutral dicomplexes [101]. The reversibility of such transformations can be utilised for the technical purification of metals, since in alkaline solution these neutral complexes are readily extracted.

Terpyridine forms complexes not only with iron(II) and cobalt(II) but also with quadrivalent platinum [$PtCl_3$terpy].Cl, as well as five-coordinated complexes of the type [MX_2terpy] (M = Co, Cu, Cd), the mechanism of whose formation has not been adequately clarified [45].

One of the most sensitive reagents for iron(II) is 4,4′,4″-triphenyl-2,2′,2″-terpyridine (terrosite) [102] ($\epsilon_{583} = 3.02 \times 10^4$), but the sparing solubility and poor extractability of the complexes obtained restricts its analytical application. The search for highly sensitive reagents whose complexes could be readily extracted has involved the study of numerous hydrazine and triazine derivatives, data on which are briefly summarised in Tables 3 and 4. The most sensitive reagents for the determination of iron(II) were 2,4,6-derivatives of 1,3,5-triazine of general formula

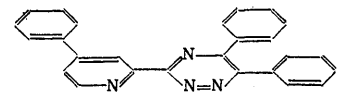


the complexes of which have values of $10^{-4}\epsilon$ of 2.26, 2.44, and 2.52 respectively depending on whether R = H, 4-C_2H_5, 4-C_6H_5. The comparative availability of 2,4,6-tripyrid-2′-yl-1,3,5-triazine has been responsible for its widespread use to determine iron in various materials [104].

The presence of amino-groups in the triazine ring strongly diminishes the complexing power of the ligand, the decrease being an additive function of the number of such groups. Whereas the extinction coefficient for the iron complex of 4,6-dipyrid-2′-yl-1,3,5-triazin-2-amine is more than halved ($\epsilon_{497} = 8000$) in comparison with tripyrid-2′-yl-1,3,5-triazine, we have $\epsilon_{455} = 300$ for 6-pyrid-2′-yl-1,3,5-triazine-2,4-diamine, and 1,3,5-triazinetriamine (melamine) does not form an iron(II) complex at all. The introduction of ethyl and phenyl substituents into the pyridine ring slightly increases the extinction coefficients of the complexes, as was to be expected. Use of the polar extractant nitrobenzene also enables the intensity of absorption of the complexes to be raised [105]. Values calculated for the extinction coefficients from refractometric data were then rather higher than the observed values, which was shown to be due to the involvement of water in formation and extraction of the complex.

Calculation of the most important sites of association in the complexing molecule will probably permit the planned introduction of substituents to obtain extractable complexes having specified properties [106,107].

Among other triazine derivatives the most effective was found to be the bidentate ligand 5,6-diphenyl-3,4′-phenylpyrid-2′-yl-1,2,4-triazine



which is inferior in the sensitivity of its reaction with iron(II) ($\epsilon_{561} = 2.87 \times 10^4$) only to terrosite, but possesses considerably better solubility in organic solvents [102,108].

Complexes of *N*-heterocyclic amidrazones, containing the ferroin grouping, are usually unstable even with a large excess of the reagent. In several cases, however, they can be used as acid–base indicators, since they contain a hydrogen atom which can be detached in alkaline medium [101].

A combined method has been worked out for the simultaneous determination of copper and iron by means of 5,6-diphenyl-3-pyrid-2′-yl-1,2,4-triazine and the ability of copper to form a stable complex with cyanide ions in the presence of this reagent [109]. The concentration of copper was found from the decrease in optical density at the wavelength of absorption by its complex with the reagent ($\epsilon_{488} = 7900$), and that of iron(II) from the optical density of the solution after the addition of sodium cyanide ($\epsilon_{555} = 2.35 \times 10^4$). Use of the above reagents to determine cobalt(II) was relatively ineffective, because of inadequate sensitivity.

Isomeric phenanthrolines and bipyridyls used in spectrophotometric methods are 6-hydroxy-1,7-phenanthroline (an analogue of 8-hydroxyquinoline) to determine iron and vanadium [110,111] and 2,3′-bipyridyl to determine niobium and titanium as mixed complexes with salicylic acid and catechol [112], germanium [113], and uranyl [114].

4,4′-Bipyridyl, in contrast to the 2,2′-isomer, forms with metals of the platinum group microcrystalline precipitates suitable for their microcrystalline detection [115]. The arrangement of the nitrogen atoms in 4,4′-bipyridyl favours the formation of polynuclear compounds with many metals [116].

6. Physicochemical Properties of Mixed Complexes and Their Application to Extractive Photometric Analysis

The sensitivity and the specificity of the extractive photometric analysis of metals can in many cases be considerably increased by the use of phenanthroline (or bipyridyl) mixed with various oxygen-, sulphur-, and nitrogen-containing ligands, since the stability and the light absorption of the mixed complexes are frequently far greater than those of the simple complexes. Thus the adduct of ferroin with a sulphophthalein dye molecule (bromophenol Blue) is intensely coloured [117] ($\epsilon_{630} = 5.9 \times 10^4$) and is readily extracted by a mixture of chloroform and isopentanol (4 : 1) within a narrow pH range (8.7–8.9). Traces of iron in hypophosphite ($\sim 10^{-8}$%) are determined in this way. Dithizone (Dz) is an extremely sensitive but relatively unspecific reagent. Nickel, like many other metals, gives an intensely coloured dithizonate ($\epsilon = 3.4 \times 10^4$), but in the presence of phenanthroline a chloroform-extractable blue complex $NiDz_2$phen is formed, which is more intensely coloured ($\epsilon = 4.91 \times 10^4$) than is the dithizonate [118].

Whereas Cu^+, as a consequence of stereochemical uniformity is characterised by simple complexes with polarised ligands such as phenanthroline and bipyridyl, the easily deformable Cu^{2+} ions readily form mixed complexes by establishing stable covalent bonds with different ligands. Examples are complexes of copper(II) with bipyridyl and glycine, pyridine-2-carboxylic acid, 8-hydroxyquinolinesulphonic acid, pentane-2,4-dione,[119-123] biguanidine, and diacid Schiff bases[124,125]. These are of especial interest, since they are readily soluble in such organic solvents as dimethyl sulphoxide, pyridine, dimethylformamide, and ethanol, and possess high molar absorption coefficients—$\epsilon = (5-12) \times 10^3$.

One of the most sensitive photometric methods for determining copper is based on the fluorescence of the mixed complex CuRBE$phen_2$ (where RBE represents the xanthen acid dye Rose Bengal—tetrachlorotetraiodofluorescein), which can be extracted by chloroform and by ethyl acetate ($\epsilon_{570} = 7.8 \times 10^4$). This method enables 1 μg of copper to be determined in 500 ml of solution on extraction with 25 ml of chloroform. Iron is masked by excees of phenanthroline, since it forms a more stable complex with the latter. Sometimes copper is first extracted as its neocuproin complex in the presence of ethylenediaminetetra-acetic acid in order to improve the selectivity[126]. Since many metals form complexes of this type with phenanthroline and Rose Bengal[127,128] (Table 6), masking agents must be used to enhance the selectivity of this method.

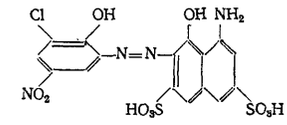
Table 6. Comparative absorption intensities by metal dithizonates by their mixed complexes [M$phen_2$RBE].[127]

Cation	Absorption $10^{-4}\epsilon$		Extractant
	dithizonate	mixed complex	
Cd^{2+}	8.8	9.2	ethyl acetate
Co^{2+}	5.9	9.2	ethyl acetate
Cu^{2+}	4.5	7.8	ethyl acetate
		6.25	chloroform
Mn^{2+}	3.2	6.5	ethyl acetate
Ni^{2+}	3.4	5.0	chloroform
Ag^+	—	4.0	chloroform
Pb^{2+}	7.2	7.0	nitrobenzene
Zn^{2+}	9.4	9.5	ethyl acetate

A highly sensitive method has been developed for determining silver(I) by means of other fluorescein derivatives: the intensity of absorption of the mixed complex Ag$phen_2$BPR is fivefold that of the simple Bromopyrogallol Red complex AgBPR ($\epsilon_{635} = 5.1 \times 10^4$ and $\epsilon_{390} = 1.0 \times 10^4$ respectively). In the presence of excess of phenanthroline iron(II) does not interfere with the determination[129].

Stable cyanide complexes of silver are easily formed in the presence of phenanthroline and either dye (Bromopyrogallol Red or Rose Bengal), a fact which is utilised to determine cyanide ions at concentrations of 0.1–0.00001 M. The end-point of the titration is determined either photometrically or visually from the fluorescence of the mixed complex Ag$phen_2$BPR or Ag$phen_2$RBE.[130] Silver concentrations of 0.2–15 μg ml^{-1} are determined as a mixed complex with bipyridyl and sulpharsazen (the sodium salt of 2-arsono-4′-*p*-nitrophenyltriazenoazobenzene-4-sulphonic acid), which is tribasic[131]. Preliminary extraction with dithizone eliminates the effects of the cations Hg^{2+}, Cu^+, and Pd^{2+}, and of the anions SO_4^{2-}, Cl^-, NO_2^-, and CH_3COO^-.

Galloin, a hydroxylated aromatic sulphonic acid



(H_3R), has also been suggested as a third component for the mixed complex. The formation of $(Ag\,phen_2)_3R$ can be used to determine silver[132] ($\epsilon_{630} = 4.0 \times 10^4$). Pyridine and ammonia are stated not to form analogous ternary compounds with galloin. The stepwise complex formation, depending on the pH of the solution, rather complicates the choice of optimum conditions.

Since most of the above methods for determining copper and silver have approximately the same sensitivity, the choice of reagent must obviously depend on the presence of intefering ions in the specimen[133] (brief data on the effect of foreign ions are given in Table 3).

The widespread use of mixed complexes in chemistry led to a series of studies on the influence of the electronic structure of metals, the nature of ligands, and the interaction of coordinated groups on the stability, solubility, redox behaviour, and other analytical properties of these complexes. The combined application of physicochemical and physical methods to solve these problems enables laws of complex formation to be established, which stimulates the further development of analytical methods using mixed complexes.

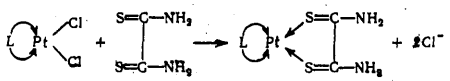
The effect of the nature of the amines on the stability of the mixed compounds has been studied with nickel(II) as example. Thus the replacement of pyridine by ammonia occurs more easily in complexes of this metal with ethylenediamine and pyridine than in those with phenanthroline and pyridine. Complexes in which the ligands are both heterocyclic or both aliphatic are more stable than mixed complexes, in which the π-bonds are regarded as destroying the symmetry of the complexes[134], which diminishes their stability. These results are consistent also with the fact[135] that complexes with 8-hydroxyquinoline or with bipyridyl are more stable than the mixed compounds with these ligands[136]. Nevertheless, the stability of the mixed compounds of cobalt(II) and zinc(II) is the same, while with copper the mixed complexes are the more stable.

Whereas the character of the bond in the copper complexes changes little on passing from bipyridyl to biquinolyl (biqu), while steric factors play the main part with iron, favourable conditions for increasing covalency of the bond are created in gold(III) complexes with biquinolyl. This is apparent, for example, in the fact that the complexes $[AuX_2bipy]^+$ are electrolytes[136], whereas $[AuX_3biqu]$ are non-electrolytes[137]. Study of complex formation between monocomplexes of nickel with phenanthroline and its derivatives on the one hand, and with diethylenediamine and nitrilotriacetic acid on the other, showed[138] that, although the rate of formation of the mixed complex is affected by the nature of the substituent in the phenanthroline, the rate-determining stage of the process is dehydration of the cation $[Ni\,phen]^{2+}$. The infrared spectra of the complexes $Fe(CN)_2(5\text{-}Xphen)_2$ (where X = Cl, NO_2, CH_3, C_6H_5) indicate that the presence of acceptor substituents strengthens the Fe–NC bond and diminishes the electron density on the nitrogen atoms in the phenanthroline molecule[139]; donor groups have the opposite effect. The degree of π-bonding of cyano-groups with the

central metal atom in this series of compounds intensifies from iron(II) through ruthenium(II) to osmium(II).[140] Increase in covalency of the metal–ligand bond and in the stability of the bivalent state in the same sequence is characteristic also of compounds[141] of the type MCl_2bipy_2, and in the sequence $Ni^{2+} < Pd^{2+} < Pt^{2+}$ of the compounds $[MX_2amin]$, where amin = phen, bipy.[42,142,143]

In most cases substitution of a ligand in platinum complexes takes place according to the equation[144,145] $k = k_1 + k_2[Y]$, where k_1 is the aquation [rate] constant and k_2 a constant depending on the nature and the three-dimensional structure of the ligands, while Y is the attacking ligand.

Kinetic study of the exchange interaction between dithio-oxamide and dichlorodiamineplatinum complexes with bipyridyl, pyridine, and ethylenediamine (L)



has shown[146] that the bipyridyl complex is the most reactive, although infrared spectroscopy indicates the most stable platinum–chlorine bond in this particular complex[147]. Obviously, the peculiarities of the metal–ligand (L) bond develop in this case only at the instant of attack on the complex by the second ligand (i.e. at the instant of the transition state).

Salt isomerism has been found among mixed complexes[148] of palladium(II) and platinum(II) of the type $[MX_2bipy]$, where $X = SCN^-$, $SeCN^-$. In aqueous solution thiocyanates in which the metal is coordinated with the nitrogen atom are the more stable, and selenocyanates in which coordination is effected between the metal and the selenium atom.

Mixed complexes with phenanthroline and bipyridyl are used for the analytical determination of scandium, rare-earth metals, and uranyl. Many eight-coordinate compounds of scandium and rare-earth metals with phenanthroline and 4,4,4-trifluoro-1-thienylbutane-1,3-dione[149], pentane-2,4-dione[150], cupferron, and 5,7-dibromo-8-hydroxyquinoline[151] are readily extracted by benzene and other solvents in acid media. These complexes are usually slightly coloured, but differences in extractability associated with the ionic radii of rare-earth metals can probably be used for extractive determinations with the application of isotopes. Several mixed complexes of europium, samarium, terbium, and dysprosium with bipyridyl and 4,4,4-trifluoro-1-thienylbutane-1,3-dione, dibenzoylmethane, etc. fluoresce, generally more strongly than do the simple complexes[152,153]. The bipyridyl molecules probably create asymmetric fields that favour f–f transitions[154]. The complex of uranyl with phenanthroline and 4,4,4-trifluoro-1-thienylbutane-1,3-dione is also extracted well by benzene, and its solutions fluoresce in long-wavelength ultraviolet radiation[155].

Highly charged cations generally form unstable complexes with ligands such as phenanthroline, which usually stabilise the lowest oxidation states—iron(II), copper(I), ruthenium(II), and titanium(III). The stabilisation of tervalent titanium, which is extremely unstable under normal conditions, enables it to be determined in the presence of titanium(IV) and a hundredfold excess of phenanthroline or bipyridyl as the tricomplex. In the presence of oxalic acid, quadrivalent titanium bound into an anionic complex is not extracted by bis-2-ethylhexyl hydrogen phosphate, but the complex of tervalent titanium is readily extracted[156] ($K_{distrib} \simeq 1000$). A metal indicator method has also been used to study the stability of phenanthroline complexes of titanium and zirconium[157,158].

Mixed complexes of highly charged cations are more stable. An alcoholic solution of bipyridyl is used with iron(III) chloride to detect phenols in paper chromatography[159]. Many complexes are known[160–163] of vanadyl with phenanthroline and anionic ligands (4,4,4-trifluoro-1-thienylbutane-1,3-dione, chromotropic acid, collidinic acid, tiron, etc.), which are of interest in connection with their extractability and their electrical conductivity.

Niobium(V) and titanium(IV) form anionic complexes which, with aliphatic and aromatic bases in weakly acid solution, yield precipitates extractable by chloroform[164]. Fairly sensitive methods have been developed for determining niobium as mixed complexes with phenanthroline and catechol or thiocyanate ions[165]. No definite relations could be detected between the pK values of the bases and the stability and extractability of the mixed adducts, since these properties are subject to the simultaneous influence of many factors (the basicity of the ligands, the polarising properties of the medium, the dipole moments of the molecules, etc.), which cannot be allowed for because of the absence of systematic investigations on the combined effect of these factors on the properties of complexes of this type.

Study of the mechanism of complex formation is considerably complicated by the tendency of multivalent cations to undergo hydrolysis in solution and form polynuclear compounds, by their enhanced affinity for oxygen. Therefore an empirical method must frequently be used to standardise the reaction conditions.

For example, the addition of phenanthroline and a solution of tin(II) chloride in 3–5 N hydrochloric acid to a solution containing molybdate ions produces a fairly intense coloration ($\epsilon_{508} = 6290$). However, although this reaction is quite sensitive, its application is extremely restricted owing to the instability of the coloration (~0.5 min). The reaction mechanism has not been elucidated, but it has been established that the most intense colour is observed with the ratio $[Mo^{VI}]/[Mo^{V}] = 1:5$ and the use of phenanthroline. Derivatives of phenanthroline cause the absorption to diminish; with terpyridine $\epsilon_{508} \simeq 880$; and bathophenanthroline forms an insoluble white precipitate. The same reaction is used as a spot test for the detection of 0.2 μg of molybdenum in 0.5 ml of solution, from the colour of a benzene extract[166,167].

Chromium(III) forms complex dinuclear compounds with phenanthroline[61,168], but the mechanism of these processes has also remained univestigated.

III. GRAVIMETRIC AND TURBIDIMETRIC METHODS

In the presence of alkali and alkaline-earth metals, ammonium, aluminium, chromium, beryllium, and scandium, the bivalent metals—cobalt, zinc, nickel, copper—and also bismuth(III) form insoluble mixed complexes with phenanthroline and thiocyanate ions, which are suitable for the gravimetric determination of these metals[169–171].

Milligram quantities of phosphorus are determined by means of the reaction of dodecamolybdophosphoric acid with phenanthroline, which yields an insoluble yellow crystalline precipitate $phen_4H_3PMo_{12}O_{40}$, of high molecular mass and therefore an ideal form for weighing[172]. Uranyl is determined by a combined method involving preliminary precipitation of a mixed complex with phenanthroline and m-aminobenzoic acid $UO_2(m\text{-}NH_2C_6H_4COO)_2phen_4$ and subsequent titration of the complex with nitrite[173]. Mixed complexes, but more soluble, are formed also by p- and o-amino-acids.

The heterometric titration of tungstophosphoric acid with phenanthroline[174] enables 0.0025 M heteropoly-acid or 0.001 M phenanthroline to be determined. The structure of the resulting complex has not been studied. Methods have been worked out also for the heterometric titration of palladium, platinum, and gold as mixed complexes with phenanthroline and thiocyanate or chloride ions[175]. A gravimetric method for determining lead is based on the formation of an insoluble precipitate by the interaction of the bulky quadruply charged anion $[Pb(S_2O_3)_3]^{4-}$ with ferroin[176]. The insolubility of the mixed complexes of scandium and vanadyl with phenanthroline and 4,4,4-trifluoro-1-thienylbutane-1,3-dione forms the basis of turbidimetric methods[149,163] for their determination in aqueous solution. Mercury(I) forms with phenanthroline the insoluble compound[177] $Hg_2(NO_3)_2$phen (solubility product 10^{-24}).

Table 7. Gravimetric methods using 1,10-phenanthroline and 2,2′-bipyridyl

Reagent	Species estimated	Quantity	Error, %	Ref.
Ferroin	$[Pb(S_2O_3)_3]^{4-}$	0.007—0.024 g	0.7	176
1,10-Phenanthroline (or 2,2′-bipyridyl) and thiocyanate	Cu^{2+}	0.0005—0.003 g	0.1—0.6	169
	Zn^{2+}	0.0005—0.003 g	0.1—0.6	169
	Ni^{2+}	0.0005—0.003 g	0.1—0.6	169
	Co^{2+}	0.0001 g	—	170
	Bi^{3+}	0.005—0.020 g	1.5	171
1,10-Phenanthroline and *m*-aminobenzoic acid	UO_2^{2+}	0.01 g	0.2	173
1,10-Phenanthroline and Na molybdate	$H_2PO_4^-$	0.001—0.01 g	—	172
1,10-Phenanthroline	tungstophosphoric acid	$2.5 \cdot 10^{-3}$ M	—	174
K_2[FePhen $(CN)_4$]	Zn^{2+}	10^{-5} M	0.4	249

The sparing solubility of certain compounds of metals with phenanthroline is utilised for their preliminary concentration, after which the metals are determined by spectrophotometric or redox methods. For example, this procedure is used to determine iron with Bromophenol Blue[146]. Since the adduct of ferroin with this dye is extracted over the narrow pH range 8.7—8.9, the iron is first precipitated as ferroin iodide. An indirect method[80] for determining lithium involves precipitation of $KLiFeIO_6$ followed by decomposition and the determination of iron with phenanthroline.

A method[178] for recovering phenanthroline (up to 86%) from ferroin complexes is based on precipitating $CuSO_4$. .phen, decomposing it with ammonia, and extracting the phenanthroline with chloroform.

A turbidimetric method[179] for determining cadmium(II) is based on the insolubility of CdI_2phen. Gravimetric methods have been proposed also for determining cadmium(II) and uranyl with 2,3′-bipyridyl.[143]

Differences in the solubility of ruthenium and osmium complexes in different oxidation states are of industrial interest[180,181]. The optical *D*- and *L*-isomers of osmium(II), ruthenium(II), and nickel(II) triphenanthrolinates not only differ in biological activity but also give compounds with antimonyl *d*-tartrate differing very markedly in solubility, a property which is used for their separation[182].

While considerably less sensitive than other methods, gravimetric methods using various complexes of phenanthroline and bipyridyl derivatives can be applied in combined procedures to enhance the selectivity of reagents. Table 7 gives examples of the most widely used gravimetric methods involving complexes with phenanthroline.

IV. ANALYTICAL METHODS BASED ON THE REDOX PROPERTIES OF METAL COMPLEXES OF 1,10-PHENANTHROLINE AND 2,2′-BIPYRIDYL

The use of solvents varying in donor power—dioxan, alcohols, oxolan, formamide, dimethylformamide, sulpholan, etc.—in preparations and in electrochemical investigations[183–186] enables several compounds of phenanthroline and its derivatives with transition metals to be obtained in different oxidation states. Besides their theoretical interest these complexes are of great practical interest as catalysts. All this leads to the development of methods for determining the different valency forms of metals and use of the redox properties of such complexes for analytical purposes. Among well known examples is the ability of phenanthroline and bipyridyl to stabilise the lower states of oxidation of metals, which has enabled titanium(III) to be determined in the presence of titanium(IV)[156] and various anions to be estimated by means of ferroin $[Fe\,phen_3]^{2+}$, whose redox potential is $E_0 = -1.06$ V, whereas

$$E_{0Fe(H_2O)_6^{2+}/Fe(H_2O)_6^{3+}} = -0.77 \text{ V}.$$

2,3,4-Substituted phenanthrolinates of iron and copper(II) exhibit a linear relation between the redox potential and the dissociation constant of the ligand[187]. Use of substituted phenanthroline complexes has enabled a series of oxidimetric indicators (Table 8) to be produced[22].

Table 8.

Indicator	E_0 in 1 M H_2SO_4, V
$[(5\text{-}NO_2phen)_3Fe]^{2+}$	1.25
$[(5\text{-}SO_4phen)_3Fe]^{2+}$	1.20
$[Fe\,phen_3]^{2+}$	1.06
$[(5\text{-}CH_3phen)_3Fe]^{2+}$	1.02
$[\{5,6\text{-}(CH_3)_2phen\}_3Fe]^{2+}$	0.97
$[\{4,7\text{-}(CH_3)_2phen\}_3Fe]^{2+}$	0.88
$[\{3,4,7,8\text{-}(CH_3)_4phen\}_3Fe]^{2+}$	0.81

The stable vanadium complex $[V\,phen_3]^{2+}$ is also used as a redox indicator[188] in the titration of iron trichloride with bivalent chromium. The corresponding bipyridyl complex is not suitable for this purpose, since its rate of dissociation depends on the acidity of the medium.

Many compounds of tervalent titanium with bipyridyl have been prepared. In view of their low electrical conductivity in non-aqueous solutions, they are assumed to have a bridged structure[189].

The rhenium compound $Na_2[Re(CN)_4bipy]$ is extremely stable in aqueous solution, although the metal is present in the uncharacteristic bivalent state. The acid $H_2[Re(CN)_4bipy]$ is very strong ($pK_2 = 2.23$); it gives

insoluble precipitates with many cations [190]—iron(II), iron(III), copper(II), silver(I), cobalt(II), nickel(II), zinc(II), cadmium(II), mercury(II), etc. Compounds of rhenium with bipyridyl in which the metal is present in its lower oxidation states have typically a dinuclear structure [191]. The number of compounds with phenanthroline and bipyridyl in which the metals—manganese, technetium, rhenium—are present in higher states of oxidation increases in this sequence, which is consistent with the known tendency for the stability of such compounds to increase in the same sequence.

Manganese can be determined by a combined method [192], involving preliminary extraction as $Mn(SCN)_2phen_2$ followed by titration of this complex in acid medium with potassium permanganate. Although the Mn^{2+} ion is very stable in acid solution as a consequence of its d^5 configuration, in the presence of phenanthroline this titrant [193,194] oxidises it in concentrated hydrochloric acid to Mn^{3+}. In ammonium acetate buffer manganese(II) is more firmly bound by ethylenediaminetetra-acetic acid than by phenanthroline, a property that is used to mask manganese [5] in the determination of nickel and cobalt.

Redox systems often catalyse reactions between two other systems if they have an intermediate redox potential. Thus the system $[Co\,bipy_3]^{2+} \rightleftharpoons [Co\,bipy_3]^{3+} + e$ ($E_0 = -0.91$ and -1.2 V in 50% alcohol and in water respectively) is a catalyst for the reduction of aromatic nitro-compounds by sodium tetrahedroborate [195]. The trisbipyridyliron complex catalyses the chain decomposition of hydrogen peroxide [46], and copper complexes act as catalysts of chemiluminescence [90].

The complex $[Fe(C_2H_5)_2bipy_2]^{3+}$ has been prepared by the interaction of iron acetylacetonate and diethylaluminium ethoxide in ether. This is a very active catalyst of the cyclopolymerisation of butadiene, acetylene, and acrylonitrile [196]. Polymerisation has been shown to involve the intermediate formation of a bond between the substrate and the iron atom.

Establishment of the mechanism of the oxidation–reduction reactions of these compounds may be of great value for elucidating the nature of their catalytic action [197]. Thus it has been shown by an isotope method that hydrogen peroxide is formed when the cation $[Cu\,bipy_2]^+$ undergoes oxidation by oxygen: water molecules play no part in the reaction [198]. This fact is very important for understanding the role of this complex cation in chemiluminescence.

In the presence of phenanthroline, cobalt(II) chloride acts as an oxygen carrier [199]. The high rate of electron transfer in complexes of metals with ligands of this type is responsible also for the high rates of redox reactions involving such complexes. This is evidently due to the small difference in size between reduced and oxidised cations, which requires no considerable reorientation of the solvate structure; furthermore, the π-character of the metal–ligand bond also facilitates electron transfer [22,200]. The rates of electron transfer in such complexes far exceed those of complex formation [46].

Study of the optical properties of the D-$[Os\,bipy_3]^{2+}$–L-$[Os\,bipy_3]^{3+}$ system showed that loss of optical activity and electron transfer take place simultaneously and at the same rate [201,202].

The large difference in potential between the Co^{2+}/Co^{3+} and Fe^{3+}/Fe^{2+} systems in the presence of phenanthroline and also the stabilisation of the cobalt(III) and iron(II) states by this ligand, so that a clear end-point is obtained (Δv = 600 mV), are exploited in the potentiometric titration of cobalt(II) with tervalent iron [203]. Cobalt can be determined in metallic nickel by this method. The ferroin that is formed is determined spectrophotometrically or by back-titration with cerium(IV). [204] It is possible also to titrate a bivalent cobalt salt directly with a quadrivalent cerium salt in the presence of ferroin as redox indicator [205]. Similar indirect methods using iron(III) chloride in the presence of phenanthroline have been employed also in determining uranium(IV), [206] niobium [207], vanadium [208], and vitamin E. [209]

A sensitive method [210] for determining traces of hydrogen peroxide is based on its reactions with ferroin or with iron bathophenanthrolinate.

The low potentials of the transition $Cu^{2+} \rightleftharpoons Cu^{+} \rightleftharpoons Cu^{0}$ are responsible for the use of complexes of copper with biquinolyl and 2,9-disubstituted phenanthrolines for the determination of oxidants and reductants (glucose, creatine, ascorbic and uric acids [211]).

Table 9. Combined methods of analysis based on photometric and redox properties of complexes with 1,10-phenanthroline

Reagent	Species determined	λ, nm	$10^{-3}\varepsilon$	pH	Sensitivity	Ref.
Ferroin	H_2O_2	510	11.1	2—9	10^{-5} M	210
Fe bathophenanthrolinate	H_2O_2	533	22.4	4	10^{-6} M	210
	Reductants				μg/100 ml	
$H[Fe(CN)_4Phen]$	quinol	462	—	2	60—300	212
	ascorbic acid				100—500	
	tannin				16—190	
	hydroxylamine				30—300	
	hydrazine				4—50	
	$Na_2S_2O_3$				130—550	
	$K_4[Fe(CN)_6]$				400—1800	
	Oxidants				μg/100 ml	
$K_2[Fe(CN)_4Phen]$	Ce^{IV}	462	—	2	60—560	212
	Cr^{VI}				10—70	
	MnO_4^-				30-120	
	IO_4^-				110 - 460	206
1,10-Phenanthroline and $FeCl_3$	U^{IV}	510	11.1	1.5—5	—	

The pair of complexes—$K_2[Fe(CN)_4phen].4H_2O$ (I) and $H[Fe(CN)_4phen].H_2O$ (II)—is most suitable for the determination of oxidising and reducing agents. The potential of this system ($E_{0,I/II}$ = 0.656 V) is almost independent of pH. The first complex has a sharp absorption maximum at 462 nm; the second hardly absorbs in this region. Many substances can be determined (Table 9) by measuring the optical density at this wavelength in solutions of complex (I) or (II) in the presence of oxidants or reductants respectively. The only limitation of this method is that the rate of redox processes may not be high enough in the determination of a particular substance [212]. The nature of a substituent has an appreciable influence on the kinetics of the oxidation of ferroins by quadrivalent cerium [46]: 5-nitroferroin is oxidised more slowly than ferroin itself by several orders of magnitude.

The rate of oxidation of ruthenium(II) by tervalent thallium is considerably lower in deuterium oxide than in water, which probably indicates that the proton plays a part in the oxidation [213].

Phenanthroline and bipyridyl accelerate the oxidation of malic and lactic acids [214] by chromic acid. It is important to study the mechanism of this reaction in order to elucidate the part played by these acids in biochemical processes.

A kinetic study of the reduction of platinum(IV) by the trisbipyridyl complex of bivalent chromium has established [215] that in aqueous solution stable platinum(IV) compounds usually contain two hydroxy-groups.

We may note in conclusion that redox processes involving complexes of metals with ligands such as phenanthroline and bipyridyl cannot be adequately characterised because of the lack of sufficient quantitative data.

V. VALUE OF 1,10-PHENANTHROLINE AND 2,2′-BIPYRIDYL DERIVATIVES IN ANALYSIS AND IN APPLIED CHEMISTRY

Analysis and technology make widespread use of the ability of 1,10-phenanthroline and 2,2′-bipyridyl to stabilise various oxidation states of metals and also of the catalytic properties of the complexes formed by these ligands with metals [3,4,90,156,188,216–218].

The use of non-aqueous solutions for inorganic preparations has yielded several complexes of metals with these ligands possessing valuable catalytic properties. Thus $[Fe(C_2H_5)_2bipy_2]^{3+}$ effectively catalyses the cyclopolymerisation of butadiene and acetylene [196]. Many complexes of Group VIII metals with ligands containing bipyridyl and imino-groups are also effective biological catalysts. The biological activity of these compounds depends on the nature of the coordinated metal, which is utilised in the production of pharmaceutical preparations [219]. The ability of the imino-hydrogen atom in such ligands to be replaced reversibly by a metal can be used for the technical purification of metals and in analysis [219].

The analytical possibilities are considerably extended by the use of phenanthroline and bipyridyl derivatives containing various donor and acceptor substituents, which have an active influence on the sensitivity and the selectivity of these reagents. The application of non-aqueous solvents and extractants also assists the controlled variation of the analytical properties of the metal complexes [44].

Metal complexes are becoming increasingly widely used in analysis as a consequence of the growing application of non-aqueous solutions in chemistry and technology. Thus dicyanodiphenanthrolineiron(II) (ferrocyphen) and the corresponding ruthenium(II) complex, because of their rapid and reversible protonation accompanied by a sharp change in spectral properties, serve as indicators for acid–base titration in non-aqueous media (acetic acid, chloroform, chlorobenzene, etc.) [220,221]. It is interesting that diethylzinc can be determined selectively (in the presence of its hydrolysis products) with phenanthroline in toluene (spectrophotometrically or thermometrically) [222].

The simultaneous application of different methods using various properties of complexes is acquiring increasing importance in analysis. In iodometric titration, for example, a complex of ruthenium with phenanthroline or a methyl derivative is used as fluorescent indicator, since at the equivalence point the red–orange fluorescence of the initial complex disappears owing to formation of an insoluble iodide complex [223].

Traces (10^{-7}%) of iron have been separated from nickel, chromium, manganese, tin by adsorption of an iron complex on silica gel, and then determined spectrophotometrically [224].

The determination of organic compounds is a separate problem in analysis, for which various methods are used. Thus microgram quantities of phenol are determined in alcoholic solution with bipyridyl and iron trichloride by paper chromatography [159]. Phenanthroline and bipyridyl derivatives themselves are most often determined by gravimetric or spectrophotometric methods using various metal cations [221].

Phthalic acid (10^{-5} M) can be determined by an indirect atomic adsorption method with preliminary extraction of the complex neocuproincopper(I) phthalate with 4-methylpentan-2-one. [225]

The brown dinuclear complex of iron(III) with phenanthroline has found practical application in radiodosimetry. Under the influence of γ-rays it decomposes with the formation of a definite quantity of ferroin proportional to the radiation dose [226].

The number of investigations involving new physical methods has grown considerably during recent years [227–230]. In several cases the use of the results of nuclear magnetic and electron spin resonance, mass spectroscopy, and quantum-chemical calculations enables the effects to be elucidated of electronic and structural factors, the nature of the solvent, the temperature, and the pressure on the analytical properties of the systems formed by metals with these ligands [231–234]. The establishment of relations between the kinetic and thermodynamic parameters of these systems and their analytical properties will make it possible to elucidate the mechanisms of many analytical reactions, to find correlations between the structure of the ligands and the state of the complex ions in solution, and to predict the physicochemical properties of novel complexes as functions of the nature of the ligands and the solvent.

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High-temperature Exciton Superconductivity : Synthetic Aspects

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The present review examines for the first time the state of chemical synthetic studies directed towards the production of compounds and systems in which, in accordance with the proposed theoretical models, we may expect to realise the exciton mechanism of superconductivity and hence an increase in the critical temperature of the superconductivity transition. The bibliography contains 197 references.

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I. INTRODUCTION

The phenomenon of superconductivity is manifested in the disappearance of the electrical resistance of a substance when it is cooled below a definite so-called critical temperature (T_c). Superconductivity was first detected in mercury 60 years ago. It has now been established that most metals and several hundred alloys are superconductors[1].

The extensive utilisation of superconductors in technology is prevented by the fact that the critical temperatures of all known superconductors lie at very low temperatures. The highest value of T_c attained is $\sim 21°$ K [for the pseudo-binary compound Nb $(Al_{0.75}Ge_{0.25})$][2]. This is the first superconductor for which T_c lies above the boiling point of liquid hydrogen ($T_h = 20.3°$ K). All other superconductors have $T_c < 21°$ K (helium temperatures). Despite the large number of published papers, little progress have been made in this field: in the last 16 years, the maximal value of T_c has been raised by only 3 deg.

Theoretical calculations show that the critical temperatures of the known types of superconductor apparently cannot exceed 40° K.[3] This is related to the characteristic features of the phonon mechanism, which is responsible for superconductivity in metals, alloys, and a number of inorganic compounds.

At the present time, an extremely attractive approach to the production of high-temperature superconductors with $T_c \geqslant 80°$ K is provided by the preparation of compounds and systems in which it might be possible to realise a fundamentally different mechanism—the exciton mechanism—of superconductivity[3]. This mechanism and the related problem of the preparation of high-temperature superconductors has been discussed extremely intensively in recent years[3–5]. The extreme scientific and technical importance of the problem has been emphasised: in its possible importance for technology, the problem of the production of high-temperature superconductors takes second place only to the problem of producing controllable thermonuclear reactors[4, 6]. The possible existence of high-temperature superconductors has not yet been strictly proved theoretically, but it has not been refuted. Exciton superconductors have not been obtained even at low temperatures. Some authors have been extremely sceptical regarding the possibility of preparing high-temperature superconductors[2, 7], but the importance of the problem has recently been leading an increasing number of research workers to take up its experimental study.

The present review will deal chiefly with the state of chemical synthetic studies directed towards the production of compounds and systems in which, in accordance with the proposed theoretical models, we might expect to realise the exciton mechanism of superconductivity.

II. MECHANISMS OF SUPERCONDUCTIVITY

1. Phonon Mechanism

In 1957, Bardeen, Cooper, and Schrieffer[8, 9] developed the microscopic theory of superconductivity (the BCS theory). According to the BCS theory, the realisation of the superconducting state requires that two basic conditions be satisfied[5]. In the first place, between the conductivity electrons close to the Fermi surface there should be produced an attractive interaction exceeding their direct Coulombic repulsion. The attraction must be sufficiently strong for the formation of combined pairs of electrons. In the second place, all the pairs of electrons must be in the same quantum-mechanical state. Superconductivity is a collective effect: the pairing of two electrons takes place only when a large number of other pairs of electrons are in the same state.

The attraction between electrons in metals arises as a consequence of the interaction of the conductivity electrons with lattice vibrations—phonons. A "free" electron, moving through the ionic metallic lattice, attracts the positively charged metal ions and hence brings about deformation of the lattice close to itself. This leads to the appearance, in the lattice, of a region of excess positive charge, produced by the higher density of ions at the point where the lattice has been deformed. Since the ions move much more slowly than electrons, this region follows at a considerable distance behind the first electron. A second electron attracts the excess of positive charge, and hence interacts indirectly with the first electron

(attracting it). In other words, the interaction of the electrons with the positively charged ions creates vibrations in the lattice (phonons). The exchange of phonons between two electrons leads to their attraction to one another.

The binding energy of the paired electrons determines the critical temperature of the superconductivity transition. Theoretical estimates of T_c show that for the phonon mechanism of superconductivity, the critical temperatures apparently cannot exceed 40° K.[3] This conclusion is confirmed experimentally: in 60 years of research on superconductivity, all metals and a large number of metallic and semiconducting alloys have been studied, but values of $T_c > 21°$ K have not been detected. It should of course be noted that these theoretical estimates are somewhat arbitrary[3], since they are based on an examination of metals with known properties. The development of the technology of high and superhigh pressures has led to the possibility of creating new superconducting phases and compounds which are not formed under "ordinary" conditions[10]. Particularly promising in this connection is the production of metallic hydrogen[11], for which calculations give values of $T_c \sim 30-300°$K. In this connection, the preparation and study of heavy metal hydrides, which can be regarded as alloys based on metallic hydrogen, are of considerable interest[12]. It may be noted that superconductivity was recently detected in polyhydrides and polydeuterides of thorium (T_c = 8.05–8.35° K)[12].

2. Exciton Mechanism

In 1964, Little suggested the possibility of an electron-electron (exciton) mechanism of superconductivity[13–16], in which the attraction between the conductivity electrons arises not as a consequence of phonon exchange, but as a consequence of exciton exchange (electronic excitation). According to some estimates, the realisation of the exciton mechanism should lead to much higher values of T_c (~300° K or more)[14,15].

In contrast to the situation for the phonon mechanism, which is universal in character, the manifestation of the exciton mechanism of superconductivity requires a definite combination of two sub-systems, one conducting, and the other dielectric with a corresponding exciton spectrum. At the present time several models, in which an exciton mechanism may be established in principle, have been proposed[3].

III. MODELS OF ONE-DIMENSIONAL EXCITON SUPERCONDUCTORS

Little examined the chief characteristic features of the exciton mechanism of superconductivity and the possibility of its realisation for the example of a model organic macromolecule (Fig. 1)[5,13–16]. This macromolecule consists of a polyene chain, which plays the role of a one-dimensional metal or semiconductor, and readily polarised substituents, which ensure effective attraction between the conductivity electrons. The "free" electron of the conducting polyene chain ("core"), moving close to one of the substituents, polarises it in such a way that a positive charge is induced at the end of the substituent nearest the conducting chain. This charge attracts another electron of the "core", so that there is effective attraction of this electron to the electron which produced the initial polarisation of the substituent. The attraction may be greater than the direct Coulombic repulsion between the conducting electrons, so that the overall interaction between the electrons of the "core" will be an attraction, and this should bring the system into the superconducting state.

The idea of an exciton mechanism of superconductivity, and Little's quasi-one-dimensional model itself, attracted considerable attention and led to lively discussion[3–5,17–19].

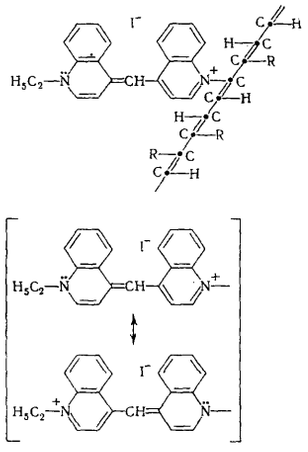


Figure 1. Little's hypothetical superconducting macromolecule.

The main objections are related to the one-dimensional nature of the model[5]. At the present time the question of which states can actually exist in the one-dimensional case with allowance for electron-electron and electron-phonon interactions is far from clear[18,20]. Thus Dzyaloshinskii and Larkin[20] have shown that, depending on the nature of the interaction between the electrons, a quasi-one-dimensional system may exist in different states: metallic, dielectric, antiferromagnetic, or superconducting.

One of the chief objections to Little's model is that in the one-dimensional system the fluctuations of electron density are large and should break down the superconducting state or at least lower T_c considerably. The fluctuations will be much smaller in fibrous structures[21], consisting of accumulations of conducting fibres in a three-dimensional non-conducting medium (the conductivity along the fibres being much greater than that in the perpendicular direction). In these structures, the advantages of the one-dimensional systems proposed by Little will be preserved, since the conducting fibre can be surrounded on all sides by molecules with appropriate electronic polarisability. The fluctuations of electron density, however, will in this instance be three-dimensional in character, and should not break down the superconducting state[4,21]. Structures of this kind are apparently more realistic for experimental realisation than Little's model.

IV. CHIEF REQUIREMENTS TO BE SATISFIED BY THE ELEMENTS OF LITTLE'S MODEL

It can be seen from Figs. 1 and 2 that Little's model consists of two interconnected parts: the quasi-one-dimensional conducting "core" and the readily polarised substituents. In principle, it is possible to use as "core" conjugated polymer chains of different types[16, 22–24]; chains of atoms[25, 26] of molecules [27–29] formed by appropriate arrangement of these units in a molecular crystal; quasi-metallic chains of iodine atoms[16]; etc. In its conducting properties, the "core" should be a metal or a semiconductor with a small gap[26]. For polymer systems, in Little's opinion, highly ordered stereoregular structures are not essential[26]. The length of the macromolecule may be of the order of 100 Å. Superconductivity in the entire specimen will possibly be produced as a consequence of the Josephson effect[26] (tunnelling of electron pairs between individual superconducting molecules through a non-superconducting phase[9]). The fundamental problem of the manifestation of superconductivity in a specimen consisting of superconducting macromolecules has not in fact been examined.

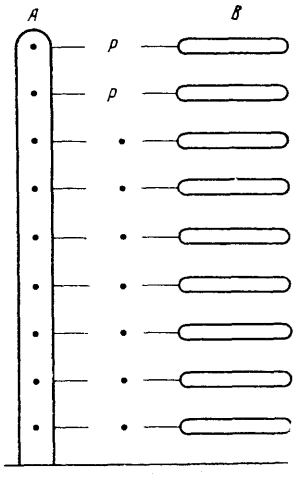


Figure 2. Model of a "one-dimensional exciton superconductor". A) Conducting "core", B) readily polarised substituents, P) connection between the elements of the model.

The substituents must satisfy certain requirements. They must be readily polarised, so that electronic excitations (excitons) which are not readily quenched can arise in them[3, 4]. This means that the substituents should have at least one low-lying excited level exhibiting a high dipole moment[17]. As substituents of this kind it is possible to use molecules (of the cyanine dye type) with a narrow absorption band in the region of ~ 1200 nm and an extinction coefficient of ~ 10^5.[18] It should, however, be noted that although dyes with intramolecular electronic transitions in the region of 1000 nm and above are known, they are generally sparingly soluble and insufficiently stable, so that it is extremely difficult to use them for preparative purposes. Other suggested possible substituents are nitroso-compounds, zwitter-ions, and dithiolene complexes of metals[30]. The latter have absorption bands in the near infrared range[31, 32]. In our opinion, it is also possible to use for the same purpose various organic and organometallic complexes of the semiconductor type, exhibiting a high polarisability (for example radical-ion salts of 7, 7, 8, 8-tetracyanoquinodimethane, and various complexes of iridium and platinum)[33, 34].

The problem of the spatial arrangement of the substituents in Little's model is important. For steric reasons, they cannot be placed on every carbon atom of the core. It is important, however, that the substituents be as close to one another as possible[16]. Moreover, the exciton system should be sufficiently close to the conducting core, since the effect of the induced charge decreases rapidly with separation[16]. There is however a limit to the distance between the polarised substituents and the conducting core, since at sufficiently small separations, exchange interaction between the conductivity electrons and the polarisation is possible, and this decreases the attraction between the conductivity electrons[16]. In Little's model, a decrease in exchange is achieved by having the lateral substituents arranged in a plane perpendicular to the core; there is then no conjugation between the core and the lateral substituents.

V. APPROACHES TO THE SYNTHESIS

At the present time there have been three general approaches to a synthesis based on Little's model. The first of these involves: 1) the creation of a one-dimensional conducting system (core); 2) the selection or synthesis of suitable readily polarised substituents; and 3) the synthetic combination of the two elements. This approach is not yet fully practical, even if only because linear conducting polymer chains are generally non-uniform and sparingly soluble. It is therefore unlikely that they could be subsequently used in a synthesis. In another approach, the aim is first to obtain a conducting chain containing relatively stable dye precursors, and then to convert these into the desired dyes. The third approach involves: 1) the synthesis of certain molecules containing readily polarised groups of substituents, and 2) the controlled polymerisation or crystallisation of these molecules.

We can now examine specific chemical approaches to the synthesis of Little's model. We shall also examine various types of quasi-one-dimensional systems which may prove to be suitable candidates for the role of the core in Little's model.

1. Polymers with a System of Conjugated Bonds

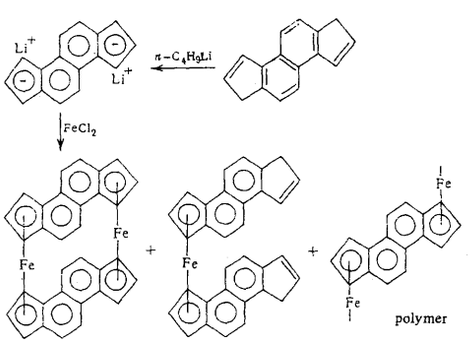
A large number of linear polymers with conjugated bonds, exhibiting semiconducting properties, have been described[35–38]. These properties are determined by two factors: the structure of the polymeric molecule (the system of conjugated π-bonds) and the supermolecular structure of the substance[37]. In most instances it is impossible to obtain polymers with a molecular weight $>$ 3000; the degree of polymerisation usually does not exceed 10.[37] The average extent of the effective intramolecular conjugation is usually less than the average degree of polymerisation, because the arrangement of the structural elements is frequently not coplanar[39]. Existing methods for the synthesis of polymers with conjugated bonds do not make it possible to obtain homogeneous

polymers with a given structure, a high molecular weight, and a narrow molecular-weight distribution. The problem of creating organic superconducting polymeric molecules probably requires fundamentally new approaches to the synthesis of polymers with conjugated bonds, which would make it possible to control closely the actual polymerisation process and to obtain conducting polymers with a rigorously defined structure.

We shall not examine in detail the various linear polymers with conjugated bonds, which formally can lay claim to the role of core in Little's model (polyacetylenes, polyynes, polyphenylenes, polyacenes). These polymers, in our opinion, are unsuitable for this purpose, since for the most part they have a high resistance ($\rho \simeq 10^5 - 10^{12}$ Ω.cm, $E \simeq 0.4-1.0$ eV)[38] and are amorphous, sparingly soluble, and somewhat unstable substances (particularly the polyacenes).

One of the most highly conducting linear polymers is polymeric sulphur nitride $(SN)_x$.[40] The polymer forms fibrous crystals with a metallic lustre, and is diamagnetic. Unfortunately, conductivity measurements have up to the present been carried out only with compressed tablets ($\rho_{0°C} \simeq 0.040-6$ Ω.cm, $E < 0.02$ eV)[40]. The study of the conducting properties of individual oriented fibres or crystals of polymeric sulphur nitride would be of considerable interest in view of its fairly high conductivity, which approaches that of metals.

Schneider[22] has discussed the advantages and disadvantages of various types of polymer with conjugated bonds, capable of laying claim to the role of core. In his opinion, alicyclic systems with a large number of possible degrees of freedom are undesirable, since in these compounds the maximal conjugation cannot be realised, because the polymer chain is insufficiently rigid. Aromatic cyclic systems exhibiting a high rigidity are suitable. Polyacenes are attracting attention in this connection, but these compounds have a low resistance to oxidation and low thermal and photochemical stability. Polyphenylenes are more stable, but in this instance loss of coplanarity is possible, and this influences the degree of conjugation. Another possibility is provided by metallocene polymers, in which polyconjugated groups are joined by metal atoms (Fig. 3). In an attempt to realise Little's model by synthesis, Schneider[22] prepared a metallocene polymer by the following scheme:



The main product was an insoluble amorphous polymer with high molecular weight. Because of its extremely low solubility, it could not be purified and was not well characterised. The disadvantages of this approach are immediately apparent: a conducting polymer core can probably be obtained in this way, but it is difficult to characterise and, which is more important, it is not clear how readily polarised substituents can be attached to it.

Another type of polymer is exemplified by polychelates, in which the metal atom is in the main polymer chain, forming a chelate unit in the conjugation chain.

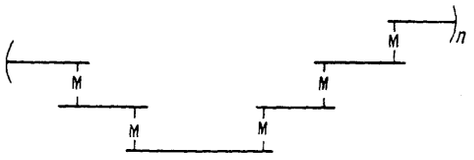


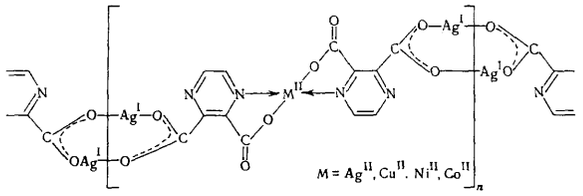
Figure 3. Polymeric metallocene: alternating planar aromatic hydrocarbon rings and metal atoms.

Dewar and Talati[41, 42] suggested that it is possible to prepare chelate polymers with a high conductivity from a suitable transition metal and an aromatic ligand capable of binding two metal atoms. To create conjugation in this system, each metal must form $d\pi - p\pi$ bonds with two neighbouring ligands, using the same d orbital. The conditions are satisfied if the ligands are coplanar and are situated in the *trans*-position relative to one another in an octahedral or square-planar complex. On this basis, the authors cited prepared polymeric chelate complexes of Cu^{II}, Ni^{II}, and Pd^{II} with 1,5-diformyl- and 1,5-diacetyl- 2,6-dihydroxynaphthalene dioximes[41, 42]. Some of the complexes obtained showed a relatively high conductivity ($\sim 10^{-4} - 10^{-5}$ Ω^{-1} cm^{-1}, $E = 0.23$ eV). The molecular weights of the polymers were low, and their degree of polymerisation did not exceed 10. Polymeric complexes of analogous type were also prepared by Kanda and Kawaguchi[43].

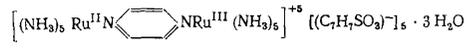
Electron transfer in these systems can probably be intensified by introducing suitable metals in different oxidation states into the chain. In particular, Bolto and Weiss[44] suggested that the higher conductivity of the Fe-containing polymer compared with the polymers of other metals obtained by the reaction of chloranil with *o*-phenylenediamine in the presence of the metal salts is due to the presence of two different oxidation states of iron in this polymer.

It may be noted that a large number of inorganic compounds containing ions of the same element in different oxidation states are now known[45, 46]. Many of these mixed-valency compounds exhibit characteristic chemical and physical properties (colour, magnetism, conductivity, and reactivity). Thus the metal–metal distances in the crystal lattices of Fe_2O_3 and Fe_3O_4 are almost the same (3 Å), but the conductivity of Fe_3O_4 (a compound with mixed valencies Fe^{II} and Fe^{III}) is greater by six orders of magnitude than that of Fe_2O_3.[47] The high conductivity (2.5×10^2 Ω^{-1} cm^{-1}) of Fe_3O_4 is attributed to rapid valency charge exchanges between iron atoms in different oxidation states[48].

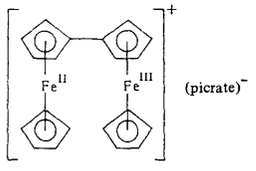
Chelate polymers containing metal ions in different oxidation states were recently prepared[49, 50]. Pyrazine-2, 3-dicarboxylic acid was used as model ligand:



Study of these polymeric complexes by static magnetic susceptibility and NMR methods at helium temperatures showed, however, that the unpaired electrons of the paramagnetic metals interact weakly with one another[51]. The probable reason is that in these complexes the conjugation chain is broken at the ends of the individual fragments. Despite this result, chelate polymers containing ligands with conjugated chains and metal ions in different oxidation states are extremely promising materials for the preparation of highly conducting linear compounds. In fact, in complexes of the type M–L–M′, where M and M′ are ions of the same element in different oxidation states, and L is a ligand with conjugated bonds, it has been possible to detect electron transfer between the metal ions. Creutz and Taube[52] made this observation for the ruthenium complex:

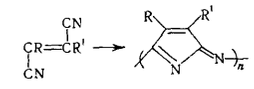


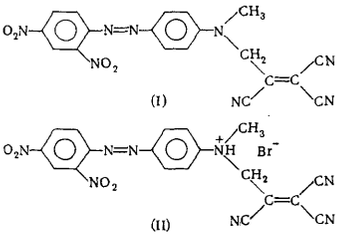
Analogous electron transfer between iron atoms in different oxidation states was observed by Kaufman and Cowan[47] in bis (ferrocinium) picrate:

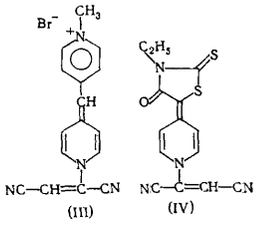


The conductivity of the latter was greater by 5–6 orders of magnitude than that of ferrocene or ferrocinium picrate. Also noteworthy is the existence of electrically conducting complexes containing linear chains of metal ions with different valencies, joined by bridging groups[53] (Cl, Br) (for example, $Pd^{II}(NH_3)_2.Cl_2Pd^{IV}(NH_3)_2Cl_4$). Some of these complexes exhibit anisotropic conductivity, the greatest conductivity being observed along the linear M^{II}–Cl–M^{IV} chains.

An interesting attempt to obtain possible superconductors was made by Liepins and coworkers[23], who prepared nitrile monomers (I–IV) containing dyes as substituents, and then carried out the polymerisation of these monomers at the nitrile groups:

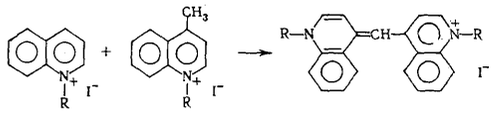




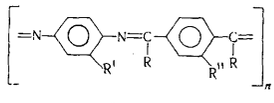


The polymers obtained had a low conductivity ($\sim 10^{-8} - 10^{-12}\ \Omega^{-1}\ cm^{-1}$), however, and superconductivity was not detected. These polymers are apparently non-uniform and disordered; their structure is not known exactly. This is the chief disadvantage of the "polymer" approach: it is impossible to obtain conjugated polymers with a strictly defined structure.

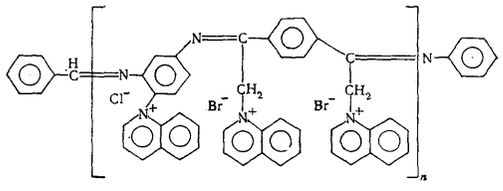
Hodgkin and Heller[24] suggested the initial preparation of a conjugated polymer chain containing relatively stable dye precursors, followed by their conversion into the desired dyes. Cyanine dyes were chosen, since they are readily obtained by the reaction of two quaternary heterocyclic bases, one of which contains an active methyl group:



Thus the first stage of the problem reduced to the preparation of polymers with a system of conjugated bonds, having as substituents quaternary heterocyclic bases, in particular quinoline bases. Polymers based on aromatic Schiff's bases were selected. The aim of the work was primarily to prepare polymers with a high molecular weight and the introduction of substituents to increase the degree of conjugation. The authors cited prepared a number of model Schiff's bases and their polymers, including a polymer containing quaternary quinoline nuclei as substituents:



(R, R′, R″ = H or dye)



In this polymer, one of the quinoline nuclei is joined directly to the aromatic ring, and this is undesirable, since exchange is then possible between the conducting system and the readily polarised system. Subsequently, Hodgkin and Heller proposed the preparation of monomers in which the quaternary quinoline nuclei are separated from the aromatic rings of the main conjugation chain by a methylene group[24]. An analogous approach has been used for the preparation of polymeric polymethine dyes[54].

In the systems examined above, the conducting core is polymeric; we shall now describe compounds in which the conducting chains are formed from atoms or molecules as a consequence of their appropriate arrangement in a molecular crystal. In our opinion, these compounds exhibit definite advantages over polymers, since they can be obtained in the form of single crystals and with a high degree of purity.

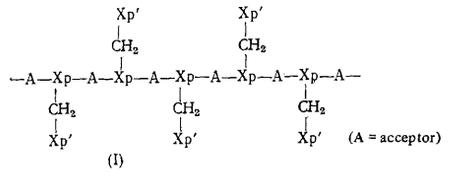
2. Charge-transfer Complexes

Charge-transfer complexes (CTC) are extremely varied[55–57], and many exhibit semiconducting properties[35, 36]. A characteristic feature of the structure of electrically

conducting CTC is the presence, in the crystal, of stacks consisting of alternating molecules of a donor and an acceptor, the distances between which are usually slightly less than the normal van der Waals' distances[35, 36, 58–61]. Thus in the ferrocene–tetracyanoethylene (TCE) complex the distance between the parallel planes of the TCE molecules and the cyclopentadienyl rings is 3.14 ± 0.1 Å[61]. The "stack" structure of the CTC should lead to anisotropy of the electrical conductivity of their single crystals, and this has been observed experimentally[62, 63]. For example, the maximal value of the conductivity ($\sigma = 10^{-5}\ \Omega^{-1}\,cm^{-1}$, $E = 0.23$ eV) in single crystals of the complex of perylene with bis [1, 2-di (trifluoromethyl) ethylene-1, 2-dithiolato]-nickel is observed along stacks consisting of alternating molecules of perylene and the complex acceptor[63].

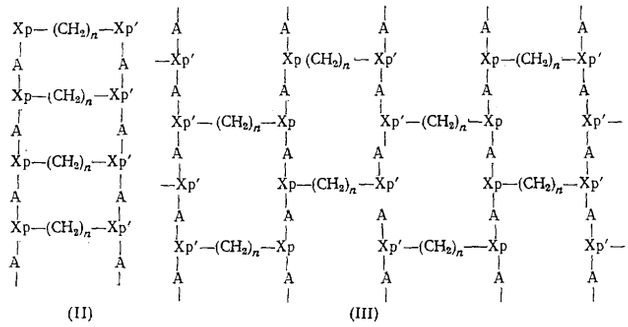
The ability of CTC to form electrically conducting stacks of alternating molecules of a donor and an acceptor in a crystal can apparently be used as a basis for the preparation of various compounds which are models of Little's molecule.

It is to be expected, for example, that in CTC containing bis-dyes with isolated chromophores as the donor component[14], one chromophoric system (Xp) will take part in the formation of the CTC, forming the electrically conducting stack in the crystal, while the other (Xp′) will act as the readily polarised substituent (structure of type I):



(I)

Since the chromophores are isolated, electron exchange between the conducting and polarised electrons in this system is unlikely; at the same time, exciton interaction is possible between two electronic systems at distances of the order of 3 Å. When bis-dyes with bridges longer than $-CH_2-$ between the chromophores are used, other types of structure (II and III) are not excluded:



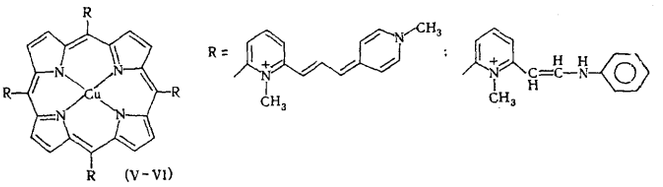
(II) (III)

For bis-dyes with one CH_2 bridge, CTC structures of types (II) and (III) are unlikely, because of the steric hindrance created by the acceptor molecules. Structure (II) is of interest, since of the two stacks connected to one another, one can be regarded as conducting, and the other as polarised. As analogous situation is observed in the double spiral of DNA. In the opinion of some authors[65, 66], the production of increased conductivity of the superconductivity type is possible in certain regions of one DNA spiral as a consequence of the excitation of electrons of another spiral.

The network structure (III) consists of conducting filaments (stacks) joined to one another; the conductivity along the filaments is greater than that in the perpendicular direction (fibrous structures)[21].

The chief difficulties are apparently associated with the preparation of highly conducting donor-acceptor stacks and the production of a structural correspondence between the components of the CTC. Very few charge-transfer complexes based on dyes have yet been described[67, 68], and almost no studies have been made of the conducting properties of this type of CTC.

The preparation of CTC using not bis-dyes but porphyrin molecules (V–VI) containing dyes as substituents[69] is of interest:



R (V-VI)

Porphyrin CTCs, in particular with nitro-compounds as acceptors, have been described[70, 71]. Complexes of etioporphyrin and its copper and nickel derivatives with 7, 7, 8, 8-tetracyanoquinodimethane (TCQM) were recently prepared[25]. The use of porphyrin molecules (V, VI) as CTC components is of particular interest, since exciton interaction between the electronic systems of the dyes and the porphyrin has apparently been detected in these complexes[69]. The position of the so-called Soret band in the absorption spectra of porphyrins usually remains unchanged when electron-accepting or electron-donating substituents are introduced into the ring at the methine bridge. In the spectra of compounds (V, VI), however, the Soret band was displaced appreciably towards longer wavelengths[69]. These shifts were attributed to exciton interaction between the electronic systems of the dye and the porphyrin ring: an electron in the ring generates an exciton in the dye, which can then interact with another electron of the ring. This should lead to a decrease or increase in the Coulombic repulsion between the electrons of the porphyrin ring, and hence to a change in the position of the energy levels in the molecule. The experimentally determined directions and magnitudes of the shifts corresponded to the calculated values[69].

3. Radical-ion Salts

Radical-ion salts represent a limiting case among CTC, where complete separation of the charges between the components of the complexes takes place even in the ground state[35, 55–57].

A characteristic feature of the crystal structure of a number of radical-ion salts is the presence, in the crystal, of stacks consisting of only radical-cations in the case of radical-cation salts[72–74] or only radical-anions in the case of radical-anion salts[75–84]. In contrast to the situation for a CTC, the stacks are formed in this instance from the same molecules (radical-ions of a given sign), the distances between which are usually slightly shorter than the normal van der Waals' distances. Strong interactions may arise within the stacks, and these are responsible, in particular, for the conductivity[85, 86], magnetic properties[86–90], and spectroscopic properties[91–95] of compounds of this type. In those instances where both components of the radical-ion salts are paramagnetic, the stacks

usually consist of alternating radical-cations and radical-anions[96–98].

Information is now available on a number of conducting radical-ion salts, based on strong π-donors: tetrathiotetracene[99], dibenzophenothiazine[100], and derivatives of N,N′-diphenyl-p-phenylenediamine[101], or based on strong π-acceptors: 7,7,8,8-tetracyanoquinodimethane (TCQM)[102], 11,11,12,12-tetracyano-2,6-naphthoquinodimethane[103], 9-dicyanomethylenepolynitrofluorenes[104], etc.[105]. Many of these compounds have a fairly high conductivity ($\sigma \geqslant 10^{-2}\ \Omega^{-1}\ cm^{-1}$, $E \leqslant 0.1$ eV). Radical-ion salts based on TCQM have attracted particular attention[85,86,106–114]. Organic salts of TCQM include compounds for which the conductivity approaches that of metals ($\sigma = 10^{2}\ \Omega^{-1}\ cm^{-1}$, $E = 0.02–0.05$ eV)[85,86].

7,7,8,8-Tetracyanoquinodimethane forms three types of conducting compound: π-complexes and simple and complex radical-ion salts[102]. TCQM forms π-complexes (charge-transfer complexes) with aromatic hydrocarbons, amines, phenols, and various other compounds. These compounds are for the most part poor conductors[102]. ($\rho = 10^{7} - 10^{10}\ \Omega.cm$), and their crystal structure is the same as that of most CTC: it consists of stacks formed by alternating molecules of a donor and an acceptor[58]. The second type of compound formed by TCQM consists of simple radical-anion salts with the general formula $K^{+}(TCQM)^{\cdot}$, where K^{+} may be a metallic, organometallic, or organic cation.

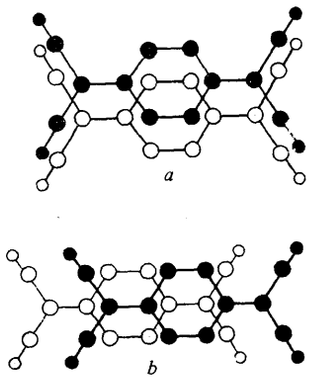


Figure 4. Two basic types of overlap between molecules of TCQM and its salts.

Most simple salts have a relatively high resistance[102] ($10^{4} - 10^{11}\ \Omega.cm$), but they also include some good conductors ($\sigma \leqslant 10^{-1}\ \Omega^{-1}\ cm^{-1}$)[85,108,113,115].

X-ray diffraction study[78,80,84] of the salt [bis (toluene) chromium]$^{+}(TCQM)^{\cdot}$ ($\rho = 3.5 \times 10^{8}\ \Omega.cm$)[110] showed that the TCQM radical-anions form stacks within which it is possible to distinguish pairs formed by TCQM molecules with an interplanar spacing equal to 3.37 Å. The distance between the pairs is 3.43 Å. The overlap of two neighbouring TCQM molecules in the stack is of type a in Fig. 4. The conductivity of this salt along the direction of the stacks is about two orders of magnitude greater than that of a compressed tablet. The TCQM spin system is here diamagnetic[88] at room temperature, indicating strong magnetic interaction in the $TCQM^{\cdot}$ chain (paired interaction).

In general, most poorly conducting simple salts of TCQM containing diamagnetic cations either are diamagnetic at room temperature or exhibit weak paramagnetism, which increases with increase in temperature (singlet-triplet behaviour)[87]. It should be noted that stacks are not always present in crystals of simple salts of TCQM[84,116]. In those instances where they are not formed, the radical-anions are still arranged in individual pairs[84,116].

The tendency for TCQM radical-anions to undergo dimerisation both in the solid state and in solution[117] is apparently a fairly general property of organic radical-ions[118]. An interesting feature is that the organometallic radical-anions of the chelate dithiolene complexes of metals also form stacks in crystals of salts with organic cations. Pairs of these radical-anions can be distinguished within the stacks[119]. The magnetic behaviour of these salts is effectively described by paired interaction[119].

The TCQM salts examined above are the poorly conducting simple salts, but, as we have already noted, some simple salts of TCQM are good conductors. Thus $(N\text{-methylphenazinium})^{+}(TCQM)^{\cdot}$ is one of the most strongly conducting organic compounds ($\sigma \simeq 10^{2}\ \Omega^{-1}\ cm^{-1}$)[86,108,113]; this salt is similar to the conducting complexes of TCQM[86].

Complex salts with the general formula $K^{+}(TCQM)^{\cdot}(TCQM)$ form the most interesting type of conducting compounds of TCQM. In addition to the TCQM radical-anion, they contain the formally neutral TCQM molecule[102]. K^{+} may be an organic or organometallic cation (metal cations, with the exception of Cs^{+}, do not form complex salts)[102]. A characteristic feature of these TCQM salts is their conductivity, which is unusually high for organic compounds ($10^{2} - 10^{3}\ \Omega^{-1}\ cm^{-1}$)[102].

The complex salts can be regarded as compounds of TCQM with mixed valency (-1 and 0), in which one electron is delocalised over two TCQM molecules $[(TCQM)_{2}^{-}]$.

The ability of the TCQM radical-anion to form complex salts is not apparently a specific property of TCQM molecules alone. Complex salts based on other radical-anions are now known[103,105].

A characteristic feature of the crystal structure of most complex salts of TCQM is the presence, in the crystal, of stacks consisting of TCQM molecules arranged one above the other, with a slight displacement[76,77,79–84]. The conductivity of the salts is generally strongly anisotropic and has a maximal value along the direction of the stacks[85,86]. The dimensions and geometry of the cation have a significant influence on the mutual arrangement of the TCQM molecules in the stack and on the distance between them, and hence on the conductivity and magnetic properties of the salts[120]. The highest conductivity ($\sigma \simeq 10 - 100\ \Omega^{-1}\ cm^{-1}$, $E = 0.025 - 0.050$ eV)[85,86,114] is shown by complex salts of TCQM, containing as cations planar aromatic heterocyclic bases with H- or CH_3- (but not $-C_2H_5$) substituents attached to the nitrogen atom[106,107]. The paramagnetic susceptibility of the highly conducting salts of TCQM depends little on temperature in the range above 30°K[86,87].

In the crystals of these salts, the distances between the TCQM molecules in the stack are equalised, and are much shorter than the normal van der Waals' distances, and the TCQM molecules overlap one another in characteristic fashion: the centre of one molecule is

situated above the centre of the double quinodimethane bond of another molecule[75, 79, 82, 84] (overlap of type *b* in Fig. 4). Thus in the complex salt (quinolinium)$^+$-(TCQM)$_2^-$, which is one of the most strongly conducting organic compounds (σ = 100 Ω^{-1} cm^{-1}, E = 0.03 eV)[85, 86, 114], the TCQM molecules are equivalent (each can be assigned a charge of $-\frac{1}{2}$), the interplanar spacings in the stack are equal (3.22 Å)[82], and the overlap is of type *b*. Analogous packing of the TCQM molecules is observed in the stacks in the complex salt [bis(toluene)chromium]$^+$(TCQM)$_2^-$ (Fig. 5)[79, 80], but the distance between the TCQM molecules is here greater than 3.29 Å, and the molecules are crystallographically non-equivalent. The conductivity of this salt is lower by almost two orders of magnitude than that of (quinolinium)$^+$(TCQM)$_2^-$ [110]. On going from the simple salt of bis(toluene) chromium to the complex salt, the interplanar spacings in the stack are equalised, and become slightly shorter; at the same time there is a change in the nature of the overlap, which becomes more effective. The conductivity increases by five orders of magnitude, and the activation energy decreases by a factor of four[110]. Packing analogous to that in (quinolinium)$^+$(TCQM)$_2^-$ is shown by the highly conducting simple salt (N-methylphenazinium)$^+$(TCQM)$^-$ [75], and also by (N, N, N′, N′-tetramethyl-*p*-phenylenediamine)$^+$ - (TCQM)$_2^-$ [77]. The conducting properties of the last compound have not yet been studied, but it may be assumed that the compound has a high conductivity.

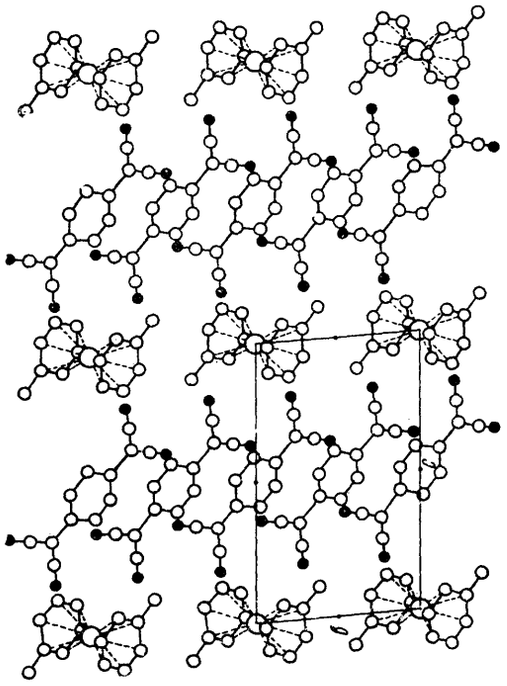


Figure 5. Projection of the structure of the complex salt [bis (toluene) chromium]$^+$ (TCQM)$_2^-$ on the [100] plane [79, 80].

Unlike the complex salts of TCQM with heterocyclic bases containing H- or CH_3-substituents attached to the nitrogen atom, complex salts of TCQM in which the cations are formed by metals, aliphatic bases, or various other non-planar systems generally exhibit a lower conductivity[85, 86], and their paramagnetism is singlet-triplet in character[86, 87, 121]. In these complex salts there is an alternation of spacings between the TCQM molecules in the stack, and these molecules in the stack form structurally repeating groups of two[84, 122, 123], three[76], or four[81, 83]; there is strong overlap within the pairs, but there may be no overlap at all between the pairs[122, 123].

The ability of the TCQM radical-anion to form quasi-one-dimensional conducting stacks in crystals can be used to prepare compounds which provide models of Little's molecule. In 1967, Khidekel' and coworkers[27, 28] and Lupinskii and coworkers[29] suggested that the radical-ion salts of TCQM with dyes may exhibit superconducting properties, since they formally satisfy the necessary conditions for the production of superconductivity: the presence of a linear conducting system (stacks of TCQM molecules) and readily polarised groups (dye cations). The compounds prepared, however, did not exhibit superconducting properties[27–29, 114], although some of them had a high conductivity ($\rho \simeq 10$ Ω. cm, $E \simeq 0.04-0.05$ eV)[27, 28, 124]. The problem of why the compounds obtained do not exhibit superconducting properties is extremely complex: here we shall restrict ourselves to an examination of some possible factors. In the first place, the dyes used[27–29, 124] are not highly polarisable ($\lambda \simeq 500-600$ nm). According to the latest calculations[16], it is necessary to have dyes with absorption bands in the region of 1200 nm. Unfortunately, complex salts of TCQM with cyanine dyes, which absorb light in the region of 700 nm and above, cannot be prepared. This is due to the fact that with increase in the length of the conjugation chain there is an increase in the basic nature of the dye, that is in its ability to undergo oxidation, so that these dyes are oxidised in their reaction with TCQM.

In contrast to Little's model, in which the bond between the conducting chain and the dye is covalent, with length ~ 1.5 Å, the bond in the compounds being considered is predominantly ionic, with length greater than 3 Å. It should however be noted that distances of the order of 3 Å may not be a significant obstacle for exciton interaction. A cardinal problem is the mechanism of conductivity in the highly conducting ($\sigma = 10^1-10^2$ Ω^{-1} cm^{-1}) radical-ion salts of TCQM. If these compounds exhibited conductivity of the metallic type, as suggested earlier[85], they would be almost ideal starting materials for the preparation of organic superconductors. Recent studies[33, 86, 113, 114] of the conducting properties of single crystals of these complexes over a wide range of temperature (4 – 300° K), however, showed that these compounds are semiconductors with a low conductivity activation energy (0.022–0.05 eV) in the range below 200 – 150° K (there is no activation energy of conductivity in the region of room temperature) (Fig. 6). In these compounds the conductivity apparently involves a jump mechanism[86, 114], and not a zone mechanism, that is there is a system of localised current carriers, the movement of which at each stage must necessarily include a thermally activated jump. It should however be noted that in the opinion of some authors[125], the simple salt (N-methylphenazinium)$^+$(TCQM)$^-$ is a "metal", which at temperatures below 200° K is gradually converted into a semiconductor. The problem of the mechanism of conductivity is fundamental, since in a system of localised current carriers the transition to the superconducting state is impossible.

On the whole, the class of compounds based on TCQM and its analogues are extremely interesting materials for

further study. There exist considerable synthetic possibilities for the preparation of new radical-ion salts. Of the greatest interest are TCQM salts containing cations with a high polarisability. Highly conducting complexes of TCQM with tetrathiotetracene (TTT) have now been prepared[126]. The TTT radical-cation introduced into the complexes has absorption bands in the near infrared range (λ = 1000–1300 nm)[99]. The compounds obtained are also of interest in connection with the fact that each of the ionic components of the complex is individually capable of forming highly conducting radical salts.

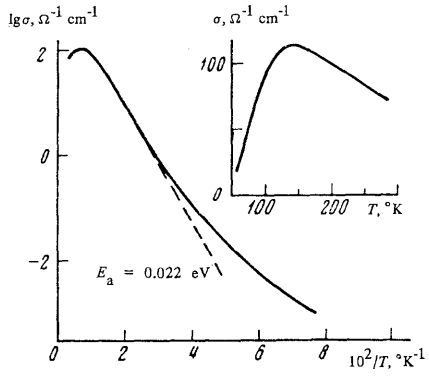


Figure 6. Temperature dependence of the conductivity of single crystals of the complex salt $(acridinium)^+ (TCQM)_2^-$ (constant current). The dependence is typical of that for highly conducting ($\sigma_{293°K} \sim 10^2\ \Omega^{-1}cm^{-1}$) TCQM salts.

An increase in the exciton interaction between the stacks of cations and the stacks of radical-anions in TCQM salts can apparently be achieved by the introduction, for example into the cation, of substituents capable of forming hydrogen bonds[127].

It is also not excluded that with the appropriate choice of cation it will be possible to prepare conducting stacks of TCQM with distances of less than 3.22 Å between the planes of the TCQM molecules (the distance of 3.20 Å is apparently not limiting: shorter intermolecular distances are known, for example 3.10 Å[72]). A decrease in the distances should lead to even stronger exchange interaction between the TCQM molecules in the stacks, and hence possibly to new effects related to the electrical and magnetic properties of these compounds (possibly the production of actual metallic conductivity). The production of an "organic metal" would be a great step forward on the road to the production of organic superconductors (this is particularly interesting in that the question of the possibility that a one-dimensional metal can exist has not yet been finally resolved). Moreover, organic compounds exhibiting a high conductivity may reveal new and previously unknown properties. In this connection, mention may be made of an unusual property detected in highly conducting radical-ion salts of TCQM: the anomalously high value of the dielectric constant (ϵ) at a frequency of 10^{10} Hz at low temperatures [for $(acridinium)^+(TCQM)_2^-$, $\epsilon_{4.2°K}$ = 800 ± 100, and for $(N\text{-methylphenazinium})^+ (TCQM)^-$, $\epsilon_{4.2°K}$ = 350 ± 50], so that these compounds can be called superdielectrics[33].

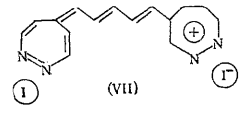
4. Poly-iodine Chains

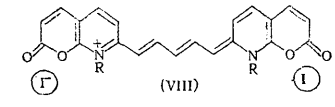
Linear chains of iodine atoms provide another possibility for the production of a conducting core[16]. It is well known that iodine can react with starch and other polysaccharides to form coloured complexes (so-called inclusion compounds)[128]. The macromolecules of amylose (a component of starch) apparently have a structure consisting of a screw or spiral with approximately six glycoside residues in each loop. Inside this loop there is a vacant cavity (or channel) with diameter 5 Å, into which the iodine is introduced. The iodine atoms are arranged linearly inside the amylose spiral with an interatomic distance of 3.1 Å[126]; all the I–I bonds are equalised[126]. In the opinion of some authors, this poly-iodine chain can be regarded as a quasi-one-dimensional metal[16, 128, 129]. The amylose–triiodide complex has been found to give an EPR signal assigned to Pauli paramagnetism, characteristic of metals[129] but these observations were subsequently not confirmed[130].

The question of the possible existence of the metallic state in poly-iodine chains is very important in connection with the problem of exciton superconductivity. To answer this question it would be necessary to study the electrical and magnetic properties of these compounds over a wide range of temperatures.

Although the metallic state has not been observed experimentally in poly-iodides, the semiconducting properties of poly-iodine compounds are familiar[131]. A complex of iodine with pyridazine, with a high conductivity ($\rho \leqslant 50\ \Omega$. cm, $E \leqslant 0.15$ eV) was recently described[132]. The study of the highly conducting ($\sigma = 3.4 \times 10^{-1}\ \Omega^{-1}\ cm^{-1}$, E = 0.07 eV) complex of iodine with N,N′-diphenyl-p-phenylenediamine showed that the electronic conductivity of this complex in the range between +50° and −50° is determined by the poly-iodine chains, in which the distances between the iodine atoms are non-equivalent: 2.99 Å and 3.77 Å[133].

Iodine can form inclusion compounds not only with polysaccharides, but also with other macromolecules: nylon, polyvinyl alcohol, and polyvinyl borate[128]. X-ray diffraction study of the polyvinyl alcohol–iodine complex showed poly-iodine chains with I–I distance equal to 3.1 Å[128]. Many relatively simple organic molecules also form complexes of this kind with iodine. Thus the compounds formed by iodine with diphenylpyrone and coumarin contain linear chains of iodine atoms with I–I distance equal to 3.06 Å[128]. For the diphenylpyrone complex it is suggested that the iodine is situated between the four phenyl groups of two pyrone molecules. These iodine atoms form a chain in the crystal[16]. A similar structure was recently proposed for the complex of bis (diphenylglyoximato) palladium(II) with iodine[134]. In Little's opinion, exciton interaction between the conductivity electrons and the polarisation electrons is possible in iodine complexes of this type, and this should lead to attraction between the conductivity electrons of the quasi-metallic poly-iodine chain, and hence to conversion of the system into the superconducting state[16]. Kagan[135] recently suggested the possibility of preparing superconductors from the starting materials (VII) and (VIII):





These compounds are extremely interesting, since they combine a high polarisability with the ability to stabilise quasimetallic poly-iodine chains.

5. Chains of Metal Ions

A number of complex compounds contain linear chains of metal ions[136–144]. Some of these compounds exhibit a high conductivity ($\sim 10^2\ \Omega^{-1}\ cm^{-1}$) along the metallic chain[34, 145–147]. A number of authors have therefore suggested that the polyene core in Little's model be replaced by a system of stacks of metal ions[25, 148–150].

Electrically conducting organometallic complexes containing chains of directly interacting metal ions can be divided into two groups: 1) complexes in which all the metal ions in the linear chain are in the same oxidation state[151–159] (Table 1), and 2) complexes containing metal ions in a linear chain in formally different oxidation states[34, 86, 145–147, 160–162].

Table 1. Electrical conductivity (σ), activation energy (E), and metal–metal distance in various complexes containing linear chains of metal ions in the same oxidation state.

Complexes	M–M distance, Å	Refs.	Conductivity, $\Omega^{-1}\ cm^{-1}$: single crystal $\sigma_{\parallel}$ (25°C)	single crystal $\sigma_{\perp}$ (25°)	powder σ_{tablet} (25°C)	$E_{\parallel}^{a}$, eV	References (conductivity data)
$Ni(DMG)_2$[b]	3.245	136	$1.01\cdot10^{-10}$	—	10^{-15}	0.57	157
$Pd(DMG)_2$[b]	3.26	136	$3.3\cdot10^{-10}$	—	10^{-15}	—	
$Pt(DMG)_2$[b]	3.23	138	10^{-12}	—	10^{-15}	—	
$Ir(CO)_2$ (acac)[c]	3.23	151, 152	10^{-5}	$2\cdot10^{-8}$ [d]	—	0.27	151, 152
$Rh(CO)_2$ (acac)[c]	3.26	141	10^{-11}	10^{-13} [e]	—	0.44	151, 152
$Rh(CO)_2$ (8-oxq)[f]	3.1	142	—	—	—	—	
$[Pt(NH_3)_4][PtCl_4]$	3.23	137	$4.54\cdot10^{-4}$	$2\cdot10^{-6}$	$2.0\cdot10^{-8}$	0.3	157
$[Pd(NH_3)_4][PtCl_4]$	3.25	139	$2.4\cdot10^{-8}$	—	—	—	157
$[Pt(NH_3)_4][PdCl_4]$	3.225	140	$5.0\cdot10^{-9}$	—	—	—	157
$K_2[PtCl_4]$	4.13	157	$4\cdot10^{-12}$	$2\cdot10^{-12}$	10^{-14}		157
$Sr[Pt(CN)_4]3H_2O$	3.09	144	—	—	—	—	—
$Be[Pt(CN)_4]2H_2O$	3.16	144	—	—	—	—	—

[a] Activation energy of the conductivity generally isotropic[152, 156]; [b] (dimethylglyoximate)$^-$; [c] (acetylacetonate)$^-$; [d] $\sigma_{\parallel} : \sigma_{\perp} > 500$; [e] $\sigma_{\parallel} : \sigma_{\perp} > 100$; [f] (8-quinolinolate)$^-$.

Complexes of the first group (with square-planar structure) (Table 1) have a characteristic crystal structure[136, 138, 171, 142, 151, 152, 157]: the molecules are arranged one above the other, forming chains of metal ions along the C axis of the crystal with a relatively short metal–metal distance (3.1–3.4 Å). In Magnus' salt $[Pt(NH_3)_4]^{2+}[PtCl_4]^{2-}$ and its analogues, the stacks consist of alternating planar anions and cations[137, 139, 140]. In salts of the $K_2[Pt(CN)_4]$ type, the stacks are made up of identical anions[144].

Complexes of this type exhibit anisotropy of their conductivity (Table 1), the conductivity being a maximum along the chain of metal ions ($\sigma_{\parallel}$). The mechanism of conductivity in Magnus' salt, and also in the dicarbonylacetylacetonato-compounds of Ir^{I} and Rh^{I} has been treated by a number of authors within the framework of the zone theories[152, 157, 159], as follows. The d_{z^2} orbitals of the metal atoms overlap and form a valency zone[139], which in square planar complexes of metals with the d^8 electronic configuration is completely filled. The valency zone is separated by a large gap (ΔE) from the conductivity zone formed by the overlapping p_z orbitals; the doubled value of the activation energy for conduction corresponds to the magnitude of the gap between the valency zone and the conductivity zone. For Magnus' salt, ΔE = 0.6 eV (4840 cm^{-1})[157]. The absorption spectrum[139, 163] of the complex along the *c* axis shows a band with a maximum of 6400 cm^{-1} (the start of the absorption lies at 4500 cm^{-1}), which is close to the magnitude of the energy gap obtained from the temperature dependence of the conductivity. Moreover, Magnus' salt shows photoconductivity with a threshold at 4500 cm^{-1}.[152]. All this provides evidence in support of the zone mechanism, but the overall problem of the mechanism of conductivity in these complexes has not been finally elucidated, and requires further study[152, 156].

It can be seen from Table 1 that the conductivity of the complexes depends markedly on two factors: the characteristic features of the electronic structure of the metal and the magnitude of the metal–metal distance in the linear conducting chain. Although the dicarbonylacetylacetonato-compounds of iridium and rhodium are isostructural[152] and have identical ligand environments, the conductivity increases by five orders of magnitude on going from the rhodium complex to the iridium complex[151, 152]. This is apparently due to the fact that the outer $5d_{z^2}$ orbitals of iridium overlap more effectively than the outer $4d_{z^2}$ orbitals of rhodium[152] (the overlap in this instance is determined by the size of the *d* orbitals). A similar increase in conductivity is observed on going from palladium complexes to platinum complexes in Magnus' salt and its analogues, and this can also be attributed to the better overlap of the $5d_{z^2}$ orbitals of Pt compared with the $4d_{z^2}$ orbitals of Pd[152, 157]. This correlation is not observed, however, for the dimethylglyoximato-complexes of Ni, Pd, and Pt^{II}; the platinum complex has a lower conductivity than the nickel complex[157]. This may be due to defects in the linear conducting chain; these should have a greater influence on the conductivity in one-dimensional systems than in two- or three-dimensional systems[157].

The influence of the magnitude of the metal–metal distance on the conducting properties is clearly shown by a study of the structure and conductivity of complexes at high pressures (up to 170 kbar)[159]. With increase in pressure to 100–120 kbar, the conductivity of Magnus' green salt and the dicarbonylacetylacetonato-compound of iridium(I) increases sharply (by about 3–5 orders of magnitude)[159]. This is due to a decrease in the distance between the metal ions (by $\sim$ 8–10%) and the corresponding increase in the interaction between them[159, 164]. The p_z and d_{z^2} levels approach one another, the magnitude of the gap decreases, and the conductivity increases. At very high pressures, changes in the metal–ligand distances, which are less sensitive to pressure, begin to have a significant influence on the electronic structure of the complexes. Decrease in these distances has the opposite influence[164]: the p_z and d_{z^2} levels move apart, the magnitude of the gap increases, so that the conductivity should decrease, as is in fact observed experimentally at pressures above 100–120 kbar.

A fairly large number of complexes in which interaction between metal ions with the same valency in a linear chain is assumed have now been prepared[165, 166]. These are chiefly square-planar d^8 complexes of iridium and rhodium with various ligands. Up to the present, however, complexes with a metal–metal distance less than 3.1 Å have not been obtained in this series of compounds.

A second group of electrically conducting complexes containing the complex-forming metal in formally different oxidation states[144] is of considerable interest (Table 2). In these compounds the linear conducting chains are made up of squares with Pt or Ir metal ions at the centres, and

the ligands (CN, CO, etc.) at the corners (Fig. 7). Crystallographically, all the metal atoms in the chain are equivalent, although formally, for example, in the $K_2[Pt(CN)_4]Br_{0.3}\cdot 2.3H_2O$ complex, approximately five out of six platinum atoms are in the bivalent state (Pt^{II}), and one is in the quadrivalent state (Pt^{IV})[144].

Table 2. Electrical conductivity (σ), activation energy (E), and metal–metal distance in various complexes containing linear chains of metal ions in formally different oxidation states.

Complexes	Oxidation state of metal	M–M distance, Å	Refs.	$\sigma_{\parallel}^{a}$ (25°), $\Omega^{-1}\,cm^{-1}$	$E_{\parallel}$, eV	Refs. (conductivity data)
$K_2[Pt(CN)_4]Cl_{0.32}\cdot 2,6H_2O$	+2.32	2.880	160	—	—	—
$K_2[Pt(CN)_4]Br_{0.3}\cdot 2,3H_2O$	+2.30	2.887	160	$(3.5\pm0.5)\cdot10^{2}$[b]	0.07[b]	34, 86, 147
$Mg[Pt(CN)_4]Cl_{0.28}\cdot 7H_2O$	+2.28	2.985	144	—	—	—
$K_{1.74}[Pt(CN)_4]\cdot 1.8H_2O$	+2.26	2.960	144	—	—	—
$Li_{1.64}[Pt(C_2O_4)_2]\cdot 6H_2O$	+2.36	2.81	144	—	—	—
$K_{1.62}[Pt(C_2O_4)_2]\cdot 2H_2O$	+2.38	2.85	144	—	—	—
$K_{1.64}[Pt(C_2O_4)_2]\cdot XH_2O$	+2.36	2.82—2.83[d]	144	0.01—42	0.07—0.086	146
$Mg_{0.82}[Pt(C_2O_4)_2]\cdot 5.3H_2O$	+2.36	2.85	144	—	—	—
$H_{1.6}[Pt(C_2O_4)_2]\cdot 2H_2O$	+2.40	2.80	144	—	—	—
$H_{1.6}[Pt(C_2O_4)_2]\cdot 3H_2O$	+2.40	2.82	144	—	—	—
$Ir(CO)_{2.9}Cl_{1.1}$[e]	+1.1	2.85	161, 167	0.2	0.064	146

[a] Measured by the four-contact method. [b] $\sigma_{\parallel} : \sigma_{\perp} \sim 200$ (measured by the two-contact method)[147, 162]. [c] $E_{\parallel} \simeq E_{\perp}$. [d] Depending on the water content. [e] $0.95[Ir(CO)_3Cl]\cdot 0.05[Ir(CO)Cl_3]$.

The distances between neighbouring metal atoms are shortened considerably (2.8–2.9 Å), due to the appreciable overlap of the d_{z^2} orbitals (strong metal–metal interaction)[144]. A zone is formed in which the upper levels are only partly filled. Examination of the electronic structure of the complexes has shown that they can be regarded as one-dimensional metals [144, 161].

It was recently shown[34, 86, 146, 147] that compounds of this class have a high conductivity ($\sim 10^2\ \Omega^{-1}cm^{-1}$) along the chain of metal ions ($\sigma_{\parallel}$) (Table 2) and have an activation energy for conduction[34, 86, 146], indicating that these compounds are semiconducting in character[34, 146]. On the other hand, Kuse and Zeller[147], who studied the optical properties of single crystals of the complex $K_2[Pt(CN)_4]Br_{0.3}\cdot 2.3H_2O$ at a frequency of the order of 10^{14} Hz, concluded that the complex is a one-dimensional metal. These authors[147] attributed the activation energy of the conductivity to defects in the linear chain.

An interesting feature is that platinum complexes with mixed valencies are similar in many respects to the highly conducting radical-ion salts of TCQM[34, 86]. They are also characterised by anomalously dielectric constants at a frequency of 10^{10} Hz at liquid helium temperatures[34, 86]. This apparently indicates that highly conducting linear chains exhibit various common features, which are due to the presence of the quasi-one-dimensional electronic system.

Yet another type of highly conducting complex with mixed valencies was discovered recently[168]. Compounds with the compositions $K[Ir_2(CO)_4Cl_4]$ (IX) and $K_2[Ir_2(CO)_4Cl_5]$ (X), in which the iridium atoms are in oxidation states 1 and 2, have been studied[169]. For polycrystalline specimens at room temperature, the conductivity has the values 1.5–5 $\Omega^{-1}cm^{-1}$ and 0.2–0.3 $\Omega^{-1}\,cm^{-1}$ for complexes (IX) and (X) respectively[168]. The activation energy of the conductivity is the same for the two compounds ($\sim$ 0.035 eV). The crystal structure of the complexes is unknown, but it may be expected that the metal ions form a linear chain. The true conductivity of these compounds in a single crystal should be much greater than that found for the polycrystalline specimens.

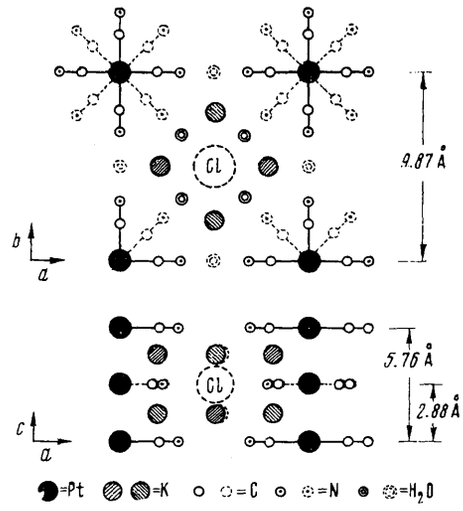


Figure 7. Crystal structure of $K_2[Pt(CN)_4]\ Cl_{0.32}\cdot 2.6H_2O$. Projections along the c and b axes.

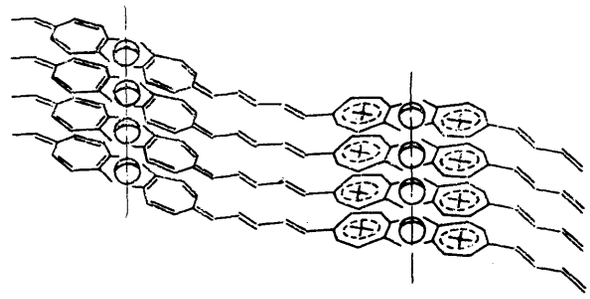


Figure 8. Suggested structure of an exciton superconductor based on metal complexes with readily polarised dyes, containing substituents of the chelate type.

The existence of highly conducting complexes containing linear metallic chains suggests that it may be possible to prepare compounds, based on metal complexes, satisfying the requirements of Little's model[149, 150].

In particular, it is proposed to prepare platinum complexes with mixed valencies, containing a chain of platinum ions and highly polarised ligands[149].

The approaches to the preparation of high-temperature superconductors based on metal complexes have been examined[135]. Various dyes containing substituents of the chelate type have been suggested as starting materials for the preparation of proposed exciton superconductors (Fig. 8). It can be seen from Fig. 8 that the metal ions form linear conducting chains, joining the highly polarised dyes. The preparation of compounds of this type will undoubtedly encounter considerable difficulties associated with solubility, purification, and crystallisation of the products. The intended products may not exhibit the required properties, because of steric complications: non-coplanarity of the dye molecules, non-coplanarity of the carbon atoms of the ring and the ligand atoms, and, which is most important, lack of correspondence between the interplanar spacings for the dyes and the dimensions of the metal atoms.

VI. MODEL OF A TWO-DIMENSIONAL EXCITON SEMICONDUCTOR

In addition to Little's model, the model of a two-dimensional exciton superconductor of the "sandwich" type[3, 4] (Fig. 9), first put forward by Ginzburgh and Kirzhnits[170], is widely known. The conductivity of the "sandwich" is due to a thin metal film ($d \simeq 10-15$ Å), and the attraction between the electrons is increased by the exchange of excitons propagated in the coatings of the "sandwich".

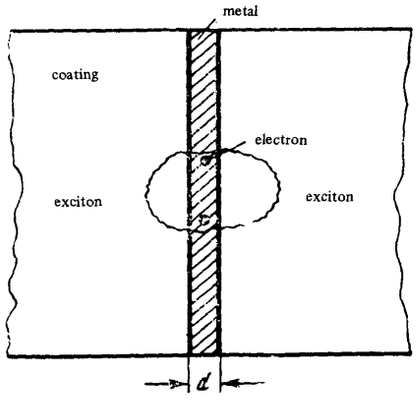


Figure 9. Model of a two-dimensional exciton superconductor of the "sandwich" type: a thin metal film between two coating layers.

The latter may consist of a dielectric, a semiconductor, or even a "poor" metal[3]. The important feature is that electronic excitations (excitons) which are not readily quenched be produced in them. The two-dimensional model of an exciton superconductor has certain advantages over Little's one-dimensional model: the fluctuations of electron density are smaller, and the Coulombic repulsion of the electrons is screened[3]. The interaction between the polarisation and conductivity electrons in the "sandwich" will possibly be weaker[3], however, than that in Little's model. To increase the interaction, the coatings must be very closely joined to the thin metal film (Fig. 9). It seems appropriate to ensure this by chemical interaction between the coating and the film[3]. The existence of chemical binding on the surface of metals has been shown, in particular, in the study of the catalytic properties of metals[171].

The possibility of obtaining high values of T_c in models of the "sandwich" type has stimulated interest in the study of the influence of organic molecules on the critical temperatures of superconducting metal films[176, 177]. The unambiguous interpretation of the changes in T_c observed in studies of this kind[172–177] is fairly complicated, since the critical temperatures of metal films depend markedly on a large number of factors (thickness, nature of the surface, particle size)[177–179]. It should be emphasised that the authors cited were dealing with fairly thick films. In addition to the selection of suitable coatings, the preparation of metal films with thicknesses of several atomic dimensions ($d \simeq 10-15$ Å) presents the main difficulty in the experimental realisation of a superconducting model of the "sandwich" type. Of considerable interest in this connection are granulated superconductors[180], in which fine metal particles are situated in a suitable dielectric matrix. In this instance there is no need to produce a continuous extremely thin metal film.

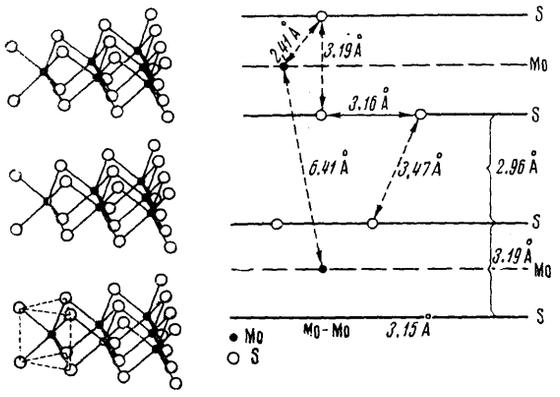


Figure 10. Structure of MoS_2.

In connection with the problem of producing a two-dimensional exciton superconductor, there has recently been an increase in interest in the study of layer compounds. A layer structure is characteristic of many dihalides and dichalcogenides of the transition metals. These include semiconductors, semimetals, metals, and superconductors[181]. Layer compounds of this type can be regarded as consisting of stacks of "sandwiches"[3]. Fig. 10 shows the structure of MoS_2, which is typical of layer dichalcogenides of the transition metals. The layer of molybdenum is situated between two layers of sulphur, and the bonding within this sandwich is strong; the Mo–S distance is equal to 2.4 Å. At the same time, the bonding between the "sandwiches" in the lattice is weak and is determined chiefly by van der Waals' forces; the distance between the sulphur atoms of neighbouring layers is 3.47 Å. The absence of continuous chemical bonding along the c axis

makes it possible to introduce into the transition metal dichalcogenides molecular or atomic layers of various substances: alkali and alkaline earth metals [182], organic bases[183–185], and amides[186]. The introduction takes place between the weakly connected "sandwiches"; the lattice expands along the c axis, with an increase in the distance between the metal layers[182–186]. Graphite, in which the bonding between the carbon layers is weak, is also capable of forming layer compounds of similar type with alkali[186, 187] and transition[188, 189] metals, acids[186], halogens[186], and metal chlorides[186, 189].

Table 3. Superconducting intercalation compounds of TaS_2 with Lewis bases[183, 185].

Bases[a]	pK_a of base	Distance between metal planes	T_c, °K
Pure TaS_2	—	6.04	0.8
$(Pyridine)_{0.5}$	5.3	11.85[b] 12.02	3.55
$(2\text{-Aminopyridine})_{0.53}$	5.2	12.09	3.25
$(2\text{-Dimethylaminopyridine})_{0.32}$		11.94	3.15
$(4\text{-Dimethylaminopyridine})_{0.34}$	9.7	12.25	2.30
$(2\text{-Ethylpyridine})_{0.29}$	6.0	9.64[b] 11.58	3.0
$(3\text{-Ethylpyridine})_{0.29}$	5.7	11.34	4.5
$(4\text{-Ethylpyridine})_{0.33}$	6.0	11.98	2.95
$(2\text{-Isopropylpyridine})_{0.25}$	5.8	11.45	3.80
$(4\text{-Isopropylpyridine})_{0.28}$	6.0	11.98	2.82
$(2\text{-Methylpyridine})_{0.34}$	6.0	11.79	2.95
$(3\text{-Methylpyridine})_{0.33}$	5.7	11.83	2.95
$(4\text{-Methylpyridine})_{0.33}$	6.1	11.76	2.70
$(2,6\text{-Dimethylpyridine})_{0.2}$	6.7	9.59	2.15
$(2,4,6\text{-Trimethylpyridine})_{0.165}$	9.6	9.67	1.95
$(2\text{-Phenylpyridine})_{0.255}$	5.1	11.92	3.15
$(4\text{-Phenylpyridine})_{0.26}$	5.2	12.31	1.6
$(2\text{-Propylpyridine})_{0.245}$	—	11.46	2.85
$(4\text{-Propylpyridine})_{0.25}$	6.1	11.85	2.75
$(Aniline)_{0.75}$	—	18.12	3.06[c]
$(Octadecylamine)_{0.58}$	—	35.02[b] 51.02	3.05[c]

[a]Number of molecules of base per molecule of TaS_2. [b]Two phases. [c]Temperature corresponding to the start of the heat capacity anomalies[185] associated with the conversion into the superconducting state.

Intercalation compounds exhibit interesting properties, particularly electrical[186, 190–195] and magnetic[186, 196, 197] properties. Thus the studies of compounds of graphite with K, Rb, and Cs has shown that these compounds (with the composition C_8M) are converted into the superconducting state at temperatures of 0.55, 0.155, and 0.135° K respectively[191, 192]. Neither the alkali metals nor graphite are superconductors. MoS_2 is a semiconductor[181], but its intercalation compounds with sodium and potassium are "metals"[193], which are converted into the superconducting state at temperatures of ~1.3° K and ~4.5° K respectively[194].

Work on the penetration of strong organic Lewis bases (of the pyridine type) into the superconducting dichalcogenides of Nb, Ta, and Pd is of considerable interest[183–185, 196]. The superconductivity did not disappear, and even a slight increase in T_c was observed (see for example Table 3). By varying the base, it is possible to alter considerably the distances between the metal layers, increasing them to 30 Å or more (Table 3). The ability to form intercalation compounds is here determined chiefly by two factors: 1) the nature of the electronic structure of the original transition metal dichalcogenides, and 2) the characteristic features of the organic Lewis bases, in particular their basic strength and dimensions[183]. Unlike the "metallic" dichalcogenides of Ta and Nb, the "semiconducting" dichalcogenides of Mo and W do not form intercalation compounds with pyridine and its derivatives[183]. TaS_2 forms stable compounds only with bases for which pK_a is greater than 4.[183]

The intercalation compounds obtained show marked anisotropy of the conducting and superconducting properties[185]. The interaction between the layers is weak, and it possibly does not have a decisive influence on the conversion into the superconducting state. There is no correlation between T_c and the magnitude of the distance between the metal planes[184, 185] (Table 3). It is not excluded that the superconductivity in these systems is a property of the two-dimensional metallic layers[187] (two-dimensional superconductivity). These materials are of considerable interest, since their study may provide an answer to the fundamental question of the possible existence of two-dimensional superconductivity. The preparation of intercalation compounds with highly polarised organic molecules appears attractive, and would be of particular interest in connection with the exciton mechanism of superconductivity, which might be produced in systems of this kind.

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The indefinite nature of the theory of the possible existence of high-temperature superconductivity of the exciton type makes it difficult to choose specific chemical routs to the preparation of possible superconducting compounds. The realisation of the models by synthesis in most instances required the development of new approaches and methods.

The results obtained up to the present, however, suggest that it may be possible to obtain compounds with structures corresponding to the existing requirements of theory. In any event, studies of this kind carried out in the field adjoining solid state physics and chemical synthesis will undoubtedly lead to interesting results.

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New Organic Ligands in Complexes of Transition Metals

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Results obtained for complexes of transition metals with unusual organic ligands—trimethylenemethane, tetramethylene-ethane, pentadienyl, and benzyl—are summarised. The chief structural and chemical features of these compounds are discussed. A list of 169 references is included.

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I. INTRODUCTION

The development of the chemistry of organic derivatives of transition metals, the vigour of which strikes the imagination, has not weakened even after twenty years have elapsed. Since the discovery of ferrocene it has become evident that any organic molecule can be in some way bound to a transition metal. Alkyl, aryl, and mixed radicals, as well as an acetylene residue, are able to combine with the metal by a simple σ-bond. Mono-, di-, and poly-enes—acyclic and cyclic, conjugated, unconjugated, and cumulated—aromatic and non-aromatic hydrocarbons and heteroatomic compounds form the most diverse π-complexes, frequently of unexpected structure. Besides such types of complex formation, which have already become usual, fresh possibilities have been revealed during recent years in this apparently exhausted field. It was demonstrated theoretically and confirmed experimentally that unstable organic species are stabilised significantly by complex formation. This provided a means of fixing and investigating such molecules as cyclobutadiene, such biradicals as trimethylenemethane and tetramethylene-ethane, and ions of the benzenonium type, which are extraordinarily difficult or quite impossible to study in the free state.

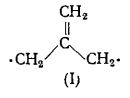
Complexes of various carbenes have been obtained. Furthermore, new possibilities have been revealed for the coordination of stable molecules. For example, an aromatic molecule is able to combine with a metal by an individual link, besides the "normal" type of bonding (as in π-arene complexes). This raises the problem of the stability of aromatic systems in the presence of transition metals.

The present Review discusses complexes with relatively new organic ligands—trimethylenemethane, tetramethylene-ethane, π-benzyl, and pentadienyl—surveying the conditions of formation as well as their physical and chemical features. Together with the π-benzyl complexes an attempt has been made to examine also the available factual information on the fragmentary coordination of aromatic molecules with metals. Work published up to December 1971 is covered.

II. π-COMPLEXES WITH TRIMETHYLENEMETHANE AND TETRAMETHYLENE-ETHANE

1. Trimethylenemethane—Structural Characteristics of the Free Biradical and of the Trimethylenemethane Ligand

The unstable reactive species trimethylenemethane (I) should theoretically have a triplet ground state (i.e. be a biradical) with a strongly delocalised system of four π-electrons[1] (delocalisation energy 1.46 β). Trimethylenemethane is important for theoretical chemistry because its central carbon atom forms a bond of maximum order ($N = 1.732$) and has the minimum free valency ($F = 0$). These are the extreme values possible for unsaturated carbon[2].

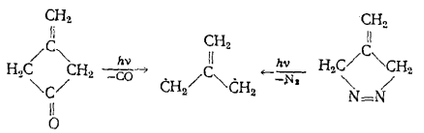


(I)

The molecule (I) has been examined as a model in various theoretical calculations[3-7] and has been assumed as an intermediate species in the thermal decomposition of 4-methylene-Δ^1-pyrazoline[8] and esters of 2-methylene-propane-1,3-diols[9], the thermal isomerisation of methylenecyclopropanes[10], the action of alkali metals on 3-halogeno-2-halogenomethylpropenes[11,12], and other reactions[13,14]. The chemical processes involving trimethylenemethane and its closest homologues and heteroanalogues have been reviewed[15].

The calculated carbon — carbon bond lengths of ~1.42 Å [6,16] and the first ionisation potential of 8.62 eV [16] have been confirmed experimentally in investigations of complexes of trimethylenemethane with the tricarbonyl-iron group[16-20]. The singlet form of trimethylenemethane is probably generated in thermal processes[16-22]. The triplet character of trimethylmethane and the equivalence of all six hydrogen atoms have been confirmed experimentally. By means of the electron spin resonance spectra Dowd observed this species among the products of

the low-temperature photolysis of 4-methylene-Δ^1-pyrazoline and 3-methylenecyclobutanone (at about −200°C):[23-25]



At this temperature the spectrum of trimethylenemethane remains for a month, but even at −150°C it changes instantly and irreversibly.

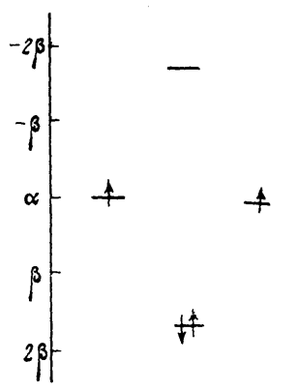


Figure 1. Energy-level diagram of the π-system of trimethylenemethane obtained by the Hückel molecular-orbital method.

Fig. 1 shows the energy levels of the π-system of trimethylenemethane.

As in other cases, this biradical is stabilised by forming a complex with a transition metal. It can reasonably be assumed that bonding occurs by interaction of the lowest filled molecular orbital with the sd_{z^2} hybrid orbital of the metal and of the doubly degenerate molecular orbital of symmetry E with the d_{xy} and d_{yz} orbitals of the metal. Probably no significant use is made of the highest molecular orbital $A_2(2)$, which is strongly antibonding, although no calculations have been made of the overlap integrals.

Existing experimental information shows that trimethylenemethane combines especially readily with the tricarbonyliron group, and its complexes are comparable with those of cyclobutadiene with respect to choice of metal and other partners. On the other hand, as will be shown below, direct transitions are possible from allylic complexes to trimethylenemethane, and *vice versa*. Thus the chemistry of compounds of this new ligand is also closely similar to that of π-allylic derivatives.

X-Ray[17,18,26,27] and electron[19,20] diffraction investigations of trimethylenemethane complexes indicate the equivalence of the bonds in the ligand, which is uniformly bound to the iron atom located exactly above the central carbon atom (Fig. 2). The $Fe-C_{(4)}$ distance is 1.93 Å both in the crystal and in the gaseous state; it is rather smaller than the distance (2.06 Å) from iron to the plane of the ligand in tricarbonyl(cyclobutadiene)iron. However, the distance from iron to the terminal carbon atoms (2.09 − 2.16 Å) is rather longer. The C − C bond lengths in coordinated trimethylenemethane are ~1.40 Å. Both methods show that $C_4H_6Fe(CO)_3$ has C_{3v} molecular symmetry with a crossed relative arrangement of the ligands (a trigonal antiprism). The central carbon atom of the trimethylenemethane system emerges to between 0.31 [18] and 0.22 [26] Å from the plane of the other three carbon atoms, on the side opposite to the metal. The phenyl-substituted complex exhibits[18] non-coplanarity of the substituent and the adjacent carbon atom (angle of deflection 59°), which should diminish the degree of $p_\pi - p_\pi$ interaction between the fragments. Possibly for this reason the introduction of a phenyl substituent into the trimethylenemethane system does not affect the positions of the absorption bands due to carbonyl groups[28].

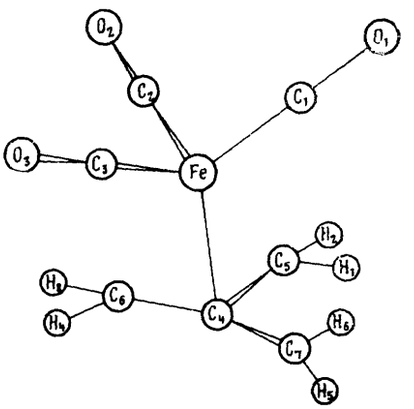


Figure 2. Structure of tricarbonyl(trimethylenemethane)-iron[20].

The nuclear magnetic resonance spectra of ^1H- and ^{13}C-tricarbonyl(trimethylenemethane)iron show that all six protons are magnetically equivalent and have a chemical shift of ~2 ppm,[29] which is in the region of absorption by the terminal protons of π-allylic and π-butadiene derivatives of iron. The spin − spin interaction constant $I_{^{13}C,H} = 162$ c/s, which is also typical of ethylenic π-complexes.

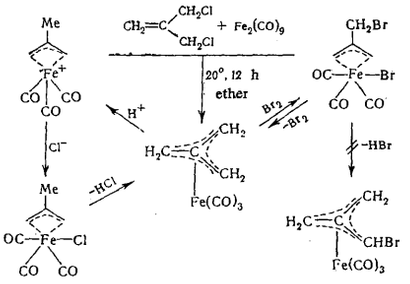
The complexes reported at the present time have in the infrared spectrum two or three carbonyl-stretching absorption bands according to the local symmetry of the carbonylmetal group $M(CO)_n$.[28-30]

2. Condition of Formation and Chemical Reactions of Trimethylenemethane Complexes

The trimethylenemethane complex was first obtained by Emerson and his coworkers[29] by the reaction of 3-chloro-2-chloromethylpropene with iron nonacarbonyl (Scheme 1). They also found that the new complex easily adds hydrogen chloride with conversion into a known allyl derivative of iron. Subsequently these workers developed this observation and found the conditions for the reverse transformation from substituted allyl complexes to trimethylenemethane derivatives[31]. This reaction occurs simply on

fractional distillation of the mixture formed by interaction between an allyl halide and iron nonacarbonyl. The first stage yields an allyl complex, which need not be isolated. The yields of trimethylenemethane derivatives obtained by this method reach 30%. Propenes and sometimes diene complexes of iron are obtained as side-products.

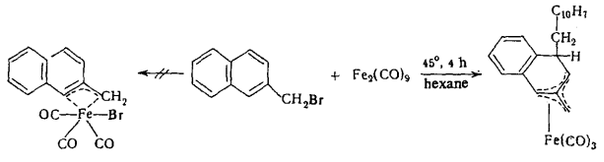
Scheme 1



Scheme 1 shows that tricarbonyl(trimethylenemethane)-iron is able also to add bromine reversibly. The resulting tricarbonyl(2-bromomethylallyl)iron bromide could be degraded in two ways—elimination of hydrogen bromide with formation of a complex containing a brominated trimethylenemethane ligand or elimination of bromine to return to the original complex—the latter of which actually occurs.

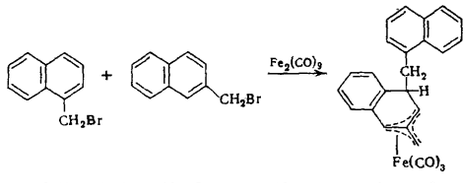
The salt $NaFe(CO)_4$ can be used instead of iron nonacarbonyl in the above reaction[30], which somewhat increases the yield of the complex.

Unusual conditions for obtaining the trimethylenemethane system have been found by Nesmeyanov and his coworkers[26,27,32,33]. This system is formed from 2-bromomethylnaphthalene, which under the conditions indicated adds the naphthylmethylene radical to one of the double bonds of the substituted ring:



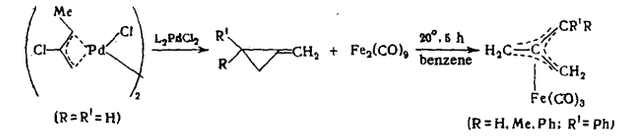
The extremely mild conditions of this transformation and the accompanying breakdown of the aromatic structure of the naphthalene molecule indicate that the nature of the trimethylenemethane ligand conforms well to the electronic and steric requirements of iron and that it is preferred to allyl.

The naphth-1-ylmethyl radical is able to take part in this reaction only as an adduct:



Formation of the trimethylenemethane system from 1-methylnaphthalene would have entailed breakdown of the aromatic structure of the second ring as well, and obviously this cannot be compensated even by formation of a bond with a metal. Several extremely stable compounds have been obtained under the above conditions, including the first complex of trimethylenemethane containing halogen in the ligand (Table 1). X-Ray diffraction examination of one of these compounds[26,27] enabled the structure of the complexes obtained to be understood correctly, and showed that the chief molecular parameters are general both for higher analogues and for the simplest complexes of trimethylenemethane.

Ring-substituted methylenecyclopropanes undergo ring-opening in the presence of iron carbonyl, and then coordinate with the iron as the trimethylenemethane form[28]:



The yields of the complexes reach 40 — 60%, but in the absence of substituents in the three-membered ring only tricarbonyl(butadiene)iron is obtained.

Table 1. Summary of data on complexes with trimethylenemethane and tetramethylene-ethane*.

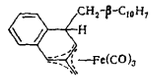
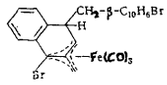
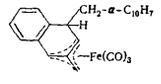
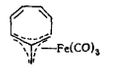
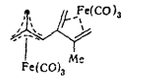
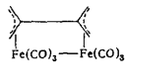
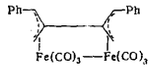
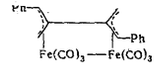
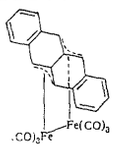
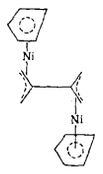
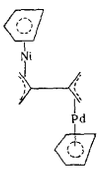
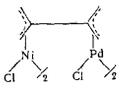
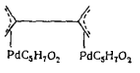
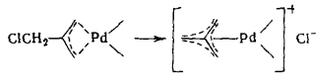
Metal	Compound	Colour	M.p., °C	Ref.
Cr	$(CH_2)_3CCr(CO)_4$	yellow	83	30
Mo	$(CH_2)_3CMo(CO)_4$	yellow	50	30
Fe	$(CH_2)_3CFe(CO)_3$	light yellow	33	19, 28–31
	$PhCH(CH_2)_2CFe(CO)_3$	—	64	18, 28, 31
	$MePhC(CH_2)_2CFe(CO)_3$	—	liquid	28
	$Ph_2C(CH_2)_2CFe(CO)_3$	—	158	28
		light yellow	142	33
		light yellow	175	33
		light yellow	100	26, 27, 33
		—	41	57
		lemon yellow	118	47
		red	89	43, 45
		dark red	131	48
		orange-red	190	48

Table 1 (contd.)

Metal	Compound	Colour	M.p., °C	Ref.
		orange	214	56
Ni		dark red	cryst.	54
Ni, Pd		red	160 (decomp.)	54
		brown	cryst.	54
Pd		white	cryst.	55

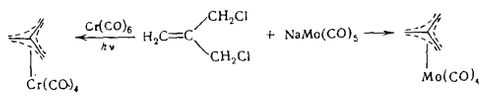
*In this and subsequent tables a dash in a column means that the characteristic is not given in the original paper.

A quite different result—formation of complexes with a π-allylic ligand—ensues when methylenecyclopropane undergoes ring-opening under the influence of palladium salts[34]. On the other hand, n.m.r. data confirm the formation of a fairly stable intermediate species, probably of the trimethylenemethane type, in the solvolysis of 2-chloromethylallyl complexes of palladium[35]:



Thus methylenecyclopropane obviously behaves differently in the presence of iron and of palladium, perhaps because of different states of the trimethylenemethane formed when the ring is opened.

A few complexes of trimethylenemethane with Group VI metals have been prepared[30]:



The conditions of their formation are clear from the above scheme. However, the yields are very low.

The list of compounds containing a trimethylenemethane ligand is not yet very long (Table 1). It is evident that they are all quite stable substances, melting at fairly high temperatures (often with decomposition). The thermal stability of the complexes is greatly improved by the introduction of phenyl substituents. The naphthalene derivatives melt without decomposition at 140 – 170°C, and are the most stable. The stability of the trimethylenemethane complexes also governs their behaviour in the mass spectrometer. All the compounds studied give molecular ions[29,33]. These compounds are considerably less stable in solution than in the solid state.

As with most other types of π-complexes, structural investigations predominate over chemical studies in this case. This is obviously due to the relative inaccessibility of these compounds and their comparative instability in solution. Besides the above addition of bromine and hydrogen chloride, the oxidation of tricarbonyl(trimethylenemethane)iron by a quadrivalent cerium salt has been studied[30], which obviously results in the liberation of trimethylenemethane. In any case, an adduct of the latter compound is obtained in the presence of tetracyanoethylene. Thus complexes of trimethylenemethane may give the free compound. Photochemical degradation of the complex with iron tricarbonyl[36] yields a complicated mixture, containing the dimer *p*-xylene, paracyclophane, and several other products. In the presence of cyclopentene 2-methylenepentalene is formed by addition of the biradical to an isolated double bond. This type of addition has hitherto been regarded as impossible.

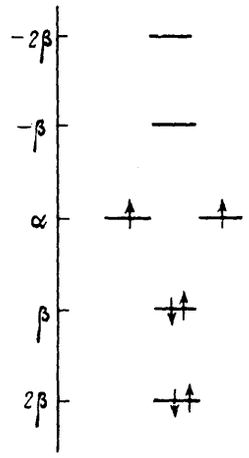
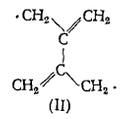


Figure 3. Energy-level diagram of the π-system of tetramethylene-ethane obtained by the Hückel molecular-orbital method.

3. Tetramethylene-ethane and its Complexes

Like trimethylenemethane, tetramethylene-ethane (II)



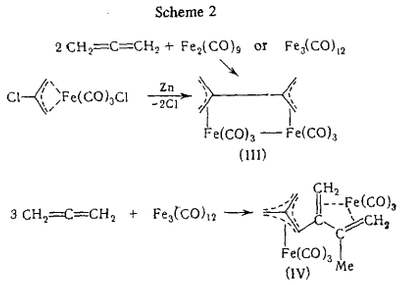
(II)

also has the triplet ground state predicted theoretically[1] and confirmed experimentally[37]. Calculation by the Hückel method gives the energy-level diagram for the π-system[38] illustrated in Fig. 3. The delocalisation energy is respectively ~2 β and 0.35 β relative to the system with two double bonds and two localised electrons and relative to two allyl radicals. This species is comparatively

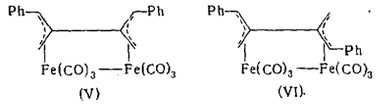
unstable in the free state, its lifetime at −196°C being about 20 min[37]. The formation of tetramethylene-ethane was suggested in a study of the degenerate thermal rearrangement of 1,2-dimethylenecyclobutane[39,40]. Tetramethylene-ethane is the central fragment of the stable bisgalvinoxyl biradical[41]. Electron spin resonance spectra have been obtained for the radical anion[42] and the radical cation[41] of tetramethylene-ethane.

The hypothesis that tetramethylene-ethane is an intermediate species in the di- and tri-merisation of allene was confirmed by isolation of the binuclear complexes (III) [43-46] and (IV) [47] in the reaction of allene with iron carbonyl (Scheme 2). The latter contains a ligand which is a kind of combination of trimethylenemethane and a tetramethylene-ethane derivative. The complex (III) can be obtained independently by eliminating the two halogen atoms from tricarbonyl-2-chloroallyliron chloride.

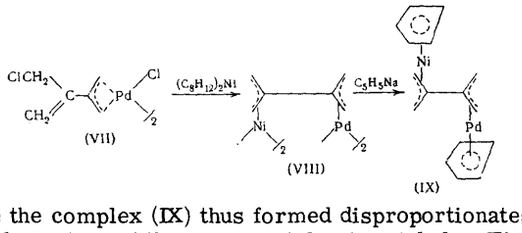
Scheme 2



Analogous complexes (V) and (VI) are obtained from phenylallene and iron carbonyl[48]. They are assumed to be isomeric, with different relative orientations of the substituents in the allyl groups

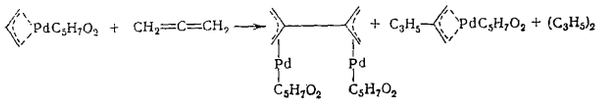


In the presence of palladium salts allene yields the complex (VII) together with other products[49-53]. If the reaction is conducted in a polar medium with excess of allene present, (VII) is the main product. The substituent in the allyl ligand of (VII) is itself a potential ligand. In fact it combines with an additional metal atom to give the tetramethylene-ethane complex (VIII),[54] which is capable of the usual reactions, e.g. rupture of the bridge by the action of C_5H_5Na:

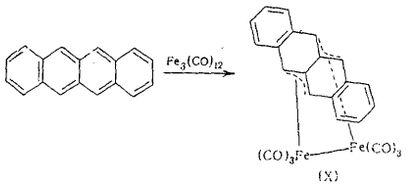


In time the complex (IX) thus formed disproportionates to give a derivative of the same metal, viz. nickel. The transoid configuration of (IX) was supported by preliminary X-ray diffraction results[54].

An analogue of (VIII) can be obtained by the incorporation of allene into an existing π-allylic type of palladium complex with an acetylacetonate group[55]:



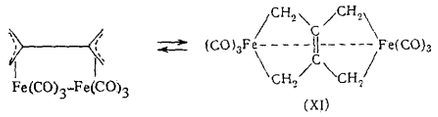
Finally, another surprising change to a tetramethylene-ethane derivative was discovered by Fischer et al.[56] When tetracene was heated with $Fe_3(CO)_{12}$, an extraordinarily stable compound containing two tricarbonyliron groups was formed, whose infrared and n.m.r. spectra suggested the structure (X):



Most complexes of tetramethylene-ethane are solids having surprising thermal stability. Their mass spectra contain peaks due to molecular ions[48].

Unfortunately there is as yet no single completed X-ray structural investigation of tetramethylene-ethane complexes. All the latter that have been described are binuclear compounds. This ligand probably cannot be coordinated other than with a few metal atoms without strong disruption of coplanarity and delocalisation. It would therefore be interesting to ascertain in what measure its fragments bound to different metal atoms are autonomous and whether the system preserves its planarity. Existing spectroscopic data seem to indicate that the two allylic systems are autonomous when the molecule contains two different metals. The n.m.r. spectrum of (IX) contains two sets of signals for each moiety of the molecule, as if each were independent. The *syn*- and *anti*-protons of each allylic group and the protons of the cyclopentadienyl rings absorb at different magnetic field intensities, and all signals for the nickel-containing moiety are displaced to a higher range than those for the moiety containing palladium.

The complex (III) possesses the properties of flexible systems. This is apparent in the variation of its spectrum with temperature and is explained[45] by a valency-tautomeric equilibrium of the type



The introduction of phenyl substituents raises the barrier to the dynamic process, and the spectra of (V) and (VI) show no dependence on temperature[47]. A third product was isolated in the preparation of complexes (V) and (VI); its spectral properties were compatible with structure (XI), and it underwent thermal rearrangement to (VI). Thus the possibility of valency tautomerism seems to be confirmed by isolation of a second equilibrium form. However, the molecules are quite complicated, and X-ray examination is very necessary to confirm these conclusions.

Complex (X) would also be interesting to examine by X-ray diffraction. The central portion of this molecule is quite analogous to (III), and the changes in the n.m.r. spectrum of tetracene after coordination are consistent with such a form of bonding. Further confirmation of the structure can be found in the infrared spectra, for carbonyl-containing complexes of iron have entirely analogous spectra in the region of carbonyl-stretching vibrations[48,56]. These workers give three bands for each of the two tricarbonyliron groups in (III), (V), and (VI)—e.g. at 2062, 2030, 1996, 1983, 1970, and 1940 cm^{-1} in the case of

(VI)—but the lower three bands are significantly less intense and are poorly resolved. The spectrum of complex (X) contains five bands, situated close to the first five bands enumerated above.

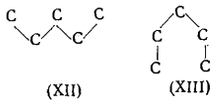
Chemical investigations of tetramethylene-ethane complexes are very sparse. These complexes are decomposed by bromine with the formation of 1,4-dibromo-2,3-bisbromomethylbut-2-ene[44,45].

III. COMPLEXES OF PENTADIENYL

A considerable number of complexes have now been prepared in which the transition metal is bound to an open chain of five unsaturated carbon atoms. These complexes can be combined under the name *pentadienyl*, although they can probably include structural variants. They have been known for about a decade, but only recently have they begun to be investigated systematically as a class.

1. Structural Characteristics of the Cation and Anion of Pentadienyl and the Pentadienyl Ligand

The simplest acyclic pentadienyl species (anion, cation, and radical) probably have the form (XII) of carbon skeleton. However, when this system is part of a ring of moderate size, (XIII) will be the more probable form of skeleton.

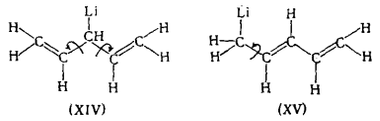


(XII) (XIII)

Fig. 4 shows the energy-level diagram of the π-system of pentadienyl. The delocalisation energy for all three species is 1.464 β.[2]

Acyclic dienyl cations are quite stable in strongly acid media, and can be observed directly by nuclear magnetic resonance[58]. At room temperature the molecules studied do not exhibit the properties of flexible systems.

The temperature variation of the n.m.r. spectrum of the pentadienyl anion (as the lithium derivative) indicates that the terminal protons become equivalent above 30°C.[59] This was explained by equilibrium between ionic and covalent forms of the lithium derivative, for which the two structures



(XIV) (XV)

were possible. Rotation about the single bond leads to interchange of the positions of the terminal protons. The spectral data show that rotation occurs more readily about inner than outer carbon — carbon bonds.

The chemical shifts for the various protons in the pentadienyl system suggest that the charge is distributed non-uniformly along the chain. In the anion the greatest electron density is concentrated on the odd carbon atoms, as predicted by theory[2,60].

Pentadienyl anions are capable of [1, 6] sigmatropic rearrangements, which conform to the Woodward — Hoffman rules. These changes are slowed down by the presence of alkyl substituents[61].

The large majority of pentadienyl complexes known at the present time contain the ligand in the form (XIII), which is probably geometrically more favourable for coordination with a single metal atom. The only example in which form (XII) of pentadienyl is fixed on a transition metal is a bis-π-allylic type of nickel complex containing two metal atoms (see below).

Benzenonium ions are stabilised as pentadienyl complexes of transition metals. Almost all known complexes with this ligand in either form (around 150 individuals have been isolated) are quite stable compounds. The following experimental results enable the relative stability of the pentadienyl cation and its complexes to be compared with other cations and complexes of other ligands.

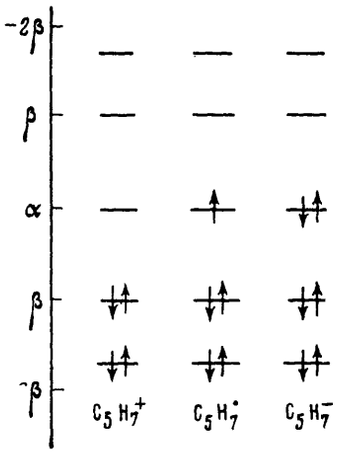
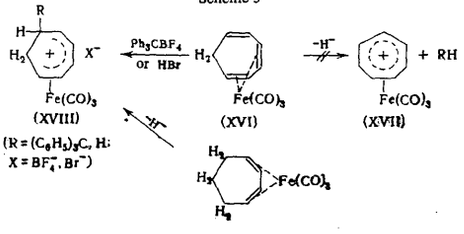


Figure 4. Energy-level diagram of the π-system of pentadienyl obtained by the Hückel molecular-orbital method.

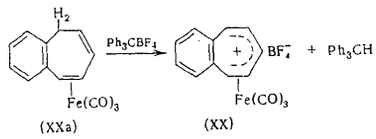
The cycloheptatriene derivative of iron (XVI) has one free double bond and an α-methylene group relative to the coordinated system (Scheme 3). However, it exhibits no tendency to change into the tropylium complex (XVII) under conditions such that a hydride ion is usually easily detached from an α-methylene group[62-64].

Scheme 3



Scheme 3 shows that (XVI) develops acceptor properties towards electophiles: it adds a proton or a triphenylmethyl cation to give the complex (XVIII) with a pentadienyl ligand[62,65]. On the other hand, the same cation and its analogue (XX) [66] can be obtained in the usual way—by

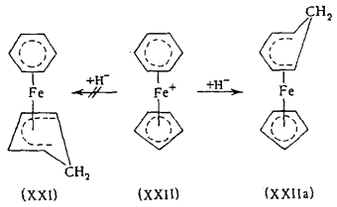
detachment of a hydride ion from (XIX) and (XXa) respectively:



(XXa) (XX)

The n.m.r. spectrum of (XX) shows that the positive charge is mainly localised in the pentadienyl system, and is not transmitted to the benzene ring: i.e. the coordinated form (XX) is probably correct, not the alternative benzotropylium form. The formation of pentadienyl complexes by the detachment of a hydride or a hydroxide[67] ion under the influence of a triphenylmethyl salt suggests that the resulting complex cations are more stable (less electrophilic) than the triphenylmethyl cation, whereas the reverse order of stability is observed for the free species. Thus the diminution in electrophilicity on passing from $C_6H_7^+$ to $C_6H_7Fe(CO)_3^+$ obviously results from the transmission of electron density from the tricarbonylmethyl group. The pentadienyl cation is preferable to the tropylium cation for iron, primarily because it is a four-electron donor. A vast quantity of experimental results confirm the special affinity of iron for organic ligands, contributing four electrons to the common electron shell. Furthermore, the pentadienyl cation contains a vacant non-bonding π-orbital, more capable than the antibonding orbital of the tropylium cation of taking part in dative bonding[2,38].

Having studied the reduction of a large number of arene-ironcyclopentadienyl (XXII) salts by hydride reductants[68-70], and also the addition to them of other nucleophilic reagents[71], Pauson and his coworkers showed convincingly that only the six-membered ligand changes, and of the two possible products (XXI) and (XXIIa) only the latter is obtained:



(XXI) (XXII) (XXIIa)

This probably applies also to the cathodic reduction of these salts[72].

Similarly, six- and seven-membered (but not four-membered) ligands add a hydride ion on the reduction of $C_7H_8CoC_4R_4^+$ and $C_6H_6CoC_4R_4^+$:[73,74] in other words, the pentadienyl ligand is preferred to the butadiene and allyl ligand respectively.

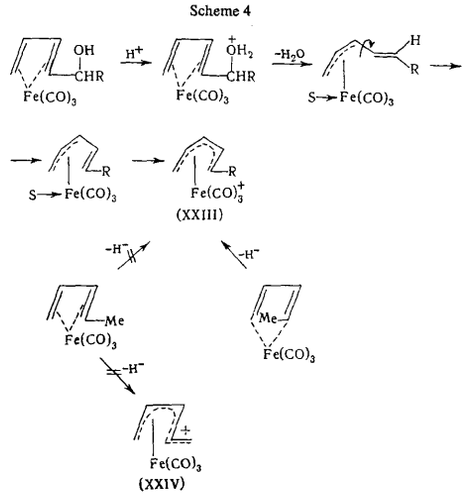
The structural problems discussed below are being studied in connection with pentadienyl complexes.

(*a*) *cis*- and *trans*-Forms of the ligand

When this ligand does not form part of a ring, it may be expected (in view of the geometry of the initial diene complexes) that *cis*- and *trans*-forms—(XXIII) and (XXIV)—will be produced. Pentadienyl derivatives of this kind are usually obtained from substituted diene complexes by the detachment of an anion from a side-chain[75-77] (Scheme 4).

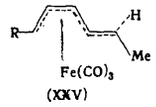
An immense quantity of experimental results shows that, independently of the initial configuration, either the *cis*-form of the complex is obtained or else the reaction does not take place at all (Scheme 4). The mechanism of inversion[76] is clear from the scheme, and involves complexes of allylic type at intermediate stages.

Scheme 4



(XXIII) (XXIV)

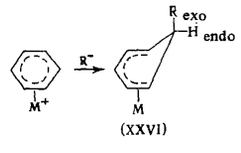
Recent spectral[78-80] and chemical[81,82] results indicate that a complex can be obtained with a ligand in the *trans*-configuration. The temperature dependence of the n.m.r. spectrum of acid solutions of tricarbonyl(2-methylhepta-3,5-dien-2-ol)iron and analogous compounds[79] shows that the *trans*-isomer exists in solution at temperatures below −50°C. The activation energy of conversion to the *cis*-form is ~13 kcal mole^{-1}. Preservation of the *trans*-configuration of the cation at low temperatures was attributed[80] to vertical stabilisation of the ionic centre by iron:



(XXV)

(*b*) Steric configuration of the ligand

The next problem, whose solution required considerable effort, involved the stereochemistry of the addition of nucleophiles (and thus the three-dimensional structure of the complexes) in the conversion of arene-containing complex cations into neutral cyclohexadienyl complexes:



(XXVI)

Spectral[68-71] and X-ray diffraction[83] results suggest that nucleophilic species (H^-, $C_6H_5^-$, CH_3^-) add on the outside of the ligand, and the ingoing substituent occupies an *exo*-position. This destroys the coplanarity of the ring, and the cyclohexadienyl ligands assume the form (XXVI). It

will be shown below that seven-membered rings buckle similarly.

The infrared spectra of cyclohexadienyl complexes have one extremely interesting feature: they contain an unusually low carbon — hydrogen stretching band (2730 — 2830 cm^{-1}),[71] which seems to be independent of the nature of the metal. Recent structural investigations show that this band is undoubtedly due to the *exo*-proton of the methylene group. The lowering of the frequency is no doubt caused by complex formation, since the free hydrocarbons do not exhibit anomalous bands. Because of the geometry of cyclohexadienyl complexes, illustrated above and to be discussed in detail later, it can hardly be supposed that the methylene *exo*-proton will interact through a tetrahedral carbon atom with the electron system of the metal[84]. Hyperconjugation is assumed to be possible in a molecule of the complex[71], as a consequence of overlapping of the σ-bonding *exo*-hydrogen — carbon orbital and neighbouring π-orbitals of the ligand directly involved in combining with the metal. The displacement of electrons from the carbon — hydrogen bond resulting from such interaction lowers the frequency of the stretching vibration. Experimental and calculated results[71] show that this phenomenon is general in character for ligands formed from five- and seven-membered rings. The cation $C_6H_7Fe(CO)_3^+$ is an exception to the general rule: its spectrum contains no anomalous band[84,85].

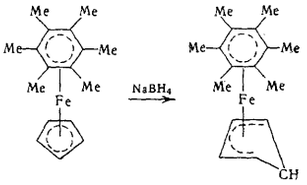
The nuclear magnetic resonance data[71] indicate that atoms and groups (hydrogen, methyl, phenyl) occupying an *exo*-position with respect to the metal are more strongly shielded than the corresponding *endo*-substituents: i.e. *endo*- and *exo*-substituents differ in their n.m.r. spectra. Protons and substituents situated in the coordinated moiety also exhibit non-equivalence, and the order of variation in shielding is opposite to that for benzenonium ions[68]. We shall return to this fact later.

Stereospecificity of addition to a complex cation may be due to spatial requirements or to an unsymmetrical distribution of electron density with respect to the plane of the ligand in the initial molecule, involving concentration on the *endo*-side, i.e. closer to the metal. Hence the approach of an anion will occur preferentially on the *exo*-side.

The direction of attack by a nucleophile on substituted arene complexes is determined to some extent by the nature of the substituents. A hydride ion usually goes towards an unsubstituted carbon atom in the benzene ring; when the number of such sites is small ($n < 3$), addition occurs also at a substituted carbon atom. When R = CH_3 ($n = 1 - 3$), the reaction involves almost exclusively unsaturated positions with a random probability distribution[68]. If methoxyl is the substituent, reduction occurs predominantly *meta* thereto. In the reduction of $CH_3OC_6H_5FeC_5H_5$, for example, the relative reactivities of the positions were found to be $o:m:p = 1:5:3$.[69] This may be due to a decrease in the local positive charge at the *ortho* and *para* positions owing to $p_\pi - p_\pi$ overlapping of the π-system of the ring and a lone pair on the oxygen.

When the nuclear substituent is a halogen, reduction occurs mainly in the *ortho* position, probably owing to the electron-accepting inductive effect of the halogen.

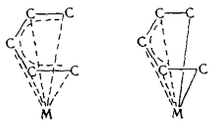
The addition of anions—$C_6H_5^-$, CH_3^-,[71,86] etc.—is in general controlled by the same rules. For example, the reaction between $CH_3C_6H_5FeC_5H_5^+$ and methyl-lithium involves unsubstituted carbon atoms, and *ortho*, *meta*, and *para* positions are equally reactive[71]. Only when all hydrogen atoms of the six-membered ring have been substituted does the behaviour of the cation on reduction change significantly: hexamethylbenzeneironcyclopentadienyl is reduced by adding a hydride ion to the five-membered ring[71]:



Similarly, only $C_6H_7MnC_6(CH_3)_6$ is obtained[87] of the two possible reduction products of the cation $C_6H_6MnC_6(CH_3)_6^+$.

(c) Possible forms of bonding with metal

The distribution of electron density in the pentadienyl ligand is of great interest. It is important to elucidate whether there is equivalent bonding of all five carbon atoms with the metal as in (XXVII) or whether the terminal carbon atoms are bound to the metal by σ-bonds, while the central portion acts as a π-allyl (structure XXVIII):



(XXVII) (XXVIII)

The latter suggestion is based on the above mentioned non-coplanarity of the rings, which may be due to rehybridisation at the terminal atoms of the coordinated portion.

Several structural investigations have been made on pentadienyl complexes, but all on derivatives in which this ligand forms part of a ring. Thus more or less complete investigations have been made on $C_6H_7Mn(CO)_3$,[84] azulene — $Mn_2(CO)_6$,[89,90] $(CH_3)_6C_6HRe(CO)_3$,[83] two azulene complexes of molybdenum carbonyl[91-93], and μ-(ππ-1, 6-dihydroheptalenebistricarbonylmolybdenum)[94]. Figs. 5 and 6 illustrate results obtained by Churchill and his coworkers for $C_6H_7Mn(CO)_3$ and guaiazulene — $Mo_2(CO)_6$ [84,93] derivatives of cyclohexadienyl and cycloheptadienyl respectively. The main features of these structures are easily seen. As already noted, the tetrahedral carbon atom in the cyclohexadienyl complexes is deflected substantially (by 42°) from the plane formed by the remaining five carbon atoms, which are arranged almost in the same plane and form an open pentagon. In $(CH_3)_6C_6HRe(CO)_3$ the deflection of the methylene group reaches 50°.[83] The deflection in structures analogous to Fig. 6 is considerably smaller (10 — 18°), which may be due to the presence of a direct metal — metal bond or of a second carbonylmetal group[90].

Like the other examples studied, the structures also show some lack of symmetry in the situation of the metal relative to the pentadienyl fragment, although the carbon — carbon bonds remain the same (~1.40 Å). As in the π-allylic complexes the metal is located closest to the central carbon atom of the system; the distances to the terminal and intermediate carbon atoms are 0.2 — 0.07 Å longer. The distances to the remaining carbon atoms, not directly bound to the metal, increase still more (difference up to 0.5 Å). The carbon — carbon distances are rather shorter in the pentadienyl than in the cyclopentadienyl ligand, while the mean metal — carbon distances are longer. This indicates stronger bonding of the metal

to the cyclopentadienyl than to the pentadienyl ligand, or else stronger bonding inside the pentadienyl than in the cyclopentadienyl fragment.

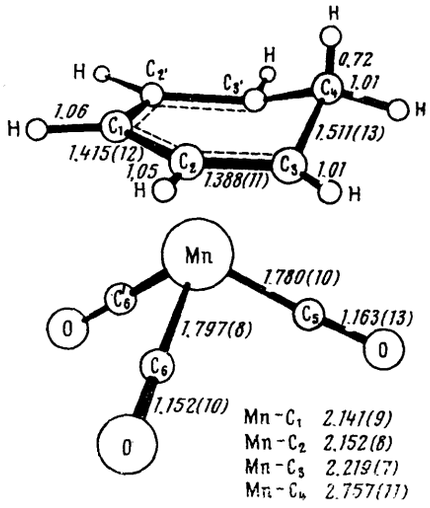


Figure 5. Structure of tricarbonyl(cyclohexadienyl)manganese[84].

The $C_{(4)}-C_{(3)}$ and $C_{(4)}-C_{(3')}$ bonds (Fig. 5) and the $C_{(4)}-C_{(10)}$ and $C_{(8)}-C_{(9)}$ bonds (Fig. 6) are elongated, and approach values corresponding $C_{sp^2}-C_{sp^3}$ bonds.

The angles in the cyclopentadienyl ring are rather smaller than the ideal angles for sp^2- and sp^3-hybridised carbon. All the azulene complexes studied exhibit shortening of the $C_{(9)}-C_{(10)}$ distances and lengthening of the $C_{(4)}-C_{(10)}$ and $C_{(8)}-C_{(9)}$ distances relative to uncoordinated hydrocarbon, which indicates that the two systems of π-electrons in the coordinated hydrocarbon are largely autonomous.

Thus the metal – carbon distances show rather weaker bonding between the terminal atoms of the pentadienyl system and the metal than with the central part of this ligand. However, no significant alternation in carbon – carbon bond lengths is observed, so that there are at present no grounds for discussing the limiting structure (XXVIII). On the other hand, the n.m.r. spectra also indicate an unsymmetrical distribution of electron density along this fragment. In fact, signals from protons attached to the terminal carbon atoms are observed at significantly higher fields than those from protons attached to the central carbon atoms of the system. With $C_6H_7MnC_6(CH_3)_6$, for example, we have the values (in ppm)—*exo*-H 1.05, *endo*-H and $H_{(3,3')}$ 1.4, $H_{(2,2')}$ 3.5, and $H_{(1)}$ 5.0 [87]—and a similar rule is observed for cycloheptadienyl complexes[88]. Furthermore, the chemical shifts depend on the nature of the solvent[95], which may be due to differences in electron density at different positions in the ligand. A final conclusion on the degree of asymmetry of bonding will obviously become possible after further structural investigations by both spectral and X-ray methods.

The first indications have been obtained that certain π-cyclohexadienyl systems are flexible[86]. However, the nature of the dynamic processes underlying such behaviour remains obscure.

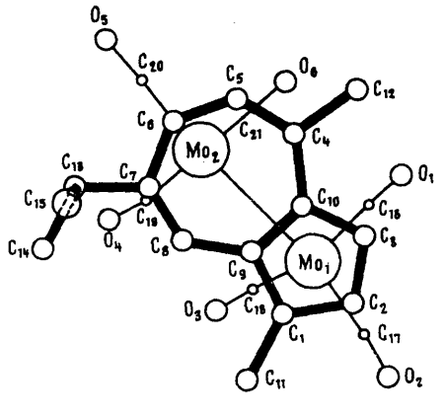


Figure 6. Structure of complex of guaiazulene with $Mo_2(CO)_6$.[93]

2. Methods of Preparation of Pentadienyl Complexes

We shall mention some general methods of preparation of pentadienyl complexes, in addition to those considered above.

1. Direct reaction between alkali-metal pentadienyl derivatives and salts of transition metals. Such a reaction has as yet been accomplished only in a single example with chromium(II) chloride[96]:

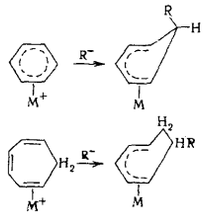
$$CrCl_2 + 2\,NaC_5H_7 \xrightarrow[-30^\circ C]{\text{oxolan}} Cr(C_5H_7)_2 + 2\,NaCl$$

The product of this reaction is very interesting. It exists as a monomer containing two pentadienyl groups and one chromium atom, is thermally stable (m.p. 122°C), and has two unpaired electrons. It resembles triallylchromium in its chemical properties: it is extremely sensitive to air, easily eliminates pentadiene on appropriate treatment, and is converted by carbon monoxide into $(C_5H_7)_2Cr(CO)_2$. No structural data are available, so that nothing definite can yet be said on the character of the bond.

Another complex of acyclic pentadienyl $(C_5H_7)_2Ni_2$ is now known, which contains two pentadienyl ligands and two metal atoms. This complex is obtained from nickel dichloride and penta-1,4-diene in the presence of triethylaluminium[97]. X-Ray results[98] show a di-π-allylic type of structure (Fig. 7). The nickel acquires its characteristic sixteen-electron shell, while the ligand is fixed in its most usual form.

2. Reduction of complex cations containing six- and seven-membered cyclic ligands. This method is used considerably more frequently[68-70,73,87,95,99-103]. Since the behaviour of the hydride anion and other nucleophilic agents is similar[71,86,88,99,104-107], this method may have even wider

application. It is suitable for the preparation of neutral cyclohexadienyl and cycloheptadienyl derivatives of all those metals for which the initial arene and cycloheptatriene complexes have been obtained:



(R = H, Alk, Ar, AlkO, CN, NR_2)

The reductants most often used are sodium tetrahydroborate, lithium tetrahydroaluminate, and sodium in liquid ammonia[102].

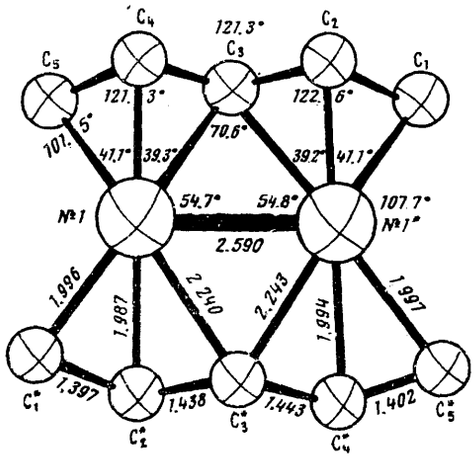


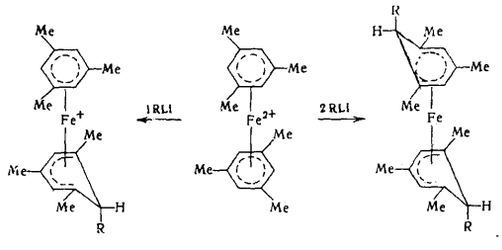
Figure 7. Structure of bispentadienyldinickel[98].

Several aspects of these reactions have been considered above. It should be added that the electronic requirements of the central atom also affect the course of these reactions. For example, reduction of the dibenzenerhenium and dibenzenetechnetium cations leads to the formation of benzenecyclohexadienyl complexes, whereas the doubly charged dibenzeneruthenium cation is reduced predominantly to benzeneruthenium cyclohexadiene[99]:

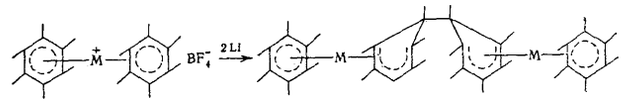
$$(C_6H_6)_2Ru^{2+} + NaBH_4 \rightarrow \underset{\text{main product}}{(C_6H_7)_2Ru} + C_6H_6RuC_6H_8$$

$$(C_6H_6)_2Re^{1+} + NaBH_4 \rightarrow C_6H_8ReC_6H_7$$

The corresponding cation of iron adds one or two moles of RLi:[86]

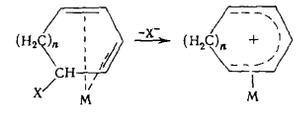


In isolated cases reduction is accomplished by an alkali metal alone, e.g. by fusing with metallic lithium[102,103]:



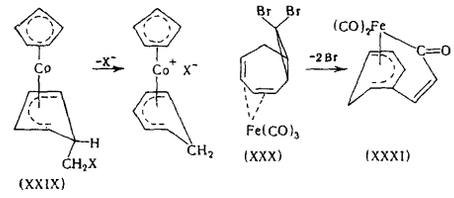
Reduction has been used to obtain all the known types of cyclohexadienyl complexes—$C_6H_7M(CO)_n$, $C_6H_7MC_5H_5$, $C_6H_7MC_6H_8$, $(C_6H_7)_2M$, $C_6H_7MC_4H_4$—in which this ligand is accompanied by carbonyl, cyclopentadienyl, arene, and cyclobutadiene ligands.

3. Detachment of an anion from an α-methylene of a diene complex. This method is suitable for obtaining cyclohexadienyl, cycloheptadienyl, and acyclic pentadienyl derivatives as cations[62,64,66,67,75–77,81,108]. The outgoing species may be hydride, methoxide, hydroxide, or halide ions. In contrast to the previous reactions, complex salts are formed here:



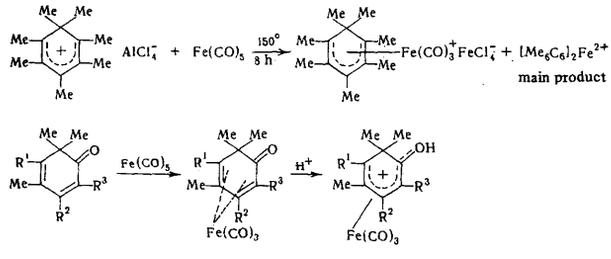
($n = 0, 1, 2$)

This method yields predominantly pentadienylcarbonyl complexes of general formula $C_5H_5[CH_2]_nM(CO)^+_m$. A proton or a triphenylmethyl cation may act as acceptor for the outgoing anions. These reactions are sometimes accompanied by enlargement[67,109–111] or contraction[112–114] of the rings. Solvolysis of (XXIX), for example, yields a cyclohexadienylcyclopentadienylcobalt cation (a cobalticinium analogue), and (XXXI) is obtained from (XXX) by treatment with methyl-lithium:

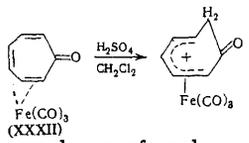


4. Addition of cations to free ethylenic group in polyalkene complexes. Salts of complex cations are obtained by the protonation of uncharged derivatives of diene type containing at least one free unsaturated group in the ligand[65,115–121] or by adding to it a carbonium ion[62,122], which has also received brief mention above. For example, complexes of bezenonium ions can be obtained by direct reaction with iron carbonyl[122] or by protonating a cyclohexadienone complex[120] (Scheme 5).

Scheme 5

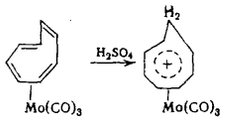


The cycloheptatrienone derivative (XXXII) is protonated at a carbon – carbon double bond[121]:

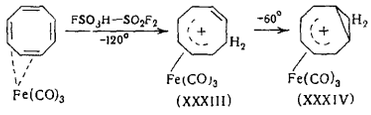


(XXXIII)

The protonation of complexes of cyclo-octatriene[119] and cyclo-octatetraene[115,117] provides a vivid example of how the electronic requirements of the metal determine the form of coordination of the organic cation. Thus the protonation of $C_8H_8Mo(CO)_3$ yields a homotropylium complex in which all six π-electrons of the ligand are involved in bonds with the metal[123]:



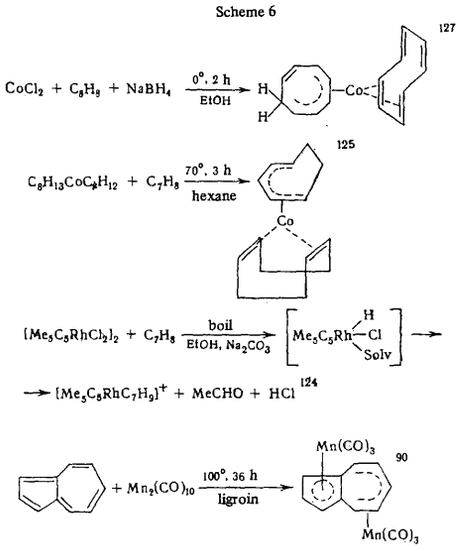
The protonation of $C_8H_8Fe(CO)_3$ [115,117] ultimately gives tricarbonyl(bicyclo[5,1,0]octadienyl)iron (XXXIV), where only four π-electrons of the pentadienyl system are used in bonding with iron:



The formation of (XXXIV) results[117] from electrocyclic ring closure in the coordinated organic ligand (XXXIII). The form of bonding in (XXXIII) is analogous to that for tricarbonyl(tropylium)iron[116].

5. Other modes of formation of pentadienyl derivatives. Pentadienyl complexes are formed in several cases of reaction between unsubstituted alkenes and various metal derivatives[90,124-128]. A few examples of such reactions are given below. The conversion of an alkene to a pentadienyl ligand requires the presence of metal hydrides, which may be introduced either directly[127] or may be formed in an intermediate stage of the process[124], the source of hydrogen being either the solvent or one of the components[125] (Scheme 6).

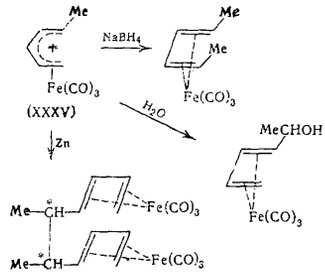
Scheme 6



3. Chemical Properties of Pentadienyl Complexes

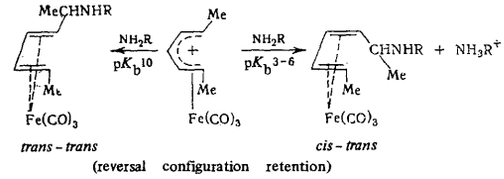
The above experimental results show that in most cases the formation of pentadienyl complexes is reversible. This does not mean that an equilibrium is established between the initial compound and the reaction product. Under suitable conditions, however, it is possible to effect the reverse change, and convert pentadienyl complexes into the diene complexes. Thus the complex (XXXV), obtained by detachment of a hydride ion from the corresponding diene complex, can be reduced by sodium tetrahydroborate[77], and also undergoes other reactions yielding diene complexes[129] (Scheme 7).

Scheme 7



The mechanisms of the reactions of complex cations with nucleophilic agents show specific differences, while conforming to general rules. For example, the reaction between $C_6H_7Ru(CO)_3^+$ and the methoxide anion begins with attack by the latter on the carbonyl group[130]. An intermediate product—the complex $C_6H_7Ru(CO)_2COOCH_3$ containing an ester group—was isolated, which gives the substituted diene complex $CH_3OC_6H_7Ru(CO)_3$ by rearrangement. However, in none of the other cases studied, those already mentioned and reported in Refs. 131 – 134, when the attacking species were nucleophiles from the hydride ion to amines, alkoxides, and β-diketones, was it possible to find any indication that the reaction followed a similar course or that the metal atom was attacked initially.

If the pentadienyl ligand does not form part of a ring, interaction with a nucleophile may involve either reversal or partial retention of the geometrical configuration of the ligand[76,77,133,134]. The geometrical form of the products obtained with amines depends on the basicity of the amine[133,134]:



(reversal configuration retention)

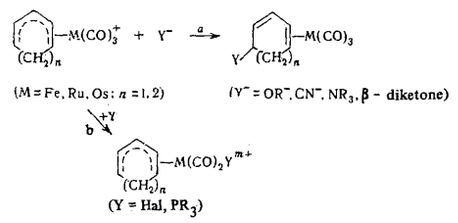
Addition is much slower when ligands possessing weaker acceptor properties than the carbonyl group are introduced into the initial complex. Increasing the size of the ring acts in the same direction: seven-membered ligands react more slowly than do six-membered ligands. The following sequence of reactivity has been found towards pentane-2,4-dione[132]:

$$C_6H_7Os(CO)_3^+ \simeq C_6H_7Fe(CO)_3^+ > C_6H_7Fe(CO)_2PPh_3^+ > C_7H_9Fe(CO)_3^+ > MeOC_6H_6Fe(CO)_3^+ \gg C_7H_9Fe(CO)_2I > C_7H_9Fe(CO)_2CN, MeOC_6H_6Fe(CO)_2I.$$

Neither β-diketones nor amines react with the later members of the series. All this suggests the probable occurrence of direct attack on the pentadienyl ligand.

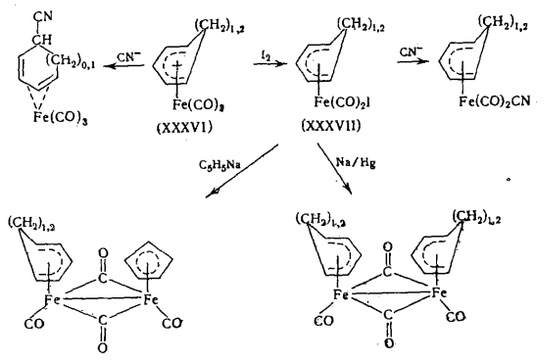
These reaction yield neutral complexes of substituted dienes (Scheme 8*a*). However, there are examples of a quite different course of reaction with nucleophiles, involving retention of the pentadienyl ligand and substitution of other groups present in the molecule (*b*).

Scheme 8

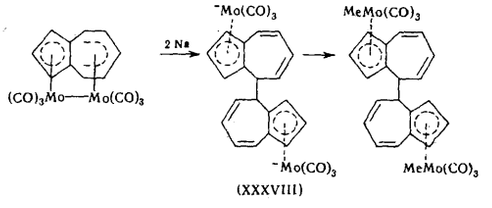


Pauson et al.[135] investigated the chemical reactions of pentadienyl derivatives of iron and compared them with those of aromatic cyclopentadienyl complexes. The cations (XXXVI: $n = 1, 2$) react with iodine, with replacement of one of the carbonyl groups and conversion into neutral compounds (XXXVII) having very similar properties to $C_5H_5Fe(CO)_2I$. These iodides are in fact able to exchange covalently bound halogen, and dimerise when reduced with sodium amalgam or treated with C_5H_5Na. This sometimes involves substitution of the pentadienyl ligand (Scheme 9). However, the above addition reactions with conversion into a diene system—quite uncharacteristic of aromatic complexes—are more characteristic of pentadienyl complexes. This constitutes their main chemical difference.

Scheme 9



When discussing the X-ray results we noted that a metal is more weakly bound to a pentadienyl than to a cyclopentadienyl ligand. This is suggested also by the formation of (XXXVIII) when the azulene complex of molybdenum carbonyl is treated with metallic sodium[93,136]:



Rupture of the molybdenum — molybdenum bond is accompanied also by cleavage of the bond with the seven-membered ring, i.e. with pentadienyl, whereas the bond with the five-membered ring is preserved.

Table 2 lists data for the complexes of pentadienyl with various metals.

Table 2. Summary of data on complexes with pentadienyl.

Metal	Compound	Colour	M.p., °C	Ref.
Ti	$C_7H_9TiC_7H_7$	green	cryst.	128
V	$C_6H_7V(CO)_4$	dark brown	66 (decomp.)	101
	1,2[a]-$Me_2C_6H_6V(CO)_4$	ditto	68 (decomp.)	101
	1,4[a]-$Me_2C_6H_6V(CO)_4$	»	—	101
	1,2,3[a]-$Me_3C_6H_4V(CO)_4$	»	73 (decomp.)	101
	1,2,4[a]-$Me_3C_6H_4V(CO)_4$	»	—	101
	1,3,5[a]-$Me_3C_6H_4V(CO)_4$	»	94 (decomp.)	101
	1,2,3,4[a]-$Me_3C_6H_5V(CO)_4$	»	75	101
	1,2,4,5[a]-$Me_4C_6H_5V(CO)_4$	»	74	101
	$Me_6C_6HV(CO)_4$	»	—	101
Cr	$(C_7H_7)_2Cr$	green	122	96
	$[(C_7H_7)_2CrCO]_2$	—	—	96
Mo	azulene-$Mo_2(CO)_6$	—	—	91, 92, 136, 137
	guaiazulene —$Mo_2(CO)_6$	—	—	91, 92
	1,6-dihydroheptalene —$Mo_2(CO)_6$	red	cryst.	94
Mn	$C_6H_7MnC_6Me_6$	red	120 (decomp.)	84
	$C_6H_7Mn(CO)_3$	yellow	78 (decomp.)	84, 95, 138
	X—$MeC_6H_6Mn(CO)_3$ (A)	yellow	liquid	95
	X—$MeC_6H_6Mn(CO)_3$ (B)	yellow–orange	liquid	95
	exo-4[c]-$MeC_6H_6Mn(CO)_3$	orange	90	104
	exo-4[c]-$CNC_6H_6Mn(CO)_3$	—	—	105
	$PhC_6H_6Mn(CO)_3$	yellow	112 (decomp.)	85, 99
	1,3,5[a]-$Me_3C_6H_4Mn(CO)_3$	orange	liquid	95
	4[b]-CN—1,3,5-$Me_3C_6H_3Mn(CO)_3$	white	109 (decomp.)	105
	exo-4[c]-CN—$Me_4C_6H_2Mn(CO)_3$	—	—	105
	$C_7H_9Mn(CO)_3$	yellow	66	88, 106
	4[b]-$MeC_7H_8Mn(CO)_3$	light yellow	39	88, 106
	4[b]-$PhC_7H_8Mn(CO)_3$	—	75	106
	4[b]-$CNC_7H_8Mn(CO)_3$	—	58	106
	4[b]-$MeOC_7H_8Mn(CO)_3$	yellow	61	88, 106
	4[b]-$EtOC_7H_8Mn(CO)_3$	—	40	106
	4[b]-t-$BuOC_7H_8Mn(CO)_3$	—	142	106
	4′, 4[b]-$C_7H_8Mn(CO)_3$—$OC_7H_8Mn(CO)_3$	light yellow	158	106
	4[b]-$Me_2NC_7H_8Mn(CO)_3$	—	38	106
	4[b]-$Me_3INC_7H_8Mn(CO)_3$	—	154 (decomp.)	106
	azulene—$Mn_2(CO)_6$	light yellow	cryst.	89, 90
	$C_{10}H_9Mn(CO)_3$	orange	10	95
	$C_7H_9Mn(CO)_2PPh_3$	yellow	110	106
Re	$C_6H_7ReC_6H_6$	orange-red	195	85, 99
	$Me_6C_6HReC_6Me_6$	orange-yellow	212 (decomp.)	102
	$Me_6C_6Re(C_6Me_6)_2ReC_6Me_6$	yellow	225 (decomp.)	102
	$Me_6C_6HRe(CO)_3$	golden	118 (decomp.)	83, 100
Tc	$C_6H_7TcC_6H_6$	yellow	178 (decomp.)	103
	$Me_6C_6HTcC_6Me_6$	yellow	235 (decomp.)	103
	$Me_6C_6Tc[C_6Me_6]_2TcC_6Me_6$	red	230 (decomp.)	103
Fe	$[PhC_6H_3Me_3]_2Fe$	orange	105	86
	[t-$BuC_6H_3Me_3]_2Fe$	orange	204	86
	$[CH_2{=}CHC_6H_3Me_3]_2Fe$	orange	132	86
	$C_6H_7FeC_5H_5$	orange–red	135	68, 72, 85, 99, 139
	exo-4[b]-$MeC_6H_6FeC_5H_5$	—	65/0, 005mmHg	71

Table 2 (contd.)

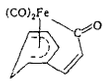
Metal	Compound	Colour	M.p., °C	Ref.
	$MeC_6H_6FeC_5H_5$[b]	—	37.70/0.005 mmHg	68
	exo-4[b]-$PhC_6H_6FeC_5H_5$	red	157	85, 99
	$MeOC_6H_6FeC_5H_5$[c]	—	55/0.005 mmHg	69
	2[b]-$ClC_6H_6FeC_5H_5$	—	72	70
	3[b]-$ClC_6H_6FeC_5H_5$	—	91	70
	3[b]-$BrC_6H_6FeC_5H_5$	—	98	70
	1,2[a])-$Me_3PhFeC_5H_5$[c]	—	65/0.005 mmHg	63, 68
	1,3[a])-$Me_2C_6H_5FeC_5H_5$[c]	—	50/0.005 mmHg	68
	1,4[a])-$Me_6C_6H_5FeC_5H_5$	—	45/0.005 mmHg	68
	1-Me-2[a])-$MeC_6H_5FeC_5H_5$[c]	—	45/0.005 mmHg	69
	1-Me-3[a])-$MeOC_6H_3FeC_5H_5$[c]	—	65/0.005 mmHg	69
	2[b])-Me-5$MeOC_6H_5FeC_5H_5$	—	50—51	69
	2,5[b])-$(MeO_2)C_6H_6FeC_5H_5$	—	47/0.005 mmHg	69
	3-Cl-5[b])-$MeC_6H_5FeC_5H_5$	—	viscous liquid	70
	3-Cl-1[b])-$MeC_6H_6FeC_5H_5$	—	viscous liquid	70, 71
	3-Cl-2[b])-$MeC_6H_6FeC_5H_5$	—	80	70
	5-Cl-2[b])-$MeC_6H_5FeC_5H_5$	—	73/0.005 mmHg	70
	2-Cl-5[b])-$MeC_6H_5FeC_5H_5$	—	viscous liquid	70
	1-Cl-3[a])-$MeOC_6H_5FeC_5H_5$[c]	—	58/0.005 mmHg	69
	3-Br-2[b])-$MeC_6H_5FeC_5H_5$	—	viscous liquid	70
	5-Br-3[b])-$MeC_6H_5FeC_5H_5$	—	viscous liquid	70
	5-Br-2[b])-$MeC_6H_5FeC_5H_5$	orange	61/0.005 mmHg	70
	2,3[b])-$Cl_2C_6H_5FeC_5H_5$	—	58	70
	1,2[b])-$Cl_2C_6H_5FeC_5H_5$	—	viscous liquid	70
	3,5[b])-$Cl_2C_6H_5FeC_5H_5$	—	84	70
	1,3[b])-$Cl_2C_6H_5FeC_5H_5$	—	viscous liquid	70
	2,6[b])-$Cl_2C_6H_5FeC_6H_5$	—	viscous liquid	70
	3,6[b])-$Cl_2C_6H_5FeC_6H_5$	—	39	70
	2-Br-5[b])-$MeC_6H_5FeC_5H_5$	orange	viscous liquid	70
	exo-4[b])-Me-2,5-$(Me_2)_2C_6H_4FeC_5H_5$	—	45/0.005 mmHg	71
	1,2,3[a])-$Me_3C_6H_4FeC_5H_5$[c]	—	32	68
	1,2,4[a])-$Me_3C_6H_4FeC_5H_5$[c]	—	—	68
	1,3,5[a])-$Me_3C_6H_4FeC_5H_5$	dark red	75/0.005 mmHg	68, 139
	exo-4[b])-Ph-2,5-$(Me_2)C_6H_4FeC_5H_5$	—	68	71
	2,6[a])-Me_2-1-$MeOC_6H_4FeC_5H_5$[c]	—	80/0.005 mmHg	69
	1,2,4,5[a])-$Me_4C_6H_3FeC_5H_5$[c]	—	55/0.005 mmHg	68
	exo-4[b])-Me-1,3,5-$Me_3C_6H_3FeC_6H_5$	—	39	71
	exo-4[b])-Ph-1,2,3-$Me_3C_6H_3FeC_5H_5$	—	99	71
	1,2,3,4,5[a])-$Me_5C_6H_2FeC_5H_5$[c]	—	viscous liquid	62
	exo-4[b])-Me-2,3,5,6-$Me_4C_6H_2FeC_5H_5$	—	60	71
	exo-4[b])-Ph-2,3,5,6-$Me_4C_6H_2FeC_5H_5$	—	90	71
	exo-4[b])-Me-1,2,3,5,6-$Me_5C_6HFeC_5H_5$	—	69	71
	$C_6H_7Fe(CO)_2CN$	yellow	91 (decomp.)	135
	$C_6H_7Fe(CO)_2I$	red-brown	96	135
	$[C_6H_7Fe(CO)_2]_2$	red	blackens 160	135
	$C_6H_7Fe(CO)_2Fe(CO)_2C_5H_5$	—	—	135
		yellow-orange	102	112—114
	$C_7H_9Fe(CO)_2I$	brown	99	132, 135
	$C_7H_9Fe(CO)_2CN$	orange	76 (decomp.)	132, 135
	$[C_7H_9Fe(CO)_2]_2$	red	198	135
	$C_7H_9Fe(CO)_2Fe(CO)_2C_5H_5$	red-brown	170	135
	$PhC_6H_3Me_3FeC_6H_3Me_3^+PF_6^-$	brown	217 (decomp.)	86
	t-Bu-$C_6H_3Me_3FeC_6H_3Me_3^+PF_6$	yellow-brown	238 (decomp.)	86
	$CH_2=CHC_6H_3Me_3FeC_6H_3Me_3^+PF_6^-$	yellow-brown	195 (decomp.)	86

Table 2 (contd.)

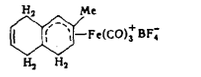
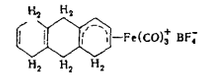
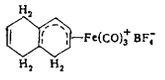
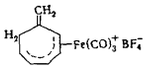
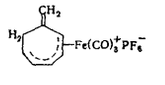
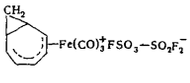
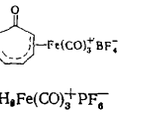
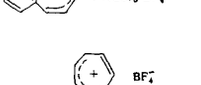
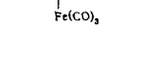
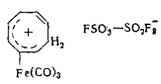
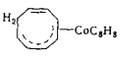
Metal	Compound	Colour	M.p., °C	Ref.
	$C_6H_7Fe(CO)_3^+ClO_4^-$	yellow	cryst.	76
	$C_6H_7Fe(CO)_3^+BF_4^-$	yellow	cryst.	76, 133
	sym-1-Me-$C_6H_6Fe(CO)_3^+ClO_4^-$	yellow	cryst.	75, 77
	sym-1-Me-$C_6H_6Fe(CO)_3^+BF_4^-$	yellow	195 (decomp.)	77
	sym, sym-1.5-$Me_2C_6H_5Fe(CO)_3^+BF_4^-$	yellow	220 (decomp.)	76, 133, 134
	$C_6H_7Fe(CO)_3^+BF_4^-$	light yellow	193 (decomp.)	63, 85, 132, 135
	$C_6H_7Fe(CO)_3^+PF_6^-$	—	—	108, 118
	1[b])-$MeC_6H_6Fe(CO)_3^+PF_6^-$	—	—	118
	2[b])-$MeC_6H_6Fe(CO)_3^+PF_6^-$	yellow	cryst.	64, 118
	2[b])-$MeC_6H_6Fe(CO)_3^+BF_4^-$	yellow	cryst.	64
	2[b])-$MeOC_6H_6Fe(CO)_3^+BF_4^-$	yellow	202 (decomp.)	64, 132
	3[b])-$MeOC_6H_6Fe(CO)_3^+PF_4^-$	yellow	—	64
	2-Me-5[b])-$MePhOFe(CO)_3^+BF_4^-$	—	—	64
	2-Me-5[a])-$MePhOFe(CO)_3^+BF_4^-$	yellow	124	64
		yellow	cryst.	64
		—	cryst.	64
	3-HO-1,4[b])-$Me_2C_6H_4Fe(CO)_3^+Al_2Cl_7^-$	—	—	120
	3-HO-2,4[b])-$Me_2C_6H_4Fe(CO)_3^+Al_2Cl_7^-$	—	—	120
		—	cryst.	64
	3-HO-1,2,4-Me_3-1[c])-$CD_3C_6H_2Fe(CO)_3^+Al_2Cl_7^-$	—	—	120
	3-HO-2,4,6-Me_3-1[b])-$CD_3C_6H_2Fe(CO)_3^+Al_2Cl_7^-$	—	—	120
	$Me_7C_6Fe(CO)_3^+FeCl_4^-$	yellow	cryst.	122
	$C_7H_9Fe(CO)_3^+Br^-$	light yellow	cryst.	65
	$C_7H_9Fe(CO)_3^+FeCl_4^-$	yellow	cryst.	65
	$C_7H_9Fe(CO)_3^+BF_4^-$	orange-red	>200 (decomp.)	62, 132, 135
	$C_7H_9Fe(CO)_3^+BPh_4$	light yellow	>240 (decomp.)	135
	$C_7H_9Fe(CO)_3^+ClO_4^-$	light orange	explodes 160	135
	$Ph_3CC_7H_8Fe(CO)_3^+BF_4^-$	light yellow	>100 (decomp.)	62
		—	cryst.	129
		—	cryst.	129
		—	—	112, 117
		—	140 (decomp.)	121
	4[b])-$MeOC_7H_8Fe(CO)_3^+PF_6^-$	—	cryst.	129
	3[b])-$MeOCOC_7H_8Fe(CO)_3^+BF_4^-$	—	—	67
	3[b])-$MeCOOCH_2C_7H_8Fe(CO)_3^+BF_4^-$	—	—	67
		yellow	230 (decomp.)	66
		yellow	112 (decomp.)	116

Table 2 (contd.)

Metal	Compound	Colour	M.p., °C	Ref.
		—	—	117
	$C_8H_7Fe(CO)_2PPh_3^+BF_4^-$	—	—	132
Ru	$(C_6H_7)_2Ru$	yellow	cryst.	85
	$Ph(C_6H_6)_2Ru$	yellow	158	85
	$C_8H_7Ru(CO)_3^+BF_4^-$	—	—	130
Co	$C_8H_7CoC_4Ph_4$	red	135	73, 74
	$C_7H_9CoC_4Ph_4$	dark red	188	73, 74
	4[b]-$BuC_6H_6CoC_4Ph_4$	orange-red	140	74
	4[b]-$BuC_6H_6CoC_4(C_6H_4Me)_4$	—	131	74
	$C_7H_9CoC_4Ph_4$	dark red	188	73, 74
	4[b]-$HOC_7H_8CoC_4Ph_4$	—	137 (decomp.)	74
	4[b]-$MeOC_7H_8CoC_4Ph_4$	orange-red	195 (decomp.)	74
	4[b]-$MeOC_7H_8CoC_4(C_6H_4Me)_4$	—	178 (decomp.)	74
	$C_7H_9CoC_6H_{12}$	red-brown	65 (decomp.)	125, 126
	$C_7H_9Co(CO)_2$	dark red	0—5	125
		black	95 (decomp.)	127
	$C_8H_7CoC_5H_5^+I^-$	red	110 (decomp.)	109, 111, 131
	$C_8H_7CoC_5H_5^+PF_6^-$	red	180 (decomp.)	109, 111, 131
	endo-4[b]-$MeC_8H_6CoC_5H_5^+PF_6^-$	—	160 (decomp.)	110
	endo-4[b]-$PhC_8H_6CoC_5H_5^+PF_6^-$	—	125 (decomp.)	110
	4,4[b]-$Me_2C_8H_5CoC_5H_5^+PF_6^-$	—	167 (decomp.)	110
	4,4[b]-$Ph_2C_8H_5CoC_5H_5^+PF_6^-$	orange	264 (decomp.)	110
Rh	$C_7H_9RhC_5Me_5^+Cl^-$	yellow	189 (decomp.)	124
	$C_7H_9RhC_5Me_5^+PF_6^-$	yellow	>260 (decomp.)	124
	$C_8H_{11}RhC_5H_5^+PF_6^-$	yellow	—	119
Ir	$C_7H_9IrC_5Me_5^+PF_6^-$	—	—	124

(a) Positions of substituents in initial hydrocarbon.

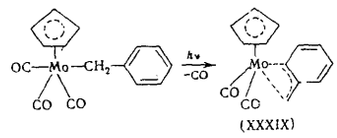
(b) Numbering as in and

(c) Mixture of isomers.

IV. THE BENZYL LIGAND IN TRANSITION-METAL COMPLEXES

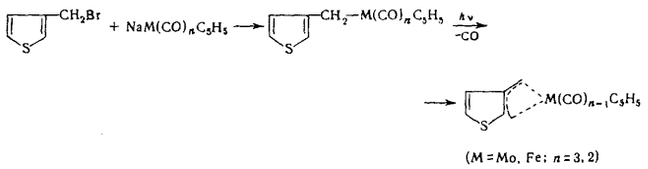
Comparatively recently a new form of coordination of aromatic molecules with transition metals—a π-allylic type of bonding involving one double bond of the benzene ring—has been discovered experimentally, and the products have been termed π-benzyl complexes.

King and Fronzaglia found that the products of prolonged ultraviolet irradiation of the σ-benzyl derivative of tricarbonyl(cyclopentadienyl)molybdenum included a small quantity of a substance containing one fewer carbonyl group than the starting material[140]:



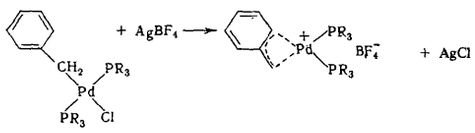
(XXXIX)

The structure (XXXIX) was suggested, and subsequently confirmed by X-ray diffraction. The same method has been used to obtain a few molybdenum and tungsten complexes substituted in the ligand[141,142] and also π-thienyl derivatives of molybdenum and iron[143]:



(M = Mo, Fe; n = 3, 2)

Complex cations in which a π-benzyl ligand is attached to palladium are obtained by a similar method[144]:



Thus in all these reactions an ethylenic group of the benzene ring occupies the coordination site vacated by the outgoing ligand. Compounds of this type that have been reported are quite stable, as indicated by their thermal constants (Table 3) and also the conditions of their preparation. In solution these complexes are unstable.

Table 3. Summary of data on complexes of π-benzyl type.

Metal	Compound	Colour	M.p., °C	Ref.
Mo	$PhCH_2Mo(CO)_2C_5H_5$	dark red	85	140
	4-$MeC_6H_4CH_2Mo(CO)_2C_5H_5$	red-orange	100	141, 142
	3,5-(i-$C_3H_7)_2C_6H_3CH_2Mo(CO)_2C_5H_5$	dark red	71	142
	β-$C_4H_3SCH_2Mo(CO)_2C_5H_5$	red-orange	127	143
	α-$C_4H_3SCH_2Mo(CO)_2C_5H_5$	red-orange	103	143
W	4-$MeC_6H_4CH_2W(CO)_2C_5H_5$	orange	127	142
Fe	β-$C_4H_3SCH_2Fe(CO)C_5H_5$	red	cryst.	143
Pd	$PhCH_2Pd(PEt_3)_2^+BF_4^-$	light yellow	cryst.	144
	2-Cl-$C_6H_4CH_2CHPd(PEt_3)_2^+BF_4^-$	yellow-orange	cryst.	144

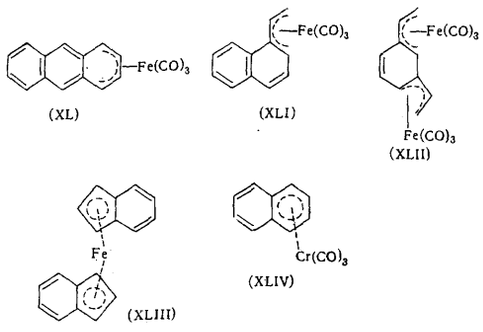
π-Benzyl complexes are easily obtained with molybdenum and tungsten, but not so well with iron. The yields of (XXXIX) and its analogues reach 25%, but the photochemical reaction of $C_5H_5Fe(CO)_2CH_2C_6H_5$ [145] involves elimination of the benzyl radical (not carbonyl) and dimerisation of the residue. The yields of thienyl derivatives of molybdenum amount to 30 — 50%, and of iron about 2% with poor reproducibility. However, the mass spectrum of $C_6F_5CF_2Fe(CO)_2C_5H_5$ includes a fragment corresponding to a π-benzyl derivative[146].

It is of considerable interest that the benzyl group can act as a bidentate ligand in complex formation. With such

coordination disturbance of the usual state of the molecule may be expected from that of delocalisation and the appearance of non-equivalence in the ethylenic groups of the ring. Therefore coordination of individual portions of an aromatic molecule would probably be determined by the donor — acceptor properties of such fragments and the metal-containing group of the complex. The very possibility of this type of interaction is being ascertained at the present time, and the first structural investigations have started.

Complexes of fused aromatic hydrocarbons have been reported, in which only part of the initial molecule is directly bound to the metal. They are represented (Scheme 10) by the structures (XL),[147] (XLI),[147] (XLII),[148] (XLIII),[149] (XLIV),[150,151] and also tricarbonyl(acenaphthylene)chromium, acenaphthylenebistricarbonyliron[152], and others.

Scheme 10



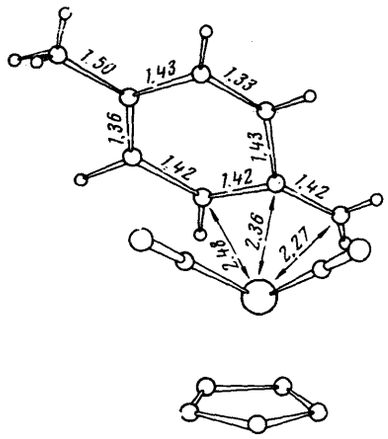
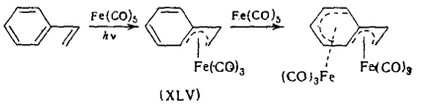


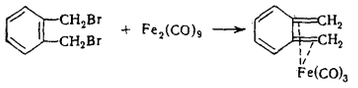
Figure 8. Structure of dicarbonyl(π-*p*-isopropylbenzyl)-cyclopentadienylmolybdenum[141].

After the structure of the π-benzyl derivatives had been established, and confirmed the breakdown in the aromatic character of this ligand, interest in such compounds grew. New examples of fragmentary coordination were found, sometimes involving fundamental reconstruction of the whole system. It was shown in particular that under severe conditions even styrene could be dismembered (formally) into two butadiene units, each of which combined with a tricarbonyliron group[153-155]:



(XLV)

If the aromatic molecule contains substituents capable of interacting with the metal, the rearrangement of the ligand may become more fundamental, as shown above in the reactions of 2-bromomethylnaphthalene and of brominated xylene with iron carbonyl[156]:



Thus an aromatic molecule is undoubtedly able to yield π-complexes involving not only the whole system of delocalised π-electrons but even part of this system.

If the π-systems of the fragments thereby become completely independent, a significant loss of delocalisation energy should occur. Calculation shows e.g. that in the formation of (XXXIX) and (XLV) such loss would exceed 1.4 β, and will be 1.23 β and 1.91 β in the formation of (XLI) and (XLII) respectively. Nevertheless, in individual cases complexes are obtained under comparatively mild conditions. This may mean that the state of the aromatic molecule does not change so strongly, or else that it changes considerably but this loss is balanced by the formation of new bonds.

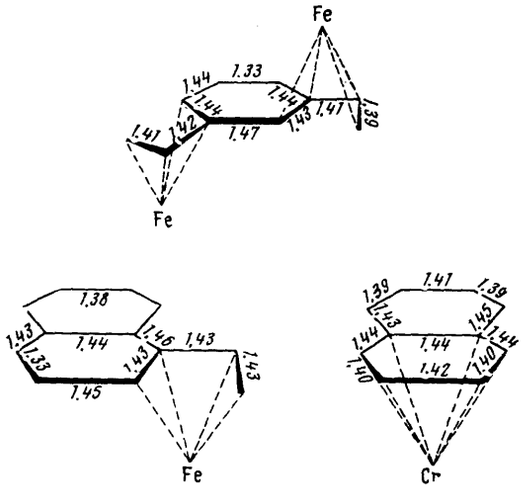


Figure 9. Some structural parameters of complexes of *m*-divinylbenzene with $Fe_2(CO)_6$, vinylnaphthalene with $Fe(CO)_3$, and naphthalene with $Cr(CO)_3$.[158]

Spectral and X-ray investigations of complexes of the benzyl type[141,157] and also of several derivatives mentioned above[158] show that fragmentary coordination may cause some localisation of π-electrons in the remaining free portion of the ring. The parameters involved are given in Figs. 8 and 9. The shortest bonds are 1.33 — 1.36 Å: i.e. they are typically ethylenic.

Comparison of data for tricarbonyl-iron and -chromium derivatives (Fig. 9) shows that the former grouping produces the more significant localisation of bonds. The short-range and long-range spin — spin interaction constants (proton n.m.r.) for these complexes[159,160] also indicate different degrees of localisation of the π-electron system under the influence of tricarbonyliron and tricarbonylchromium groups.

The carbon — carbon distances in the coordinated fragments are typical of each class of derivative. The metal atom in a π-benzyl complex is located somewhat unsymmetrically with respect to the allyl group and closer to the exocyclic atom.

It cannot at present be stated definitely whether the alternation of bonds found for these systems affects their chemical behaviour. An attempt to subject the butadiene portion of the π-benzyl ligand to the Diels — Alder reaction[142] did not give a clear result. This question merits further study; it is extremely important in connection both with the chemistry of aromatic compounds and with the role of the metal.

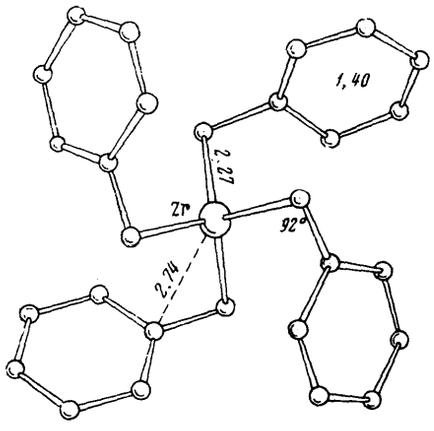


Figure 10. Structure of tetrabenzylzirconium[166].

The n.m.r. spectra of π-benzyl complexes of molybdenum and tungsten depend on the temperature, which indicates that the molecules are flexible[140,142]. At low temperatures (below −30°C) the spectrum is consistent with the suggested structure. With rise in temperature, however, it simplifies as a result of the averaging out of three pairs of protons—the two methylene protons and the ring *oo'*- and *mm'*-protons—by an intramolecular dynamic process assumed[142] to involve production of a σ-form. Quite rapid rotations about CH_2 — Mo and CH_2 — C bonds are possible in such an intermediate compound, which may be responsible for the observed averaging. The process is independent of the nature of the solvent: i.e. decrease in coordination number on passing to the σ-form is not balanced by interaction with the solvent. However, this transition restores the resonance stabilisation, so that energetically a σ-state is entirely probable. Thus the tendency to pass into a dynamic state, which is well known with allylic derivatives of metals, is characteristic also of the π-benzyl type of complexes.

π-Thienyl complexes do not exhibit the properties of flexible systems, but the existence of rotational isomers is not excluded[143].

After the discovery of π-benzyl complexes further investigation became necessary of the nature of the bond in several other benzyl derivatives of metals. The reason for this was their considerably greater stability compared with alkyl and aryl derivatives. For example, the tetrabenzyl derivatives of vanadium[161], titanium[162-164], and zirconium[165,166] have been prepared. The latter two compounds are stable, and have been studied by X-ray diffraction. Although a π-benzyl form was not confirmed in this case, the structure has noteworthy features (Fig. 10). In both cases the molecule is a distorted tetrahedron. All seven atoms within the benzyl groups are coplanar, their plane being almost perpendicular to the M — CH_2 bonds. All the M — CH_2 — C angles are significantly smaller than tetrahedral, while the distance (2.74 Å) from the metal to the first carbon atom of the ring is shorter than would be expected for a true σ-structure. The electron system of this atom is probably able to interact with vacant orbitals of the metal. According to the n.m.r. results this interaction is maintained even in solution[164].

Great interest attaches also to the extraordinarily stable triphenylmethyl derivatives of nickel—$[(C_6H_5)_3C]_2Ni$ [167] and $(C_6H_5)_3CNiCl$ [168]—on which no structural investigations have been made.

In concluding this Section mention must be made of the surprising lithium complex $C_6H_5CH_2Li.2N(CH_2CH_2)_3N$† containing a benzyl ligand and two amine molecules. Its structure[169] is analogous to the π-complex of molybdenum: i.e. it contains a π-bonded ligand. π-Complexes are not characteristic of non-transition metals; π-complexes involving separate fragments of an aromatic system are still less characteristic .

The main aim of this Review is to direct the attention of chemists of various kinds, including theoreticians, to the new opportunities and new problems which are opening up in the organic chemistry of the transition metals. The problems raised cannot be solved without combining many endeavours. The Reviewer will have achieved her aim if interest in these problems is aroused and maintained.

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[† 1,4-Diazabicyclo[2,2,2]octane (triethylenediamine) (Ed. of Translation).]

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The Ullmann Reaction

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The review describes data obtained in recent years on the synthesis of biaryls by treating aryl halides with powdered copper at an elevated temperature (the Ullmann reaction). The conditions governing the reaction, the limits of its applications at the present time, and its mechanism are discussed.
The bibliography includes 200 references.

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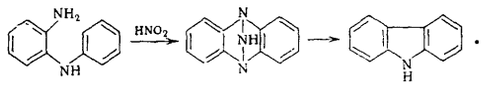
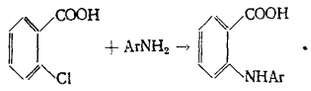
I. INTRODUCTION

There are three reactions associated with Ullmann's name[1].

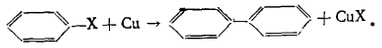
1. The Graebe–Ullmann synthesis of carbazole[2]:



2. The Ullmann condensation[3,4] which consists of the interaction of *o*-chlorobenzoic acid with phenols, thiophenols, arenesulphonic acids, and aromatic amines in the presence of catalytic amounts of copper with formation of diarylamines:



3. The Ullmann synthesis[5,6] of biaryls by the reaction of aryl halides with powdered copper at an elevated temperature:

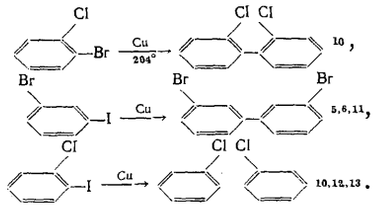


The last reaction is widely employed in organic chemistry and the number of studies dealing with it is continuously increasing. This review describes data for this reaction obtained from 1963, after the publication of Fanta's reviews[7,8], until 1971. The present limits of the applications of the Ullmann reaction (see, for example Nilsson[9]), the conditions governing its occurrence, and its mechanism are discussed.

2. REACTION CONDITIONS

a. Synthesis of Symmetrical Biaryls

Depending on the nature of the halogen atom, aromatic halides behave differently under the conditions of the Ullmann reaction. The reactivity of the halides increases in the series Cl < Br < I. Aromatic fluoro-compounds do not enter into this reaction at all[10]:



In halogenonitrobenzenes, the activating effect of the nitro-group increases in the series *m* < *p* < *o*.[8,14]

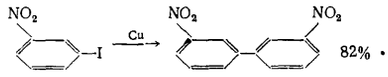
Table 1. Dependence of the yield of biaryls on the halogen and on the position of the nitro-group in the initial halogenonitrobenzene.

Halogen	Yield of dinitrobiphenyl, %		
	ortho-	*para-*	*meta-*
I	65	54	36
Br	64	36	15
Cl	40	0	0

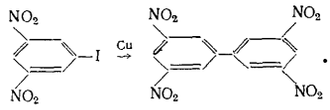
A defect of the results listed in Table 1 is that all the experiments carried out to establish the reactivity of the halogeno-derivatives were performed under severe conditions. To obtain valid data, experiments at a lower temperature using solvents are necessary. At any rate, in the synthesis of asymmetric biaryls exceptions from the rule formulated above are encountered[8]. Moreover, 2-iodopyridine is less reactive in the Ullmann reaction than 2-bromopyridine[15]. This problem will be discussed in greater detail in connection with the mechanism of the Ullmann reaction.

Highly electronegative groups such as the nitro-, carboxy-, and other groups have an activating effect when they are in the *ortho*-position relative to the halogen atom.

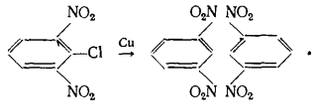
For the nitro-group, this effect decreases in the series $o > p > m$. For example, *o*-iodonitrobenzene is most reactive in the Ullmann reaction, while the *p*- and *m*-isomers are less reactive [16,17]. It has been found recently [11] that *m*-iodonitrobenzene forms under these conditions 3,3′-dinitrobiphenyl in 82% yield:



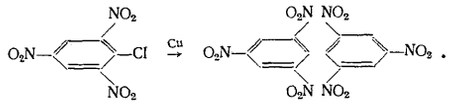
However, the presence of a further nitro-group in the *m*-position relative to the halogen greatly hinders the formation of the biaryl. Thus the yield of 3,3′,5,5′-tetranitrobiphenyl from 1-iodo-3,5-dinitrobenzene is only 15%:[18]



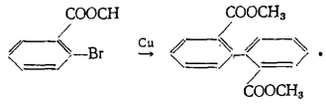
The nitro-group in the *o*-position relative to chlorine in the aromatic ring strongly activates it in this reaction; the yield of 2,2′-dinitrobiphenyl from *o*-chloronitrobenzene is 66%;[19–24] chlorobenzene is less reactive [8]. The introduction of a second nitro-group in the *o*-position relative to the halogen atom in *o*-chloronitrobenzene also reduces the yield of the biaryl; the yield of 2,2′,6,6′-tetranitrobiphenyl from 1-chloro-2,6-dinitrobenzene is 61%:[25,26]



On the other hand, the yield of the biaryl from picryl chloride is 55–58%:[19,27–29]

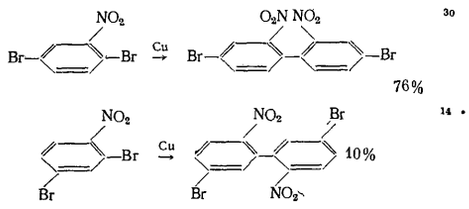


The effect of the alkoxy carbonyl group is approximately the same. Thus methyl *o*-bromobenzoate gives rise to 2,2′-dimethoxycarbonylbiphenyl in 80% yield [14]:



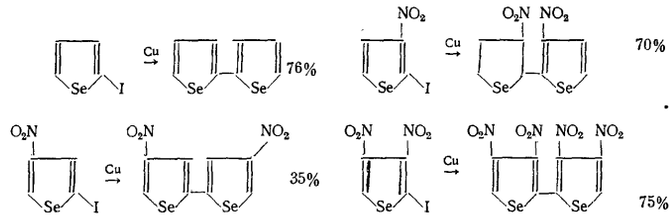
On the other hand, 3,3′- and 4,4′-dimethoxycarbonylbiphenyls are obtained from *m*- and *p*-iodobenzoate esters in yields of only 15 and 25% respectively [14].

The higher reactivity of the halogen in the *o*-position relative to the nitro-group compared with those in the *m*- and *p*-positions can be illustrated by the following examples:

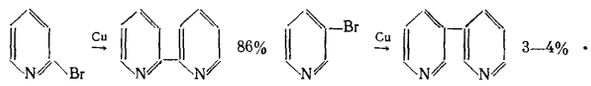


The phenyl substituent in the *p*-position relative to the halogen atom has a highly activating effect, while the same substituent in the *o*- and *m*-positions hinders the reaction. Thus, in the presence of copper at 225–260°C, *p*-, *o*-, and *m*-iodobiphenyls give rise to isomeric terphenyls in yields of 97, 50, and 16% respectively [31].

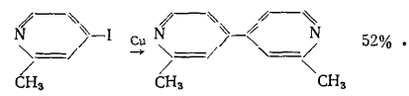
Interesting results were obtained for isomeric 2-iodoselenoles [32]:



An effect similar to that of the nitro-group is also shown by the nitrogen atom in the pyridine ring. It activates the halogen atom in the 2-position, as shown by the formation of 2,2′-bipyridyl from 2-bromopyridine (yield 87%).[33,34] 3-Halogenopyridines enter into this reaction with greater difficulty [35–37]:



A halogen in the 4-position of the pyridine ring is somewhat more reactive than in the 3-position [38]:

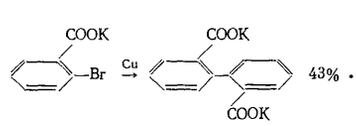


On the basis of literature data, Fanta [7] predicted that electropositive groups should deactivate the halogen in the Ullmann reaction. However, this hypothesis was disproved by later studies (see Table 2c in Ref. 8), in particular the work of Forrest [14].

The activating effect of the substituent depends both on its nature and its position relative to the halogen atom involved in the reaction.

A decrease of the yield of the biaryl is usually observed when the aromatic ring contains groups such as NH_2, $NHCOCH_3$, $NHCH_3$, SO_2NH_2, $SO_2NHC_6H_5$, COOH, and OH.[6,39] To obtain the required yields of products, the influence of the amino-group must be weakened by acylation and that of the hydroxy- and carboxy-groups by esterification (see Table 2c in Ref. 8).

Although *o*-bromobenzoic acid reacts with copper at 160°C with formation of copper benzoate and copper(I) bromide only, when the Ullmann reaction is performed with the potassium salt of this acid, it is possible to obtain a 43% yield of biphenyl-2,2′-dicarboxylic acid [40]:

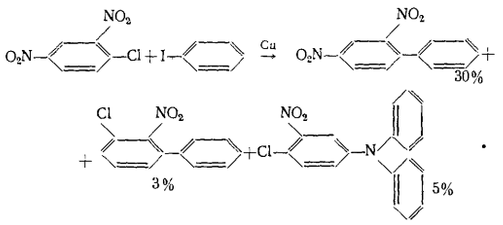


The methyl ester of this acid gives rise to the dimethyl ester of biphenyl-2,2′-dicarboxylic acid in 82% yield [6].

The yield of biaryls from aromatic compounds containing 2 or more halogen atoms is always lower than the yield from monohalogeno-derivatives [7,8].

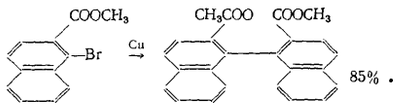
Certain halogenonitrobenzenes undergo side reactions, namely the reduction of the nitro-group. Thus when

1-chloro-2,4-dinitrobenzene reacts with iodobenzene, the following products are formed[14]:

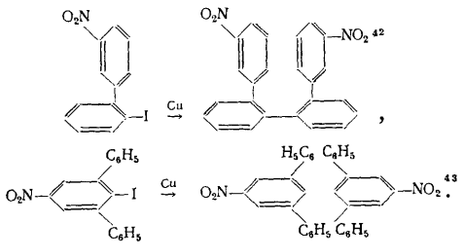


Steric factors have a definite influence on the course of the Ullmann reaction. Bulky substituents such as the nitro-, alkyl-, halogeno-, alkoxy-, and carboxy-groups do not hinder the Ullmann reaction. This is confirmed by the high yield of biaryls from 2,6-disubstituted halogenobenzene (Table 3, see also Table IIc in Ref. 8).

On the other hand, 1-bromo-2-methylnaphthalene[41] is completely inert, which is probably not caused solely by the steric influence of the methyl group. Alkyl and other electropositive groups in any position relative to the halogen atom in the naphthalene ring are known to deactivate the halogen, while electronegative (electrophilic) groups (NO_2, COOR) activate it[41]. This is also confirmed by the high yield of the dimethyl ester of 1,1′-binaphthyl-2,2′-dicarboxylic acid from the methyl ester of 1-bromo-2-naphthoic acid[41]:



Steric hindrance becomes appreciable when substituents such as the phenyl and naphthyl groups are introduced in the 2,6-positions relative to the halogen atom in the benzene ring:

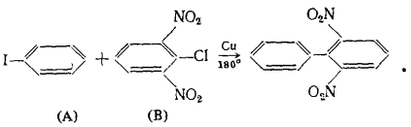


The yields of biaryls in such cases are very low.

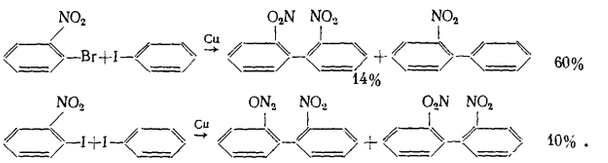
b. Synthesis of Asymmetric Biaryls

Examples of the use of the Ullmann reaction for the synthesis of symmetrical biaryls were described above (Table 4 on p. 1053; see also Table IIc in Ref. 8 and Table 1c in Ref. 7). At the same time, the reaction has been successfully used also for the synthesis of asymmetric biaryls. The results of latest syntheses of asymmetric biaryls by the Ullmann reaction are presented in Table 5 on p. 1055. For earlier results, see Table IIIc in Ref. 8 and Table 2c in Ref. 7.

Forrest[14] showed that optimal yields of asymmetric biaryls are obtained when one of the aryl halides (A) is more reactive than the other (B):



Component (B) should contain at least one electronegative group (NO_2, COOR) in the 2-position and better still two such groups in the 2- and 6-positions relative to the halogen atom. Best yields of asymmetric biaryls are obtained when component (A) contains iodine and component (B) contains bromine or chlorine, as can be seen from the following examples:

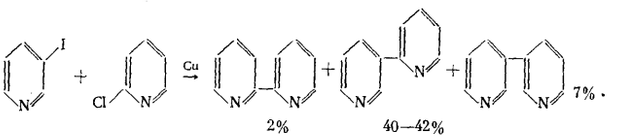


As was to be expected, the reaction of aryl halides with similar reactivities gives a mixture of three biaryls in approximately equal proportions[44-47].

When mixtures of aryl halides (A) and (B) are used, the reaction can be carried out at a much lower temperature than with component (B) alone.

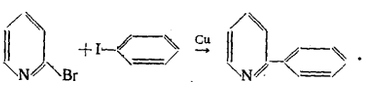
The degree of reaction increases when the reaction is performed in the presence of an excess of component (A) with simultaneous increase of the amount of asymmetric biaryls[14].

It has been established[48] that, when an inactive component (A) is heated with copper for a specific time with subsequent addition of an active component (B) in portions, the yield of the asymmetric biaryl increases sharply. In such cases component (B) is taken in an excess:



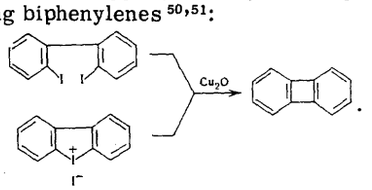
Under the usual conditions, i.e. on simultaneous heating of a mixture of components (A) and (B) in the presence of copper, 2,3′-bipyridyl is formed in a yield of only 7%.[48]

2-Bromopyridine reacts with iodobenzene, forming 2-phenylpyridine in a yield of 50–55%:[49]



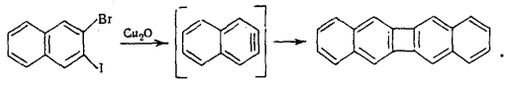
c. Synthesis of Biphenylenes

By heating 2,2′-dihalogenobiphenyls or 2,2′-biphenyliodonium iodide with copper(I) oxide, Lothrop succeeded in synthesising biphenylenes[50,51]:

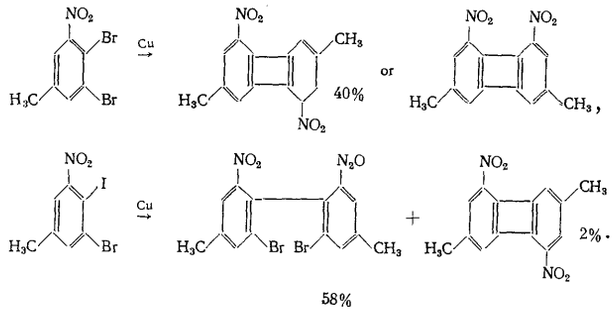


Subsequently this method was used to synthesise also many other biphenylenes [8]. In most cases the reaction is carried out in the presence of copper(I) oxide, the yields of biphenylenes depending significantly on its quality [52-54].

In view of the formation of dibenzobiphenylene on heating 2-bromo-3-iodonaphthalene with copper bronze in dimethylformamide, it was suggested that the reaction proceeds via the formation of dehydronaphthalene with its subsequent dimerisation [56]:



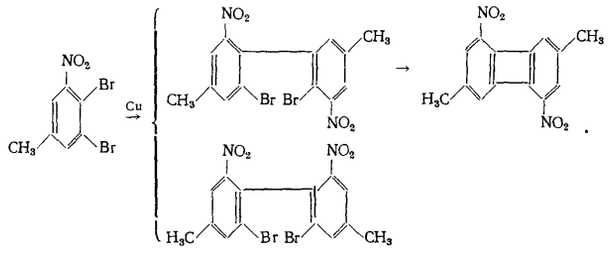
On the other hand, dihalogenonitrotoluenes yield the following products [57]:



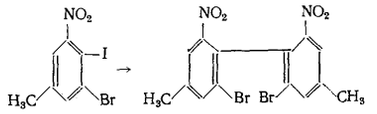
58%

According to Corbett and Holt [57], biaryls cannot serve as intermediates in the formation of biphenylenes. A more detailed examination of these investigations and the studies of recent years [58-60] reveals certain other features of the reaction. Thus contrary to Lothrop's data [50,51], Salfeld and Baume [58] established that metallic copper can also be employed in the synthesis of biphenylenes instead of copper(I) oxide. The yield of biphenylenes is then considerably higher.

The structure of biphenylenes synthesised by the method of Corbett and Holt [57] was investigated by Harrison et al. [59], who found that the product obtained under these conditions is 3,7-dimethyl-1,5-dinitrobiphenylene. Together with the main product, 2,2′-dibromo-4,4′-dimethyl-6,6′-dinitrobiphenyl is also formed in this reaction with a yield of 20%. Probably the process proceeds via the following mechanism:

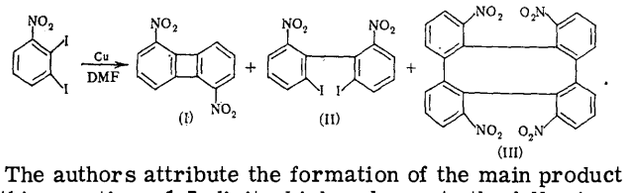


The above scheme shows that the formation of biphenylene involves the formation of a biaryl as an intermediate. Therefore it is easy to account for the formation of a biaryl and not a biphenylene from 3-bromo-4-iodo-5-nitrotoluene:

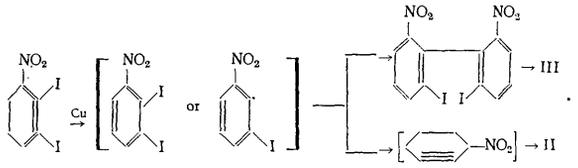


The 2,2′-dibromo-6,6′-bitolyl obtained does not enter into subsequent reactions owing to the presence of the nitro-group in the *m*-position relative to the halogen.

The reaction of 2,3-di-iodo-1-nitrobenzene with copper yielded 1,5-dinitrobiphenylene, 2,2′-di-iodo-6,6′-dinitrobiphenyl, and 4,5,12,13-tetranitroquaterphenylene [60]:

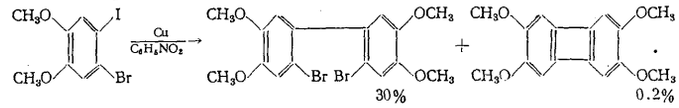


The authors attribute the formation of the main product of this reaction—1,5-dinitrobiphenylene—to the following sequence of steps:



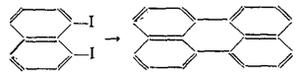
According to this scheme, biphenyl is obtained from dehydrobenzene. However, the absence of 1,2-dinitrobiphenylene (II) from the mixture is evidence against the formation of dehydrobenzene, since in this case the formation of both 1,2- and 1,5-dinitrobiphenylene (I) would be equally probable.

In addition, it has been shown [61] that, when 4-bromo-5-iodoveratrol reacts with copper bronze in nitrobenzene, biphenylene is formed in an insignificant yield (0.2%) and the main product is a biaryl:

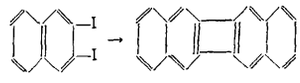


Thus a more detailed examination of the available literature data reveals a similarity of the Ullmann and Lothrop reactions. It is likely that an intermediate aryne is not in fact formed in the Lothrop reaction. The formation of intermediates of this type is usually coupled [62] with an increase in the complexity of the mixture of products obtained. Under the conditions described, this did not occur.

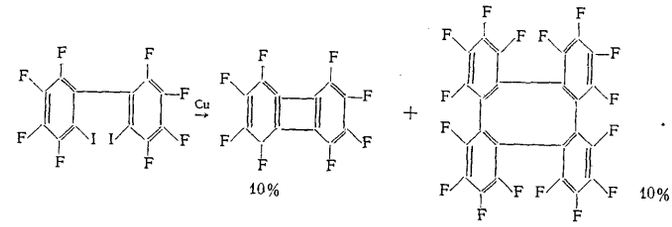
Apart from biphenylenes, other cyclic polyaryls were obtained from aryl dihalides. Thus perylene was synthesised from 1,8-di-iodonaphthalene [63]:



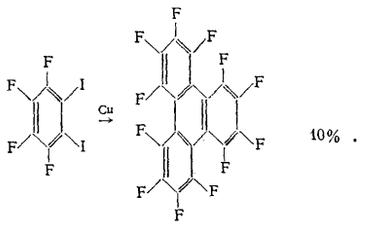
and 2,3-di-iodonaphthalene yielded dibenzobiphenylene [64]:



Octafluorobiphenylene and polyfluoroquaterphenylene were obtained from octafluoro-2,2′-di-iodophenylene [65]:

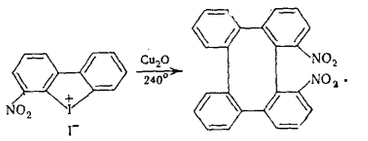


3,4,5,6-Tetrafluoro-1,2-di-iodobenzene forms a trimer:

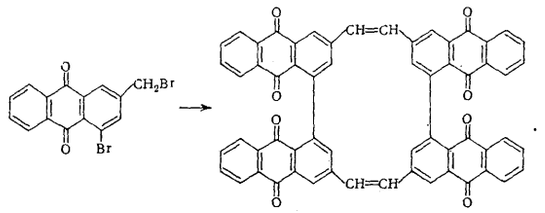


10%.

Pyrolysis of 3-nitrobiphenylene-2,2′-iodonium iodide at 340°C in the presence of copper(I) oxide yields dinitroquaterphenylene; biphenylene was not detected in the reaction products [66]:



Another interesting product was obtained from 4-bromo-2-bromomethylanthraquinone [67]:



Numerous other studies on biphenylenes have been made [68–78].

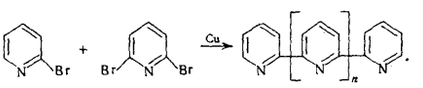
Reactions of aryl dihalides with aryl monohalides yield various polyaromatic compounds.

d. Reactions of Bifunctional Aryl Halides

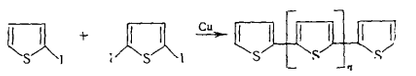
The reactions of bifunctional aryl halides can be divided into two groups: (1) synthesis of cyclic condensation products from two aryl dihalide molecules and (2) synthesis of linear products from a mixture of an aryl dihalide and an aryl monohalide.

The reactions of the first group were largely considered in the discussion of the synthesis of biphenylenes. Those of the second group give rise to a mixture of ter-, quater-, and poly-phenyls; this is best regarded as a special case of the synthesis of asymmetric biaryls. The results obtained are compiled in Table 6 (see also Table IVc in Ref. 8).

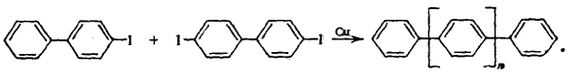
The reaction of 2-bromopyridine with 2,6-dibromopyridine yields bi-, ter-, quater-, quinque-, and sexipyridyls [79]:



Polythienyls have also been synthesised [80,81]:



as well as polyphenyls [82]:



Arylation products are formed in high yields when one of the aryl halides is reactive and the reactivity of the other is somewhat lower [83,84].

e. Experimental Conditions

In most cases copper powder is gradually added to the aryl halide at a specified temperature. An excess of copper, usually a threefold excess, is almost always employed. Sometimes a tenfold excess of copper is used [14,17]. With the exception of certain cases [41], special purification of the aryl halide is not required for the Ullmann reaction. The yield of the biaryl very often depends on the quality of the copper employed. The question of the effect of the quality of the copper used in the reaction still remains controversial. Frequently commercial copper powder, known as copper bronze, is employed [14]. A special form of copper bronze, "Naturcupfer-C", is also used [6,85].

Commercial copper bronze contains traces of oil but these impurities are readily removed by washing with alcohol or ether. According to Ullmann and Bielecki [19], preliminary treatment of the copper is not needed for the synthesis of biaryls. However, the use of commercial copper powder precludes reproducible yields of 2,2′-dinitrobiphenyl [16] and 2,2′-bipyridyl [86,87]. In such cases freshly prepared copper has been used for a long time [88].

Kleiderer and Adams [89] and Vogel [90] suggest that activated copper be used in the Ullmann reaction. The activation involves treatment of the copper bronze with iodine in acetone and subsequent washing with a mixture of acetone and hydrochloric acid and then pure acetone. When a tenfold excess of copper bronze activated in this way was used, 2,2′-dinitrobiphenyl was obtained from *o*-iodonitrobenzene in almost quantitative yield [17].

In some studies [19,91], it was stated that sometimes mechanically contaminated copper gives better results than freshly precipitated copper. Thus "lithographic copper", containing 0.2–0.5% of long-chain fatty acids (mainly stearic, palmitic, oleic, etc. [13]) is effective. Electrolytic copper treated with stearic acid has also been used [92].

Lothrop [50,51] found that in the synthesis of biphenylenes from 2,2′-dihalogenobiphenyls or from biphenylene-2,2′-iodonium iodide, copper(I) oxide gives very satisfactory results, while copper powder is completely inactive. Contrary to these results, it has been established [93,94] that freshly precipitated copper gives entirely satisfactory yields of biphenylenes. "Gatterman's precipitated copper powder" gives even better results [95].

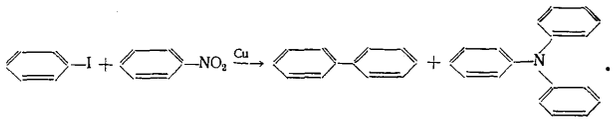
The study of the synthesis of biphenylenes in the presence of copper(I) oxide, commercial copper powder, and copper prepared by the method of Brady and McHugh [88] showed [58] that in the last case best results are obtained.

Apart from those mentioned above, one of the decisive factors governing the success of the Ullmann reaction is reaction temperature. The Ullmann reaction is carried out over a very wide range of temperatures, between 60° [17] and 360°. [96] In most cases the range is between 150° and 280°C (see Tables 4 and 5 on pp.1053 and 1055 and also the Tables in Refs. 7 and 8). Sometimes high temperature may cause the formation of side products. For example, for compounds containing the nitro-groups, the reaction temperature should not be raised above 200°C, since this promotes oxidation-reduction processes [13,14].

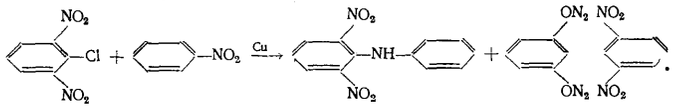
The Ullmann reaction is frequently carried out in solution. Under these conditions, side reactions, which

may occur in the case of labile aryl halides, are to some extent suppressed. The solvents employed are nitrobenzene, toluene, naphthalene, *p*-cymene, biphenyl, anthracene, dimethylformamide (DMF), and others.

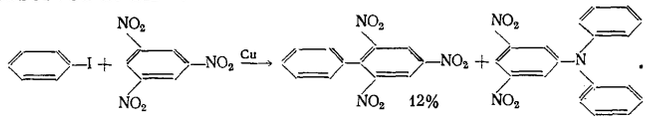
Forrest[14], who used nitrobenzene as a solvent, found that in the presence of copper iodobenzene enters into the following reaction:



When 1-chloro-2,6-dinitrobenzene was allowed to react in boiling nitrobenzene, a product corresponding to the reduction of the nitro-group and a biaryl were obtained in a very low yield[96]:



When a mixture of iodobenzene and 1,3,5-trinitrobenzene was treated with copper, the formation of a biaryl was not observed at all[14]:



Thus nitrobenzene cannot be regarded as an inert solvent in the Ullmann reaction. More suitable solvents are high-boiling hydrocarbons—biphenyl, *p*-cymene, naphthalene, and others.

Recently DMF has been employed with increasing frequency[97]. One of its advantages is its miscibility with water, which facilitates the isolation of reaction products. Moreover, certain aryl halides, which are relatively unreactive in other solvents, give high yields of biaryls in DMF.[11,33,34,41,97] For example, 3,3′-dinitrobiphenyl was obtained in a yield of 82% from the relatively unreactive *m*-iodonitrobenzene[11] (see p. 1046). 3,3′-Dimethyl-5,5′-dinitrobiphenyl was prepared in 71% yield from 3-iodo-5-nitrotoluene[98]. Bipyrrolyls[99-102], bifuryls[103], and bithienyls[104,105] have been obtained in satisfactory yields. Aryl halides containing the formyl[106], keto-[107,108], and carbamoyl[109] groups give satisfactory yields of biaryls in DMF.

Only a few studies in which DMF was used to synthesise asymmetric biaryls have been published[30,37,110,111] and the yields were relatively low. The disadvantages of DMF include its capacity to promote dehalogenation reactions[26,108,112] and halogen exchange reactions[13].

Apart from these solvents, toluene[28], benzene[102,113,114], decane, decalin, pseudocumene, tetralin[33,115-118], xylene[32,118], phenyl ether[119], bitolyl[73], pyridine[120], quinoline[121], etc. have been used in the Ullmann reaction. Sand[19,20,23] has also been employed as an inert diluent and heat exchanger. In some cases common salt has been used instead of sand, which facilitates the isolation of the product from the sintered mass[87].

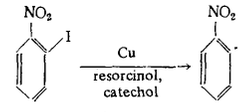
The Ullmann reaction is usually performed in air and in some cases a stream of hydrogen or nitrogen is employed[122]. Some investigators claim[123] that these precautions are superfluous when the initial and final reaction products are not sensitive to atmospheric oxygen. However, it is very likely that an inert atmosphere promotes a satisfactory yield of products, protecting the copper powder, particularly the activated powder, from oxidation[89,90].

3. REACTION MECHANISM

The mechanism of the Ullmann reaction, like those of certain other organic reactions, is still the subject of controversy and discussion[8,14]. There are several views concerning the mechanism but none is entirely convincing.

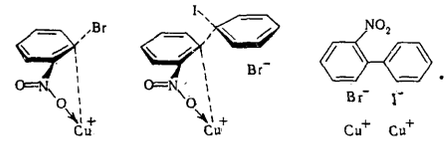
By treating halogenobenzenes with copper or sodium, Rapson and Shuttleworth[124,125] obtained the corresponding dehalogenated products. They suggested that these products are formed owing to the abstraction of hydrogen atoms from the solvent by the free radical produced in the reaction. To confirm this hypothesis, halogenobenzenes were treated with copper bronze in an excess of ethyl benzoate in a sealed tube; 2-carboxybiphenyl and 4-carboxybiphenyl were isolated from the reaction mixture. The authors concluded that a biaryl is formed in the Ullmann reaction as a result of the coupling of free phenyl radicals. Bell and Morgan[126] also believe that the Ullmann reaction has a free-radical mechanism.

To solve the problem of the intermediate in the Ullmann reaction (the aryl radical or aryl anion), the behaviour of *o*- and *p*-iodonitrobenzenes and of *o*-bromonitrobenzenes in an excess of resorcinol and catechol was examined[127]. It was shown that the yield of the dehalogenated product (nitrobenzene) in the experiments with catechol is higher than with resorcinol, although the critical oxidation constant for resorcinol (1.043) is higher than for catechol (0.742). The authors believe[127] that these results confirm a free-radical mechanism of the Ullmann reaction:



Despite these conclusions, Fanta[7,8] concluded on the basis of literature data (he examined about 500 studies) that this reaction has a clearly ionic mechanism. He believes that the reaction consists mainly of two stages, the first of which includes nucleophilic attack by metallic copper on the carbon–halogen bond as a result of which an arylcopper complex is formed on the surface of the metal. He also believes that the success of this stage depends strongly on the sensitivity of aromatic halides to nucleophilic attack in general.

The second stage involves the reaction of the arylcopper complex with a second molecule of the initial aryl halide to form the biaryl and copper halide. This stage depends mainly on steric factors.

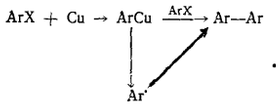


Thus Fanta rules out the formation of free radicals in the Ullmann reaction.

On the basis of a vast number of experimental data and literature results, Forrest[14] also postulates an ionic mechanism for the Ullmann reaction.

Other workers[128] formulate the mechanism of the Ullmann reaction in a somewhat different way. They believe that the reaction consists of two stages: the first involves the formation of an organocopper compound and the second, involving the formation of a biaryl, can occur in two ways, i.e. the biaryl can be formed either as a result of the attack by the initial aryl halide on the organocopper compound or as a result of the coupling of

two free radicals formed owing to the disproportionation of the organocopper compound. They believe that more than half of the biaryl is formed due to the attack by the initial aryl halide on the organocopper compound.

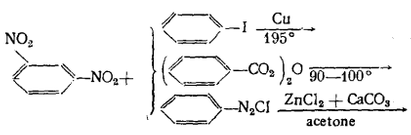


The foregoing statements clearly show that the question of the mechanism of the Ullmann reaction remains controversial.

The formation of anomalous products such as biphenyl-2-carboxylic and biphenyl-4-carboxylic acids from iodobenzene and methyl benzoate [125], 2,6-dinitrobiphenyl from iodobenzene and *m*-dinitrobenzene, and 2,4,6-trinitrobiphenyl from iodobenzene and *sym*-trinitrobenzene [11] is quoted as an argument in support of the free-radical reaction mechanism. In view of the formation of carbon dioxide in 2.6% yield on heating a mixture of benzoic acid and copper in *o*-iodonitrobenzene at 201–208 °C, Nursten concluded [127] that the dehalogenation observed in previous studies [129–131] involves the formation of intermediate free radicals. However, Forrest showed [14] that the formation of such side products is observed for highly hindered aryl halides and is virtually absent for simple halides.

Fanta [8] showed that the interaction of iodobenzene with *m*-dinitrobenzene under the conditions of the Ullmann reaction yields somewhat different proportions of products than on treatment of *m*-dinitrobenzene with benzoyl peroxide at 100 °C (a free-radical reaction) or on decomposition of diazonium chloride in *m*-dinitrobenzene (a Gomberg–Bachmann free-radical reaction) (Table 2).

Table 2.

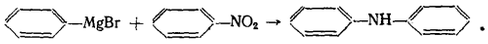
Starting materials and reaction conditions	Relative yields (%) of products (isomeric dinitrobiphenyls)	
	2,4-	2,6-
	0	8
	8	1
	2	0.2

Supporters of the ionic mechanism believe that the Ullmann reaction involves the formation of an organocopper complex or compound as an intermediate stage. Therefore their attention was attracted to the question of the synthesis and reactivity of arylcopper derivatives.

Organocopper compounds of this type were synthesised for the first time by Reich [132] and then Gilmann and Straley [133], Starkey and coworkers [134], and Costa et al. [135] In the last study, the optimal conditions for the formation of phenylcopper were established. Recently Lewin and Cohen [128,136,137] and other investigators [138–147] carried out several studies on the synthesis and properties of organocopper compounds.

Diphenylcopper and dimethyl copper were also obtained [148] and it was shown that they are stable at the boiling point of tetrahydrofuran (THF) (64 °C).

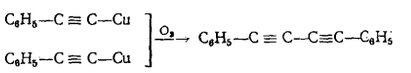
On hydrolysis, diphenylcopper yields benzene and not biphenyl. It has been shown that phenylcopper reacts with aldehydes as a typical Grignard reagent: for example, it reacts with benzaldehyde to form diphenylmethanol in 24% yield [133]. Forrest showed [14] that the addition of nitrocompounds, aldehydes, and ketones to the reaction mixture suppresses the main Ullmann reaction. The formation of triphenylamine when the reaction of iodobenzene and copper is carried out in nitrobenzene may be attributed to typical reactions of organometallic compounds with nitrobenzenes, although phenylmagnesium bromide reacts with nitrobenzene to form only diphenylamine and not triphenylamine [149]:



The thermal decomposition of phenylcopper, *p*-tolylcopper, phenylsilver, and *p*-tolylsilver has been investigated [150,151] and it has been established that the process proceeds via the formation of free radicals, since biaryls and benzenes are the products of this reaction. When a free-radical acceptor (*p*-benzoquinone) is added to the mixture, the yield of products falls sharply. The formation of free radicals is observed also when methylcopper is decomposed [150]. Other workers claim that the thermal decomposition involves a bimolecular mechanism in which a dimer is formed via an organocopper compound [151].

The thermal decomposition of *cis*- and *trans*-ethylenecopper compounds has been studied and the possibility of their dimerisation has been demonstrated [151].

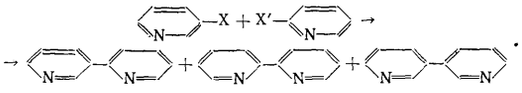
A necessary condition for the synthesis of biaryls from arylcopper is the presence of oxidising agents in the mixture. Gilmann and Straley [133] showed that phenylcopper is oxidised in air over a period of 2 h with formation of biphenyl. On the other hand, in an inert atmosphere phenylcopper is stable over a period of 36 h but the product is again biphenyl. This is also consistent with the following synthesis of diacetylenes [152]:



which has been known for a long time. Furthermore the presence of free radicals in the reaction mixture leads to the formation of side products. Lewin and Cohen [128] claim that, when the reaction of *p*-iodotoluene with copper is performed in quinoline, 8-methylquinoline, or 1-methylnaphthalene, about half of the biaryl is formed from free radicals which are generated owing to the disproportionation of phenylcopper. They did not observe the formation of side products. However, the free radicals produced in the decomposition of benzoyl peroxide in quinoline [153] and in 2-methylnaphthalene [154] gave various phenyl-substituted quinolines and 2-methylnaphthalenes. The decomposition of benzoyl peroxide in chloro- and bromo-benzenes [155] results in the formation of 2-, 3-, and 4-chloro- and 2-, 3-, and 4-bromo-biphenyls, dihydrobiphenyls, diphenyl-, chloro-, and bromo-benzoic acids, dichloro- and dibromotetrahydroquarterphenyls, etc. On the other hand, the decomposition of phenyldiazonium chloride in pyridine gives an almost 80% yield of 2-, 3-, and 4-phenylpyridines [156].

The absence of these products in the experiments of Lewin and Cohen [128] casts doubt on the hypothesis of a radical mechanism of the Ullmann reaction.

The studies by the authors of this review are useful for the estimation of the reactivities of halogen atoms [37,48,49,157-159]. Using the synthesis of 2,3′-bipyridyl as an example, a new method of synthesising asymmetric biaryls was proposed. When 3-iodopyridine was heated with copper in boiling DMF and 2-chloropyridine was added dropwise, 2,3′-bipyridyl was formed in 40–42% yield. On the other hand, when the mixture of all the reactants was heated simultaneously, 2,3′-bipyridyl was formed in a yield of only 7%: [157]



When 3-iodopyridine was replaced by 3-chloropyridine and 2-chloropyridine was replaced by 2-iodopyridine in this reaction, 2,3′-bipyridyl was not obtained. Other halogenopyridines were also employed (Table 3).

Table 3.

X in 3-X-pyridine	X′ in 2-X′-pyridine	Yield of 2,3′-bipyridyl, % of 3-bromopyridine	Yield of 2,2′-bipyridyl, % of 3-bromopyridine	Yield of 3,3′-bipyridyl, % of 3-bromopyridine
Cl	Cl	2—4	3	0
Cl	Br	Следы	70	0
Br	Cl	35	2.5	3—4
Br	Br	28—30	45	4
I	Cl	40—42	2	8
I	Br	32—35	45—47	7—8

Table 4. Compilation of symmetrical biaryls synthesised by the Ullmann reaction:

$$2ArX \xrightarrow{Cu} Ar-Ar.$$

Ar	X	Reaction temp., °C	Reaction conditions	Yield of biaryl, %	Refs.
1	2	3	4	5	6
2,3,4,5,6-Pentafluorophenyl	Cl	320—360	—	73	170
3-Bromophenyl	I	—	DMF	30	11
2-Nitrophenyl	Cl	315—325	—	66	24
" "	I	190—240	—	96	17
3-Nitrophenyl	I	—	DMF	—	11
3,4,5,6-Tetrafluoro-2-nitrophenyl	Br	—	ditto	—	171
3,4,5,6-Tetrafluoro-2-methylphenyl	Br	—	ditto	—	171
2-Cyano-3,4,5,6-tetrafluorophenyl	Br	—	ditto	—	171
2-Iodo-6-nitrophenyl	I	—	ditto	6.46	172
3-Methylphenyl	I	—	—	—	84
4-Methylphenyl	I	—	—	16	167
5-Methyl-3-nitrophenyl	I	—	DMF, stream of N_2	71	98
4-Methoxyphenyl	I	—	—	12	167
3-Methoxy-2-methylphenyl	I	—	—	—	173
3-Bromo-4-methyl-6-nitrophenyl	I	70	DMF	77	174
2,6-Dimethyl-4-nitrophenyl	I	—	DMF, stream of N_2	60	98
4-Methoxy-2-methyl-6-nitrophenyl	Br	200—230	—	65	175
" "	Br	190	nitrobenzene	59	175
2-Formyl-6-nitrophenyl	I	—	—	—	176
2,3-Dimethoxyphenyl	I	250	—	70—83	177
2,4-Dimethoxyphenyl	I	220	—	—	177, 178
	—	—	—	73	59
2,5-Dimethoxyphenyl	I	220	—	—	178
3,4-Dimethoxyphenyl	I	220—250	—	—	179
3,4-Dimethoxy-2,3-dimethylphenyl	I	260	—	13	180
2-Chloro-4,5-dimethoxyphenyl	Cl	230—250	—	31—36	177
5,6-Dimethoxy-3-methylphenyl	Br	300	—	18.5—20	177
5,6-Dimethoxy-2,3-dimethylphenyl	Br	280—300	—	17—20	177
2,5-Dimethoxy-3,4-dimethylphenyl	I	220	—	—	181
2,4,5-Trimethoxyphenyl	I	—	—	—	177
3-Formyl-4-methoxyphenyl	I	—	—	—	182
2-Bromo-4-carboxymethyl-5-nitrophenyl	I	150—225	—	40	174
2-Biphenylyl	I	—	—	—	31
3-Biphenylyl	I	225—260	—	16	31
4-Biphenylyl	I	225—260	—	97	31
3-Methyl-4-(*o*-tolyl)phenyl	I	200—240	*m*-bitolyl		83
2-(*p*-Terphenylyl)	I	230—290	—	49.5	24
2-(*o*-Terphenylyl)	I	215—225	—	28	24
4-(*m*-Terphenylyl)	I	320	—	10	24
2-(2-Azo-1-hydroxy-4-methylphenyl)-3-chlorophenyl	Cl	30	pyridine + toluene	92	183, 184
2-(2-Azo-1-hydroxy-4-methylphenyl)-3-bromophenyl	Br	—	—	—	183, 184
2-(1-Azo-2-hydroxynaphthyl)phenyl	Br	—	—	45	183, 184
2-(1-Azo-2-hydroxynaphthyl)-3-chlorophenyl	Cl	—	—	—	183, 184
2-(1-Azo-2-hydroxynaphthyl)-3-bromophenyl	Br	—	—	—	150, 184
2-Phenanthryl-	I	—	—	—	84
9,10-Dihydro-2-phenanthryl	I	—	—	—	84
3-Phenanthryl	I	250	biphenyl		172
" "	I	200—240	—	39	176
6-Nitro-3-phenanthryl	I	—	DMF	22	176
10,11-Dihydro-5-*n*-dibenzo (*a*, *b*)cycloheptane*	Cl	—	benzene	—	113
9-Methyl-9-fluorenyl	Cl	—	benzene	—	114

Table 4 (contd.)

Ar	X	Reaction temp., °C	Reaction conditions	Yield of biaryl, %	Refs.
1	2	3	4	5	6
2-Perylenyl	I	250	—	—	185
3-Benzanthronyl	Cl	280—300	—	4.3	186
" "	Br	250—270	—	6.3	186
" "	I	280—300	—	12.7	186
" "	I	300—320	—	11.3	186
2-Dibenzofuryl	I	200—220	—	58	187
2-Dibenzofuryl-3-methoxy-	I	180—220	—	65	187
2-Methoxy-5-flavonyl	I	250—260	—	—	182
4-Methoxy-3-flavonyl	I	250—260	—	—	182
5-Nitro-2-furyl	I	—	DMF	76	103
5-Formyl-2-furyl	I	—	ditto	50	103
5-Methoxycarbonyl-2-furyl	Br	—	"	68	103
5-Benzoyl-2-furyl	Br	—	"		103
5-Methoxycarbonyl-2-furyl 3-methyl	Br	—	"	62	103
5,5-Diethoxycarbonyl-3,4-dimethyl-2-pyrrolyl	I	—	"	31.6	101
4-Ethoxycarbonyl-3,5-dimethyl-2-pyrrolyl	I	—	"	17.6	101
3-Ethoxy-5-ethoxycarbonyl-4-methyl-2-pyrrolyl	I	—	"	28.6	101
4-Ethoxycarbonyl-1,3,5-trimethyl-2-pyrrolyl	I	160—225	in a sealed tube	58.6	188
3-Ethoxy-5-ethoxycarbonyl-4-methyl-2-pyrrolyl	I	—	DMF	30	101
3,5-Dimethoxycarbonyl-4-methyl-2-pyrrolyl	I	—	ditto	60	102
5-Ethoxycarbonyl-4-methoxycarbonyl-3-methyl-2-pyrrolyl	I	—	"	21	102
3,5-Diethoxycarbonyl-4-methyl-2-pyrrolyl	I	—	"	61—65	101, 102
" "	I	—	benzene	77	102
" "	I	—	nitrobenzene	38.4	102
" "	Br	180—210	in a sealed tube	54	99
5-Carboxyphenyl-3-ethoxycarbonyl-4-methyl--2-pyrrolyl	I	—	DMF	77	101
5-Carboxyethyl-3-carboxyphenyl-4-methyl-2-pyrrolyl	I	—	ditto	27	101
3,5-Dicarboxyphenyl-4-methyl-2-pyrrolyl	I	—	"	56	101
5-Carboxyethyl-2,4-dimethyl-3-pyrrolyl-	I	—	"	25	102
	Br	—	—	72—74	189
2-Pyridyl	Br	—	DMF	86	33, 34
" "	Br	—	tetralin	25	33
" "	Br	—	decane	50.6	33
" "	Br	—	decalin	60.7	33
" "	Br	—	*p*-cymene	63.4	33
" "	Br	—	pseudocumene	65.4	33
" "	Br	—	biphenyl	72	33
3-Pyridyl	Br	—	ditto	3—4	159
" "	I	—	"	7—8	48
4-Pyridyl	Cl	—	"	—	157, 158
2-Quinolinyl	X	—	DMF	—	34
4,5-Dimethyl-2-pyrimidinyl	Br	—	DMF	26	190
4-Phenyl-2-pyrimidinyl	Br	—	DMF	20	191
6-Methyl-2-phenyl-4-pyrimidinyl	I	—	*p*-cymene	28	192
2-Carboxymethyl-4-nitro-3-thienyl	Br	—	DMF	73	105
3-Nitro-2-selenolyl		—	xylene	76	193
5-Cyano-2-selenolyl	I	—	ditto	70	193
3,5-Dinitro-2-selenolyl	I	—	"	35	193
5-Acetyl-2-selenolyl	I	—	"	75	193
10(12)-*o*-Carboranyl	I	—	"	55	193
9(10)-*m*-Carboranyl	I	—	THF	—	194
Ferrocenyl	I	—	THF	—	194
" "	I	—	—	52	195
" "	Br	—	—	35	195
" "	Cl	—	—	7.1	195

*The condensation of 5,5-dibromo-10,11-dihydro-5*H*-dibenzo[*a*, *d*]cycloheptene to 5,5′-bi-(10,11-dihydro-5*H*-dibenzo[*a*, *d*]cycloheptenylidene) in the presence of alkyllithium [113] is apparently meant here (Ed. of Translation).

Thus the reactivity of halogens in the first stage, involving the formation of an arylcopper compound, increases from chlorine to iodine and that in the second stage, involving the decomposition of the arylcopper compound, increases from iodine to chlorine. The arylcopper compound is evidently formed via a free radical.

The following mechanism was proposed for the Ullmann reaction as the most probable:

$$\begin{array}{l} ArX + Cu \rightarrow Ar^{\cdot} + CuX \\ \qquad\quad \downarrow Cu \\ \qquad\quad ArCu \\ ArX + ArCu \rightarrow Ar{-}Ar + CuX \end{array} .$$

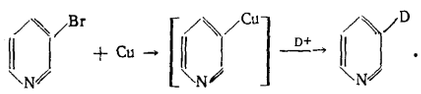
Table 5. Compilation of asymmetric biaryls synthesised by the reaction

$$ArX + Ar'X' \xrightarrow{Cu} Ar-Ar'.$$

Ar	Ar'	X	X'	Reaction temp., °C	Reaction conditions	Yield of biaryl, %	Refs.
1	2	3	4	5	6	7	8
2-Methoxyphenyl	2,3,5,6-tetrafluoro-phenyl	Br	Br	252	in a sealed tube	—	196
3,4-Dimethoxyphenyl	4-nitrophenyl	I	I	200—250	—	14—16	179
2-Methoxycarbonylphenyl	3,4-dimethoxyphenyl	Br	I	—	—	—	179
5-Carboxymethyl-2-methoxyphenyl	2,6-dimethoxyphenyl	I	I	220	—	—	197
" "	2,3,6-trimethoxyphenyl	I	I	220	—	—	197
" "	2,4,5-trimethoxyphenyl	I	I	220	—	—	197
5-Carboxymethyl-3,4-dimethoxyphenyl	2-methoxyphenyl	I	I	220	—	—	197
5-Carboxymethyl-2,3,4-trimethoxy-phenyl	4-nitrophenyl	Br	I	—	—	18	119
" "	4-methoxy-2-nitrophenyl	Br	I	250—265		11	119
4-*p*-Biphenylyl	without substituent	I	I	300	in a sealed tube	65—69	198
4-(*p*-Biphenylyl)-	2-methylphenyl	I	I	190—260	—	34	199
" "	3-methylphenyl	I	I	190—260	—	37	199
" "	4-methylphenyl	I	I	190—260	—	17	199
2-Fluorenyl	without substituent	I	I	—	—	53	84
	2-methyl-4-(*m*-tolyl)phenyl	I	I	—	biphenyl	44	83
9,10-Dihydro-2-phenanthryl	without substituent	I	I	—	—	50	84
2-Dibenzofuryl	ditto	I	I	180—220	—	58	187
" "	2-methoxyphenyl	I	I	180—220	—	57	187
" "	3-methoxyphenyl	I	I	180—220	—	60	187
3-Methoxy-2-dibenzofuryl	without substituent	I	I	180—260	—	60	187
2-Thienyl	ditto	I	I	160	quinoline	50	121
2-Pyridyl	" "	Br	I	—	—	50—55	49
" "	3-pyridyl	I	Cl	—	—	40—42	48
" "	4-pyridyl	Br	Cl	—	—	14.5—20	157, 158

According to this mechanism, the first reaction stage involves the cleavage of the carbon–halogen bond with formation of a free aryl radical. The latter then forms an organocopper compound. This is followed by the second reaction stage—the formation of a biaryl as a result of nucleophilic attack by the organocopper compound on the initial aryl halide.

The formation of an organocopper compound in the Ullmann reaction is consistent with the observed dehalogenation of the starting material [129,130,160–162] and also with the formation of pyridine from 3-bromopyridine in the presence of copper at a high temperature [35–37]. In the last case pyridine is formed owing to the decomposition by acid agents of the organocopper compound formed in the course of the reaction. When the reaction mixture obtained in the Ullmann reaction with 3-bromopyridine was decomposed with a solution of DCl in D_2O, [3-D]pyridine was obtained [163]:



The reactivities of aryl halides can also be estimated from the yields of dehalogenation products. Such dehalogenation was first observed by Ullmann [160] in the reaction of 2-chloro-3,5-dinitrobenzoic acid with copper; the main product was 3,5-dinitrobenzoic acid. Dehalogenation is observed also when the reaction is carried out in the presence of tetrahydronaphthalene [161], alcohol [162], and benzoic acid [129,130]. The last method has been used to debrominate various bromonitronaphthalenes [131]. The dehalogenation process proceeds via the mechanism

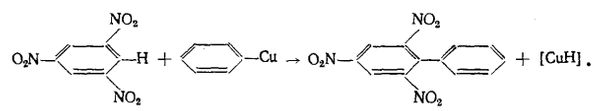
$$ArX + Cu \rightarrow ArCu \xrightarrow{H^+} ArH + Cu^+.$$

Smidt established [129] that the interaction of picryl chloride with copper in the presence of benzoic acid results in the formation of 1,3,5-trinitrobenzene in a yield of only 20%, while the reaction of 1-chloro-2,4-dinitrobenzene and *o*-chloronitrobenzene gives 1,3-dinitro- and nitro-benzenes in yields of 52 and 59% respectively. Consequently an increase of the number of electronegative constituents (in the present case nitro-groups) in the *ortho*-position relative to the halogen atom deactivates the aryl halide in the first stage of the Ullmann reaction. However, this should promote the second reaction stage, since electronegative groups in the *ortho*-position relative to the halogen should activate the carbon–halogen bond in relation to nucleophilic attack.

Indeed the interaction of iodobenzene, picryl chloride, and copper at 135°C is explosive and leads to an asymmetric biaryl [164,165].

The formation of 2,6-dinitrobiphenyl and 2,4,6-trinitrobiphenyl in the reaction of iodobenzene with *m*-dinitrobenzene and *sym*-trinitrobenzene [14] can be accounted for by the following processes:

$$C_6H_5I + Cu \rightarrow C_6H_5Cu,$$



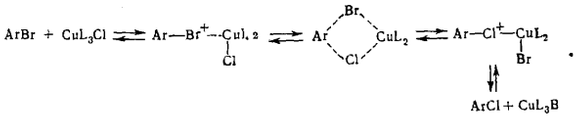
A number of 2,6-dinitrobiphenyls have been synthesised according to this scheme [167].

The reaction of *o*-bromonitrobenzene with α-iodonaphthalene gave α-bromonaphthalene (yield 40%). [14,168]

Table 6. Products obtained from bifunctional and monofunctional aryl halides.

Bifunctional aryl halide	Monofunctional aryl halide	Reaction product	Reaction temp., °C	Reaction conditions	Yield of product, %	Refs.
1,4-Di-iodobenzene	*o*-iodotoluene	1,3-dimethyl-*p*-terphenyl	220–240	bitolyl	38	83
" "	*m*-iodotoluene	1,3-dimethyl-*p*-terphenyl	–	*m*-bitolyl	33	83
" "	4-iodo-1,2-dimethoxybenzene	3,4,3",4"-tetramethoxy-*p*-terphenyl	220–250	–	–	179
" "	4-iodo-3,3'-dimethylbiphenyl	2,3,2"',3""-tetramethyl-*p*-quinquephenyl	–	–	–	83
1,3-Di-iodo-2,5-dimethoxybenzene	1-iodo-2,4-dimethoxybenzene	2,4,2',5',2",4"-hexamethoxy-*m*-terphenyl	–	*m*-bitolyl	50	178
1,3-Di-iodo-4,6-dimethoxybenzene	1-iodo-2,5-dimethoxybenzene	2,5,4,6,2",5"-hexamethoxy-*m*-terphenyl	220	–	41	83
1,3-Dibromo-2,5-dinitrobenzene	[2,4,6-D_3] iodobenzene	2,4-dinitro-*m*-[2,4,6,2",4",6"-D_6] terphenyl	190–200	in a stream of N_2	35	200
4,4-Di-iodobiphenyl	*o*-iodotoluene	2,2"'-dimethyl-*o*-quaterphenyl	200–240	*m*-bitolyl	45	83
" "	*m*-iodotoluene	3,3"'-dimethyl-*p*-quaterphenyl	–	"	42	83
" "	4-iodo-3,3'-dimethylbiphenyl	3,3"',2"",3""'-tetramethyl-*p*-sexiphenyl	–	"	43	83
4,4'-Di-iodo-3,3'-dimethylbiphenyl	iodobenzene	2',3"-dimethyl-*p*-quaterphenyl	200–240	biphenyl, in a stream of N_2	–	83
" "	*o*-iodotoluene	2,2,3",2"'-tetramethyl-*p*-quaterphenyl	–	*m*-bitolyl	39	83
" "	*m*-iodotoluene	3,2',3"',3"-tetramethyl-*p*-quaterphenyl	–	"	40	83
4,4-Di-iodo-2,2'-dimethylbiphenyl	*o*-iodotoluene	2,3,2",2"'-tetramethyl-*p*-quaterphenyl	–	–	65	83
4,4-Di-iodo-*p*-terphenyl	iodobenzene	*p*-quinquephenyl	200–240	biphenyl, in a stream of N_2	52	83
" "	*o*-iodotoluene	2,2""-dimethyl-*p*-quinquephenyl	200–240	biphenyl	47	83
" "	*m*-iodotoluene	3,3""-dimethyl-*p*-quinquephenyl	–	*m*-bitolyl	49	83
" "	4-iodo-3,3'-dimethylbiphenyl	3,3,2"",3""'-tetramethyl-*p*-septiphenyl	–	"	37	83
4,4-Di-iodo-3,3-dimethyl-*p*-terphenyl	iodobenzene	3,3"'-dimethyl-*p*-quinquephenyl	200–240	biphenyl, in a stream of N_2	42	83
2,7-Di-iodofluorene	iodobenzene	2,7-diphenylfluorene	–	biphenyl	42	83
" "	*o*-iodotoluene	2,7-di-(*o*-tolyl)-fluorene	–	*m*-bitolyl	39	83
" "	*m*-iodotoluene	2,7-di-(*m*-tolyl)-fluorene	–	"	34	83
3,6-Di-iodophenanthrene	3-iodophenanthrene	3,6-di-(3-phenanthryl)-phenanthrene	–	–	–	172,176
2,7-Di-iodo-9,10-dihydrophenanthrene	iodobenzene	2,7-diphenyl-9,10-dihydrophenanthrene	–	–	49	84
" "	*o*-iodotoluene	2,7-di-(*o*-tolyl)-9,10-dihydrophenanthrene	–	–	52	84
" "	*m*-iodotoluene	2,7-di-(*m*-tolyl)-9,10-dihydrophenanthrene	–	–	50	84
2,7-Di-iododibenzofuran	iodobenzene	2,7-diphenyldibenzofuran	–	–	30	187
" "	*m*-iodotoluene	2,7-di(*m*-tolyl)dibenzofuran	–	–	27	187

Thus there is an exchange of halogen atoms. This process can be accounted for by the following mechanism [169]:



We may note that, according to this mechanism, halogen exchange involves an organocopper halide formed in the Ullmann reaction.

The mechanism proposed above for the Ullmann reaction, involving the intermediate formation of organocopper compounds, accounts for the following typical features: (1) the Ullmann reaction takes place only with aromatic halogeno-derivatives; (2) dehalogenated products may be formed in the course of the reaction [124,125]; (3) asymmetric biaryls may be formed in high yields by the reaction of activated and non-activated aryl halides below the temperature required for the synthesis of the symmetrical biaryl from the non-activated aryl halide [14,165]; (4) the Ullmann reaction may be suppressed by the addition of proton donors [14,129–131,160]; (5) exchange of halogen atoms between the starting materials is possible in the course of the Ullmann reaction [168].

The mechanism discussed above is also consistent with the following findings: electronegative groups in the *ortho*-position relative to the halogen atom in aryl halides activate it in relation to the Ullmann reaction; the reaction of iodobenzene with copper in the presence of nitrobenzene results in the formation of triphenylamine [14]; when iodobenzene reacts with copper in the presence of *m*-dinitrobenzene and *sym*-trinitrobenzene, 1,3-dinitrobiphenyl and 1,3,5-trinitrobiphenyl are formed [14].

It is noteworthy that certain aspects of this reaction, for example the effect of solvents on the yield of product, the influence of the amount and quality of the copper on the main and side reactions, and the nature of the stabilisation of the intermediate arylcopper compound, still remain obscure. The use of new effective methods for the analysis and separation of reaction products (ultraviolet, infrared, NMR, and mass spectroscopy, gas–liquid chromatography, etc.) may and should extend significantly our knowledge in this field.

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Molecular Structures of Cyclic Organophosphorus Compounds

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The structural data for various classes of cyclic organophosphorus compounds published up to 1972 are systematically reviewed. The geometrical parameters are classified in accordance with the concepts of the valence states of atoms in the molecule and the types of chemical bonds. The dependence of bond lengths and valence angles in various cyclic systems on the number of atoms in the latter is discussed. Endocyclic parameters are compared with exocyclic parameters and also with the corresponding parameters of acyclic structures. Such comparison makes it possible, in particular, to characterise the influence of exocyclic substituents on cyclic systems which is sometimes reflected in a considerable change of the geometrical parameters. The results of studies on the conformational relations in cyclic phosphorus-containing structures are described.
The bibliography includes 274 references.

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I. INTRODUCTION

Among organophosphorus compounds, cyclic derivatives are fairly common. Much information concerning the geometrical parameters and conformational characteristics of these compounds has now accumulated and a systematic account of such data is a timely and important task. We attempted to carry this out using as a theoretical basis for the classification of the geometrical parameters the concepts of the valence state of atoms in the molecule and the types of chemical bonds (in the sense of the classical theory of structure) [1-3]. The review gives a compilation of experimental spectroscopic and diffraction data employed to determine molecular geometry and published up to 1972.

The vast majority of these data appeared after the publication of fundamental reviews on the stereochemistry of phosphorus compounds in the compilations "Topics in Phosphorus Chemistry" [4] and "Topics in Stereochemistry" [5] and also reviews on the stereochemistry of phosphorus sulphides [6], compounds with a PP bond [7], phosphonitriles [8,9], and cyclophosphazanes [10].

Data quoted in our earlier review [11] are used for comparison with the geometrical parameters of cyclic structures. Owing to lack of space, the geometrical isomerism determined by the orientation of exocyclic substituents around the phosphorus atom and other ring atoms is not discussed, although this problem is undoubtedly closely related to that of the conformation of cyclic structures.

II. PHOSPHINOBORINES [(I)-(III)]

The phosphinoborine cyclic systems consist of PB bonds, both atoms being tetracoordinate (Table 1). The comparatively scanty information concerning the structure of phosphinoborines at present available precludes a sufficiently far-reaching analysis of their chemical structure. The lengths of the PB bonds in the rings are the same in each structure within the limits of experimental error. Exocyclic PC bonds have the usual length for single bonds formed by tetracoordinate phosphorus. However, regardless of the complexity of the ring, the length of the PB bond in phosphinoborines is greater than the sum of Pauling's covalent radii (1.91 Å) [12] and also somewhat greater than the length of the analogous bond in acyclic structures (1.83-1.95 Å). Although the phosphorus atom in phosphinoborines is formally pentacovalent, the way this property is reflected in the length of the PB bonds, which cannot be regarded as single bonds, is at least unusual.

The endocyclic valence angles are determined to a considerable degree by the dimensions of the ring system. It is striking that, with increase of the number of PB units in the ring, the endocyclic BPB phosphorus valence angle increases apparently to a greater extent than the PBP boron valence angle.

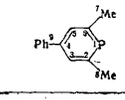
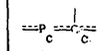
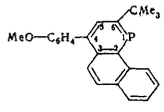
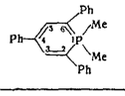
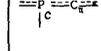
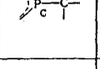
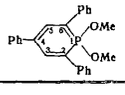
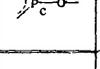
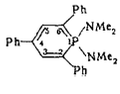
The structures of phosphinoborines have been investigated only in the crystalline state and the conformations of their ring systems have been found to be non-planar under these conditions.

Table 1. Phosphinoborines*.

Compound	Ring conformation	Endocyclic bonds		Exocyclic bonds		Endocyclic valence angles		Exocyclic valence angles		Research technique	References
		bond type	bond length, Å	bond type	bond length, Å	angle	magnitude, deg	angle	magnitude, deg		
$(Ph_2PBI_2)_2$ (I)	non-planar		2.00 (0.03)		1.81 (0.02)	BPB PBP	88.0 88.1	CPC	103.5	X-ray	13
$(Me_2PBH_2)_3$ (II)	chair	ditto	1.935 (0.009)		1.837 (0.007)	BPB PBP	118.1 (1.2) 112.2 (0.9)	CPC BPC	100.4 (0.9) 109.1 (0.6)	ditto	14
$(Me_2PBH_2)_4$ (III)	saddle	»	1.932 (0.024)	ditto	1.868 (0.012)	BPB PBP	125** 104**	CPC BPC	104.2 (1.7) 110.2 (0.7)	»	15

*Here and henceforth the subscript c denotes atoms forming part of the ring system.
**This value is quoted by Goldstein and Jacobson [16].

Table 2. Phosphabenzenes.

Compound	Rhg conformation	Endocyclic bonds		Exocyclic bonds		Endocyclic valence angles		Exocyclic valence angles		Method	Refs.
		bond type	bond length, Å	bond type	bond length, Å	angle	magnitude, deg	angle	magnitude, deg		
 (IV)	planar		1.743 (0.005)	—	—	CPC PCC	102.4 (0.2) 122.9 (0.4)	—	—	X-ray	20
 (V)	ditto	ditto	1.75	—	—	CPC PCC	103 124 (mean)	—	—	ditto	21
 (VI)	»		1.749 (0.005)		1.806 (0.006)	CPC PCC	104.72 (0.23) 119.90 (0.35)	CPC C_cPC	101.32 (0.27) 112.8 (mean)	»	22
 (VII)	»	ditto	1.72 (0.02)		1.58 (0.02)	CPC PCC	107 (2) 120 (2)	OPO C_cPO	93 (2) 114 (2)	»	23
 (VIII)	»	»	1.739 (0.004)		1.659 (0.003)	CPC PCC	105.0 (0.2) 119.9 (0.3)	NPN C_cPN	101.6 (0.2) 112.6 (mean)	»	24

III. PHOSPHABENZENES [(IV)–(VIII)]

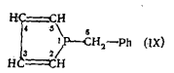
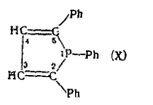
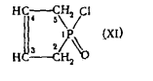
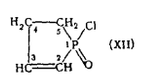
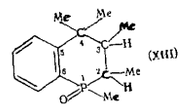
Compounds of this class are derivatives of benzene in which a phosphorus atom replaces one of the carbon atoms of the benzene ring (Table 2). The planar six-membered phosphabenzene ring is one of the first structures where the phosphorus atom was obtained in a dicoordinate state†.

† The existence of dicoordinate phosphorus in the perchlorates of phosphamethinecyanine derivatives was known previously [17–19]. In the cations $[(C_9H_9NS)_2P]^+$ [18] and $[(C_{11}H_{10}N)_2P]^+$, [19] the phosphorus atom forms two PC bonds in each case. In the first case, the cation is almost planar and has a symmetrical structure [r(PC) = 1.76 ± 0.01 Å, ∠CPC = 104.6°]. In the second case, the cation was found to be asymmetric, which is shown by a difference between the angles of rotation of the $C_{11}H_{10}N$ residues about the PC bonds and by the non-equivalence of the bonds themselves [r(PC) = 1.77 ± 0.01 and 1.81 ± 0.01 Å; ∠CPC = 100.4°].

According to X-ray diffraction data, both endocyclic PC bonds in (IV) and (V) have the same length, which is intermediate between the average lengths of $-\overset{|}{\underset{|}{P}}=C\diagup\diagdown$ bonds (1.65–1.78 Å) of single PC bonds (1.74–1.94 Å) in acyclic structures [11]. The four CC bonds in the ring also have the same length (1.388 ± 0.009 Å). The planarity of the six-membered cyclic system is achieved by an increase of the PCC and CCC angles to 122–126°, while the CPC angle is relatively small (102–103°).

In compound (IV), the displacement of the atoms in the heterocycle from the optimum mean-square plane does not exceed 0.005 Å. The displacement of the exocyclic $C_{(7)}$, $C_{(8)}$, and $C_{(9)}$ atoms from the plane of the ring is not more than 0.024 Å. All these data suggest that the phosphabenzene ring system is aromatic. The NMR and ultraviolet spectroscopic data are consistent with this conclusion [25]. With increase of the coordination number of phosphorus to four, the equivalence of the endocyclic PC (as well as

Table 3. Phospholes and phospholenes.

Compound	Ring conformation	Endocyclic bonds: bond type	Endocyclic bonds: bond length, Å	Exocyclic bonds: bond type	Exocyclic bonds: bond length, Å	Endocyclic valence angles: angle	Endocyclic valence angles: magnitude, deg	Exocyclic valence angles: angle	Exocyclic valence angles: magnitude, deg	Method	Refs.
 (IX)	envelope (weak)	$>P_c-C_c<$	1.783 (0.005)	$>P_c-\overset{\vert}{C}-$	1.858 (0.005)	CPC PCC	90.7 (0.2) 110.0 (0.4)	C_cPC PCC_{Ph}	106.0 (0.2) 116.4 (0.4)	X-ray	30
 (X)	ditto	ditto	1.822	$>P_c-C<$	1.822	—		C_cPC	105.3	ditto	31
 (XI)	envelope	$=P_c-C_c-$	1.835 (0.008)	$=P_c-Cl$ $-P_c=O$	2.040 (0.008) 1.440 (0.010)	CPC PCC	98.5 (1.5) 101.3 (1.5)	CP=O ClP=O CPCl	118.3 115.3(2.0) 101.3(1.0)	el.dif	32
 (XII)	envelope (methylene group closest to P atom displaced from plane of ring)	ditto $=P_c-C_c=$	1.830 (0.008) 1.791 (0.008)	$=P_c-Cl$ $-P_c=O$	2.057 (0.008) 1.451 (0.009)	CPC PCC CP=C	94.2 (1.0) 102.6 (calc.) 112.8 (1.0)	$C_cP=O$ ClP=O $-C_cPCl$ $=C_cPCl$	117.5(3.0) 114.8(3.0) 105.6(2.0) 97.0(2.0)	ditto	33
 (XIII)	half chair	$=P_c-C_c-$ $=P_c-C<$	1.768 (0.009) 1.762 (0.009)	$=P_c-C-$ $-P_c=O$	1.864 (0.012) 1.471 (0.007)	CPC PCC PC=C	104.3 (0.4) 108.5 (0.6) 123.6 (0.6)	$-C_cP=O$ CP=O $-C_cPC$ $=C_cPC$	113.8(0.4) 109.6(0.5) 110.2(0.5) 104.7(0.5)	X-ray	34

CC) bonds in phosphabenzene remains unaffected. Within the limits of experimental error, their length remains the same as for dicoordinate phosphorus and the endocyclic CPC angle increases only by 2–4°. However, the ring conformation deviates a little from planarity. Thus in compound (VI) the maximum displacement of a ring atom from the optimum plane reaches 0.055 Å. In compounds (VII) and (VIII), the displacement of the ring C atoms from the $C_{(3)}PC_{(5)}$ plane reaches up to 0.11 and 0.055 Å respectively. Although on passing from di- to tetra-coordinate phosphorus, the geometry of the phosphabenzene ring changes little, the problem of the aromaticity of the ring system in the latter case is more complex. This is particularly due to the ill-defined role of the *d* orbitals of phosphorus [26].

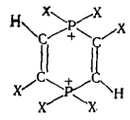
IV. PHOSPHOLES [(IX)–(X)] AND PHOSPHOLENES [(XI)–(XIII)]

According to microwave studies, the ring system of pyrrole, the nitrogen analogue of phosphole, is planar [27,28]. However, the first determinations of the structure of phosphole derivatives (Table 3) by X-ray diffraction showed that their five-membered ring with tricoordinate phosphorus and two C=C double bonds (1.350 Å) is non-planar. In particular, in compound (IX) the phosphorus atom deviates from the plane of the remaining ring atoms by 0.21 Å (the "envelope" conformation). The exocyclic $C_{(6)}$ atom is displaced relative to this plane in the direction opposite to that of the displacement of the phosphorus atom, i.e. it is, as it were, located in an equatorial position. According to one view [29], based on thermochemical data and semiempirical quantum-chemical calculations, the phosphole ring system may be aromatic. However, the barrier to the inversion of the phosphorus atom (16 kcal mole^{-1}), obtained from the NMR spectra of 1-isopropyl-2-methyl-5-phenylphosphole [35], is fairly high. The experimental structural parameters of phospholes do not indicate any significant delocalisation of electrons over the five-membered ring, although the $>P_c-C_c<$ bond in the ring is probably somewhat shorter and approaches the

length of the $=P_c-C_c\langle$ bond involving tetracoordinate phosphorus in phospholenes‡.

Phospholenes—phosphorus–carbon heterocycles with one double bond—also have non-planar conformations, the characteristics of which are determined, in particular, by the position of the double bond relative to the phosphorus atom. According to electron diffraction data, compound (XI) has the envelope conformation with displacement of the phosphorus atom from the plane of the ring. The $C_{(2)}PC_{(5)}/CCC$ dihedral angle in this structure is 13°. In compound (XII), the methylene group closest to the phosphorus atom is displaced from the P–C=C–C plane (dihedral angle 27°). In the condensed system (XIII), studied in the crystalline phase, the $C_{(4)}$, $C_{(5)}$, $C_{(6)}$, and P atoms are coplanar to within 0.05 Å, while the $C_{(2)}$ and $C_{(3)}$ atoms are 0.6 Å and 0.2 Å above and below this plane.

‡ On the basis of a combined spectroscopic study (infrared, ultraviolet, and NMR spectra)[36,37], it has been suggested that π electrons are delocalised in the six-membered PC system of the hexaphenyldiphosphoninocyclohexadiene cation.



However, X-ray diffraction data do not agree with the delocalisation hypothesis, at any rate in the analogous system with alkyl substituents[38]: $r(C=C)_c = 1.340(0.009)$ Å, $r(PC)_c = 1.788(0.008)$ Å, and $r(PC) = 1.793(0.003)$ Å, and the average valence angle of the phosphorus atom is 109.5 ± 0.5°; the average valence angle of the $\rangle C=$ atoms is 120.0 ± 2.2°. The ring was found to be planar to within 0.003 Å.

V. SATURATED PHOSPHORUS–CARBON HETEROCYCLES [(XIV)–(XXIV)]

One of the most interesting saturated PC ring systems is ethylenephosphine (XIV)—a three-membered ring with tricoordinate phosphorus (Table 4). According to microwave data, the CPC endocyclic angle in this compound is only 47.4° ± 0.5°. This is the smallest valence angle of the phosphorus atom ever found. The length of the $\rangle P_c-C_c-$ bonds is geater by 0.017 Å than in the open-chain analogue $HP(CH_3)_2$ (1.850 Å).[11]

According to X-ray diffraction data, in six-membered rings with tricoordinate phosphorus [compounds (XV) and (XVI)], the CPC endocyclic angle increases to about 98° and the $\rangle P_c-C_c-$ bonds are shortened to the usual value of 1.84–1.85 Å. Both these rings have a non-planar conformation of the chair type with an axial location of the exocyclic phenyl substituent at the phosphorus atom despite the difference between the crystal fields in their macrostructures. The deviation of the ring atoms from the average plane diminishes somewhat at its phosphorus end.

Table 4. Saturated phosphorus–carbon heterocycles.

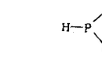
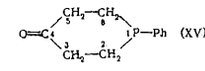
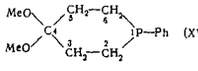
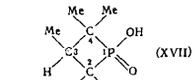
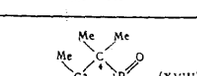
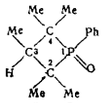
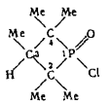
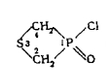
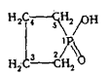
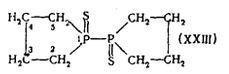
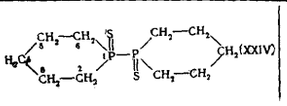
Compound	Ring conformation	Endocyclic bonds		Exocyclic bonds		Endocyclic valence angles		Exocyclic valence angles		Method	Refs.
		bond type	bond length, Å	bond type	bond length, Å	angle	magnitude, deg	angle	magnitude, deg		
 (XIV)	planar	$\rangle P_c-C_c-$	1.867 (0.005)	$\rangle P_c-H$	1.428 (0.005)	CPC	47.4 (0.5)	CPH	95.2 (0.5)	microwave	39
 (XV)	chair	ditto	1.838 (0.005)		1.837 (0.005)	CPC PCC	98.2 (0.2) 116.5 (0.2)	C_cPC	102.9 (0.2)	X-ray	40
 (XVI)	ditto	»	1.855 (0.005)	ditto	1.854 (0.005)	PCP PCC	97.7 (0.2) 116.3 (0.2)	C_cPC	102.3 (0.2)	ditto	41
 (XVII)	non-planar	$=\!\rangle P_c-C_c-$	1.83 (0.02)	$=\!\rangle P_c-O-$ $-\rangle P_c=O$	1.54 (0.01) 1.48 (0.01)	CPC PCC	82.5 (0.5) 86.0 (0.6)		(106–121)	»	42
 (XVIII) (Me/P = O *cis*-form)	ditto	ditto	1.88 (0.02)	$=\!\rangle P_c-C\langle$ $-\rangle P_c=O$	1.79 (0.01) 1.50 (0.02)	CPC PCC	84.9 (0.6) 86.7 (0.8)	$C_cP=O$ $C_{Ph}P=O$ C_cPC_{Ph}	120.0 (0.6) 110.0 (0.6) 111.4 (0.6)	»	43

Table 4 (continued).

Compound	Ring conformation	Endocyclic bonds: bond type	Endocyclic bonds: bond length, Å	Exocyclic bonds: bond type	Exocyclic bonds: bond length, Å	Endocyclic valence angles: angle	Endocyclic valence angles: magnitude, deg	Exocyclic valence angles: angle	Exocyclic valence angles: magnitude, deg	Method	Refs.
 (XIX) (Me/P = O *trans*-form)	non-planar	$=P_c-C_c-$	1.836 (0.004)	$=P_c-C$	1.809 (0.004)	CPC	81.3 (0.2)	$C_cP=O$	115.2 (0.2)	X-ray	44
				$-P_{II}=O$	1.494 (0.002)	PCC	87.1 (0.2)	$C_{Ph}P=O$	109.2 (0.2)		
								C_cPC_{Ph}	116.9 (0.2)		
 (XX)	ditto	ditto	1.84 (0.03)	$=P_c-Cl$	2.06 (0.01)	CPC	85.9 (1.4)	$C_cP=O$	122.0 (1.1)	ditto	45
				$-P_c=O$	1.48 (0.02)	PCC	84.2 (1.5)	ClP=O	110.1 (0.8)		
								C_cPCl	107.1 (0.9)		
 (XXI)	»	»	1.836 (0.015)	$=P_c-Cl$	2.032 (0.015)	CPC	86 (2)	$C_cP=O$	121	el. dif.	46
				$-P_c=O$	1.441 (0.010)			ClP=O	118 (3)		
								C_cPCl	103 (3)		
 (XXII)	half chair (twisted envelope)	»	1.786 (0.017)	$=P_c-O-$	1.567 (0.006)	CPC	94.8 (0.5)	CP=O	116 (mean)	X-ray	47
								OP=O	113.4 (0.5)		
				$-P_c=O$	1.473 (0.01)	PCC	106.0 (1.5)	CPO	107.4 (mean)		
 (XXIII)	non-planar	»	1.820 (0.007)	$=P_c-P_c=$	2.210 (0.004)	CPC	96.6 (0.3)	CP=S	117.6 (1.0)	ditto	48
				$-P_c=S$	1.950 (0.002)	PCC	105.0 (0.6)	PP=S	111.1 (1.0)		
								CPP	106.3 (1.0)		
 (XXIV)	ditto	»	1.810 (0.011)	$=P_c-P=$	2.21 (0.004)	CPC	101.8 (0.4)	CP=S	115.3 (0.4)	»	49
				$-P_c=S$	1.950 (0.004)	PCC	108.8 (0.8)	PP=S	112.7 (0.2)		
								CPP	105.2 (0.4)		

The distribution of torsion angles is as follows (in degrees):

	$PC_{(2)}C_{(3)}C_{(4)}$	$C_{(2)}C_{(3)}C_{(4)}C_{(5)}$	$C_{(3)}C_{(4)}C_{(5)}C_{(6)}$
in (XV)	−49.8	+53.0	−56.1
in (XVI)	−58.0	+62.4	−60.5

	$C_{(4)}C_{(5)}C_{(6)}P$	$C_{(5)}C_{(6)}PC_{(2)}$	$C_{(6)}PC_{(2)}C_{(3)}$
in (XV)	+56.3	−47.6	+44.3
in (XVI)	+56.1	−44.7	+45.5

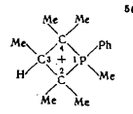
According to the NMR spectrum, in a solution of compound (XVI), one conformation also predominates, as has been suggested for the solid phase [41].

In saturated four-, five-, and six-membered rings with tetracoordinate phosphorus, the length of the $=P_c-C_c-$ bonds does not differ, within the limits of experimental error, from the values found for open-chain compounds. At the same time, the endocyclic CPC angles are determined by the ring size and increase from 82–86° in compounds (XVII)–(XXI) to 94.5–96.5° in compounds (XXII) and (XXIII) and to 102° in compound (XXIV). However, the last value is still less than the analogous angle in open-chain compounds (104–109°). [11] The ring conformations in these compounds are also non-planar. The displacement of the atoms from the optimal mean-square plane in the four-membered rings of (XVII)–(XXI) is 0.10–0.15 Å. The dihedral angles and other characteristics of the conformations of the rings§ are given in Table 5.

In compounds (XVIII)–(XX), the single methyl group at the $C_{(3)}$ atom is fixed in the equatorial position. Thus in these structures there is geometrical isomerism determined by the position of the exocyclic substituent at the P atom.

In the five-membered ring of (XXII), the P, $C_{(2)}$, $C_{(4)}$, and $C_{(5)}$ atoms are approximately in the same plane (the angle between the normals to the $PC_{(2)}C_{(5)}$ and $PC_{(5)}C_{(4)}$

§ In the cyclic cation



the $C_{(2)}PC_{(4)}/C_{(2)}C_{(3)}C_{(4)}$ dihedral angle is 24°. The remaining structural parameters have the following values: $r(PC)_c = 1.93(0.02)$ Å, $\angle(CPC)_c = 82.6°$, and $\angle(PCC)_c = 84.7°$. The methyl group at the $C_{(3)}$ atom is in the *cis*-position relative to the phenyl group.

planes is only 5°), from which only the $C_{(3)}$ atom deviates significantly. The torsion angles relative to the bonds in the ring have the following values starting from $PC_{(2)}$: 5°, 24°, 36°, 30°, and 14°¶.

Table 5.

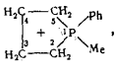
Compound	Dihedral angles, deg			Position of P=O bond	Position of CH_3 group at $C_{(3)}$ atom relative to P=O bond
	$C_{(2)}PC_{(4)}/C_{(2)}C_{(3)}C_{(4)}$	$PC_{(2)}C_{(3)}/PC_{(4)}C_{(3)}$	$C_{(2)}PC_{(4)}/XP{=}O$		
(XVII)	19.6				
(XVIII)	21.6	20.6	91.6	eq.	*cis-*
(XIX)	23.8	22.3	91.1	ax.	*trans-*
(XX)	26.4			aq.	*cis-*
(XXI)	10and35			mixture of isomers with ax. and eq. P=O bonds in proportions of 4 : 1	

VI. PHOSPHADIAZOLES [(XXV)–(XXVIII)], PHOSPHAOXADIAZOLES (XXIX), AND PHOSPHAOXAZOLES (XXX)

After phosphabenzenes, phosphadiazoles are the second class of compounds in which the existence of dicoordinate phosphorus was demonstrated (Table 6). The planarity of the five-membered ring system with dicoordinate phosphorus was studied by electron diffraction. The experimental geometrical parameters and the vibration, ultraviolet, and NMR spectroscopic data for compounds of this class [52,53,58] suggest that electrons are delocalised in the phosphadiazole rings of (XXV) and (XXVI) as in phosphabenzene derivatives.

The conformation of the five-membered rings with tricoordinate phosphorus in compounds (XXVII), (XXIX), and (XXX) is non-planar: the phosphorus atom is markedly displaced from the plane of the remaining four atoms (envelope conformation). According to electron diffraction data, the dihedral angles characterising the displacement of the phosphorus atom from the plane are respectively 28.8°, 20.0°, and 23.0°. The lengths of the endocyclic PO and PN bonds are normal for tricoordinate phosphorus [11]†. At the same time, it is striking that the endocyclic valence angle at the tricoordinate phosphorus atom is appreciably greater (by about 5°) than that at the dicoordinate phosphorus atom. The exocyclic PCl bonds in (XXVII), (XXIX), and (XXX) occupy axial positions. Their lengths (2.17–2.19 Å) are unusual for covalent bonds of tricoordinate phosphorus. They are significantly longer than in all the cases known previously (2.04–2.08 Å). [11]

¶ A fundamentally identical ring conformation was found in the cation [51]



where the torsion angles have the following values (also starting from $PC_{(2)}$): 5°, 26°, 40°, 36°, and 17°. The remaining parameters of this structure are as follows: $r(PC)_C$ = 1.765(0.02) Å, $r(PC_{Me})$ = 1.80(0.02) Å, $r(PC_{Ph})$ = 1.76(0.02) Å, $\angle(CPC)_C$ = 94.8(1.1)°, $\angle(PCC)_C$ = 101.1(1.7)°.

† Anomalous PN bond lengths were found by X-ray diffraction in the structure of the cation $Cl_4P(NCH_3)_2C^+Cl$—a planar four-membered ring system with hexacoordinate phosphorus [59]. The lengths of both PN bonds—axial (1.91 ± 0.04 Å) and equatorial (1.85 ± 0.06 Å)—are significantly greater than the sum of the covalent radii after correction for heteropolarity (1.75 Å). This can also be said of the exocyclic PCl bonds (2.15 ± 0.02 Å and 2.09 ± 0.02 Å) found in this structure.

VII. PHOSPHONITRILES [(XXXI)–(LXI)]

Phosphonitriles are cyclic structures comprising a variable number of formally unsaturated $-\overset{|}{\underset{|}{P}}{=}N-$ units formed by tetracoordinate quinquevalent phosphorus and dicoordinate tervalent nitrogen. Nevertheless there is no alternation of single and multiple bonds in phosphonitriles (Table 7).

1. Phosphonitriles with Identical Substituents at the Phosphorus Atoms [(XXXI)–(L)]‡

When the substituents at all the phosphorus atoms are the same, the PN bonds in the ring have the same length, which however is much smaller, particularly in more complex rings, when the number of ring units $n > 4$, than the $=\overset{|}{\underset{|}{P}}-N\langle$ (1.60–1.71 Å) and even $-\overset{|}{\underset{|}{P}}{=}N-$ (up to 1.64 Å) bond lengths in acyclic structures [11]. The length of the PN endocyclic bonds is significantly influenced by the substituents at the phosphorus atom. Whereas in the trimers this effect is relatively small [the average r(PN) remains within the limits 1.58 ± 0.02 Å], in the octafluorotetramer (XLIII) r(PN) = 1.507 Å and in the decachloropentamer (XLVII) r(PN) = 1.521 Å, which is far outside the range of the other values. Although the endocyclic valence angles of the phosphorus atom vary in these structures comparatively little (117–123°), these changes are also related to the properties of the substituents. A large NPN angle is obtained when the substituents are halogen atoms. The range of variation of the PNP angles is much greater (120–149°). A gradual increase in the PNP angles takes place with increase of ring size up to hexamers, but subsequently the angles appear to decrease. A systematic effect of the properties of exocyclic substituents on the PNP angles could not be discovered.

It is interesting that the ratio of the ranges of variation of the NPN and PNP angles in phosphonitriles is the reverse of the ratio of the ranges of variation of the BPB and PBP angles in phosphinoborines (see above).

The conformations of the phosphonitrile ring systems bear a definite relation to the number of PN units. The trimers (XXXI)–(XXXVIII) have planar or almost planar ring conformations, the average endocyclic angle being always close to 120°. As a rule, the deviations from the ideal symmetry D_{3h} are minimal: the displacement of the ring atoms from the plane usually does not exceed 0.07 Å. More pronounced distortions were found in only two cases. In compound (XXXII), five ring atoms lie in one plane, while one of the N atoms is displaced from it by 0.15 Å. In (XXXIII), two nitrogen atoms are displaced from the plane of the remaining ring atoms in opposite directions

‡ Symmetrical phosphonitriles with non-geminal substituents [compounds (XLI), (XLV), and (XLVI)] are also included here.

Table 6. Phosphadiazoles, phosphaoxadiazoles, and phosphaoxazoles.

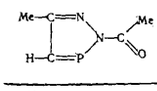
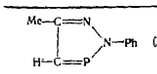
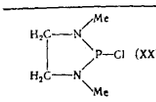
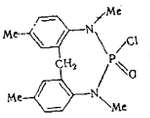
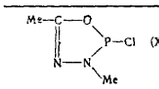
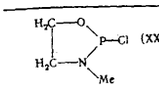
Compound	Ring conformation	Endocyclic bonds: bond type	Endocyclic bonds: bond length, Å	Exocyclic bonds: bond type	Exocyclic bonds: bond length, Å	Endocyclic valence angles: angle	Endocyclic valence angles: magnitude, deg	Exocyclic valence angles: angle	Exocyclic valence angles: magnitude, deg	Method	Refs.
 (XXV)	planar	$=P_c-N_c<$ $-P_c=C_c<$	1.68 (0.01) 1.75 (0.01)	—		NPC PNN	89.0 (1.5) 115.0 (2.5)	—		el. dif.	52
 (XXVI)	ditto	$=P_c-N_c<$ $-P_c=C_c<$	1.65 (0.03) 1.75 (0.03)	—		NPC PNN	92 110 (assumed)	—		ditto	53
 (XXVII)	envelope	$>P_c-N_c<$	1.68 (assumed)	$>P_c-Cl$	2.19 (0.02)	NPN PNC CCN	89.3 113.7 (1.0) 106.2 (1.5)	NPCl	102 (2)	»	54
 (XXVIII)	non-planar	$=P_c-N_c<$	1.644 (0.006)	$=P_c-Cl$ $-P_c=O$	2.069 (0.003) 1.492 (0.005)	NPN PNC	108.3 (0.3) 120.1 (mean)	NPCl NP=O ClP=O	103.0 (mean) 115.8 (mean) 109.2 (0.2)	X-ray	55
 (XXIX)	envelope	$>P_c-N_c<$ $>P_c-O_c-$	1.70 (0.015) 1.60 (0.015)	$>P_c-Cl$	2.170 (0.005)	NPO PNN POC	95 108 105.5	NPCl= =OPCl	101 (1)	el. dif.	56
 (XXX)	ditto	$>P_c-N_c<$ $>P_c-O_c-$	1.692 (0.013) 1.622 (0.013)	$>P_c-Cl$	2.174 (0.009)	NPO POC CCO=CCN PNC	93.9 115.6 107.8 (1.0) 112.7 (1.0)	NPCl OPCl	101.2 (1.5) 98.1 (1.5)	ditto	57

Table 7.

Compound	Ring conformation	Endocyclic bonds: bond type	Endocyclic bonds: bond length, Å	Exocyclic bonds: bond type	Exocyclic bonds: bond length, Å	Endocyclic valence angles: angle	Endocyclic valence angles: magnitude, deg	Exocyclic valence angles: angle	Exocyclic valence angles: magnitude, deg	Method	Refs.
A. Phosphonitriles with all substituents of the same type at the phosphorus atoms											
$(NPPh_2)_3$ (XXXI)	chair (weak)	$=P_c=N_c=$	1.597 (0.006)	$-P_c-C<$	1.804 (0.007)	NPN PNP	117.8 (0.4) 122.1 (0.3)	CPC NPC	103.8 (0.3) 108.6 (0.3)	X-ray	72
$[NP(-N=C=S)_2]_3$ (XXXII)	non-planar (weak)	ditto	1.58 (0.05)	$-P_c-N=$	1.63 (0.01)	NPN PNP	119 (3) 121 (4)	NPN N_cPN PNC N=C=S	100 (1) 109 (2) 152 (10) 175 (2)	ditto	73
$[NP(OPh)_2]_3$ (XXXIII)	non-planar (weak)	»	1.575 (0.002)	$-P_c-O-$	1.582 (0.002)	NPN PNP	117.3 (0.2) 121.9 (0.3)	OPO NPO POC	98.1 110.0 123.2	»	74
$[NP(OC_6H_4)_2]_3$ (XXXIV)	boat (weak)	»	1.572 (0.006)	$-P_c-O_c-$	1.584 (0.005)	NPN PNP	118.4 (0.25) 121.0 (0.25)	$(OPO)_c$ NPO $(POC)_c$	102.7 (0.25) 108.6 (0.25) 120.0 (0.4)	»	75
$(NPO_2C_6H_4)_3$ (XXXV)	planar	»	1.576 (0.002)	ditto	1.598	NPN PNP	119 122	$(OPO)_c$ NPO	97 107.0	»	76
$(NPF_2)_3$ (XXXVIa)	ditto	»	1.586 (0.013)	$-P_c-F$	1.548 (0.013)	NPN=PNP	120.0 (assume)	FPF	98.8 (3.0)	el. dif	77
$(NPF_2)_3$ (XXXVIb)	»	»	1.560 (0.012)	ditto	1.521 (0.012)	NPN PNP	119.4 (0.9) 120.3 (0.9)	FPF NPF	99.1 (0.7) 109.0 (0.6)	X-ray	78
$(NPCl_2)_3$ (XXXVIIa)	chair (weak)	»	1.582 (0.005)	$-P_c-Cl$	2.006 (0.003)	NPN=PNP	119.7 (0.2) (mean)	ClPCl	101.5 (1.5)	el. dif	79

Table 7 (continued).

Compound	Ring conformation	Endocyclic bonds		Endocyclic bonds		Endocyclic valence angles		Endocyclic valence angles		Method	Refs.
		bond type	bond length, Å	bond type	bond length, Å	angle	magnitude, deg	angle	magnitude, deg		
$(NPCl_2)_3$ (XXXVIIb)	chair (weak)		1.581 (0.003)		1.993 (0.002)	NPN PNP	118.4 (0.2) 121.4 (0.3)	ClPCl NPCl	101.4 (0.1) 108.9 (0.3)	X-ray	80
$(NPBr_2)_3$ (XXXIII)	ditto	ditto	1.576 (0.008)		2.162 (0.004)	NPN PNP	118.5 (0.6) 121.4 (0.6)	BrPBr NPBr	102.1 (0.1) 108.8 (0.5)	ditto	81
$(NPMe_2)_4$ (XXXIX)	saddle	»	1.596 (0.005)		1.805 (0.008)	NPN PNP	119.8 (0.3) 131.9 (0.3)	CPC NPC	104.1 (0.3) 108.0 (mean)	»	82
$[NP(NMe_2)_2]_4$ (XL)	ditto	»	1.578 (0.01)		1.679 (0.01)	NPN PNP	120.1 (0.5) 133.0 (0.6)	NPN PNC CNC N_cPN	103.8 (0.5) 119.1 (mean) 116.0 (1.0) 108 (mean))	»	83
$N_4P_4Ph_4(NHMe)_4^*$ (XLI)	chair	»	1.59 (0.01)	 	1.81 (0.01) 1.68 (0.01)	NPN PNP	120 (mean) 128 (mean)	CPN PNC	106.0 (0.5) 120 (0.5)	»	84
$[NP(OMe)_2]_4$ (XLII)	saddle	»	1.570 (0.01)		1.581 (0.01)	NPN PNP	121.0 (0.6) 132.2 (0.7)	OPO POC NPO	105.5 (0.5) 121.0 (0.9) 107.4 (0.5)	»	85
$(NPF_2)_4$ (XLIII)	planar	»	1.507 (0.017)		1.514 (0.015)	NPN PNP	122.7 (1.0) 147.2 (1.4)	FPF NPF	99.9 (1.0) 108.0 (1.0)	»	86
$(NPCl_2)_4$ (XLIVa) (*K*-form)	boat	»	1.570 (0.01)		1.989 (0.004)	NPN PNP	121.2 (0.5) 131.3 (0.6)	ClPCl ClPN	102.8 (0.2) 108 (mean))	»	87
$(NPCl_2)_4$ (XLIVb) (*T*-form))	chair	ditto	1.559 (0.012)	ditto	1.992 (0.004)	NPN PNP	120.5 (0.7) 135.6 (mean)	ClPCl ClPN	103.1 (0.2) 108 (mean)	»	88
$N_4P_4Ph_4Cl_4^*$ (XLV) *trans*-isomer	chair	»	1.57 (mean)	 	1.79 (mean) 2.03 (mean)	NPN PNP	120 (mean) 135.5 (mean)	ClPC	104 (mean)	»	84
$N_4P_4Ph_4Cl_4^*$ (XLVI) *cis*- isomer	crown	»	1.573 (0.008)	 	1.783 (0.010) 2.042 (0.004)	NPN PNP	121.2 (0.5) 137.4 (0.5)	ClPC	103.0 (0.5)	»	89
$(NPCl_2)_5$ (XLVII)	nearly planar	»	1.521 (0.02)	ditto	1.961 (0.01)	NPN PNP	118.3 (1.0) 148.6 (1.5)	ClPCl ClPN	102.2 (0.5) 108.7 (mean))	»	90
$[NP(NMe_2)_2]_6$ (XLVIII)	boat	»	1.563 (0.01)		1.669 (0.01)	NPN PNP	120.0 (0.5) 147.5 (0.7)	NPN PNC CNC N_cPN	102.9 (0.5) 120.1 (0.8) 113.0 (1.0) 108.2 (mean)	»	91
$[NP(OMe)_2]_6$ (XLIX)	consists of two plane and parallel segments	»	1.561 (0.005)		1.576 (0.005)	NPN PNP	116.7 (mean) 136.7 (mean)	OPO POC N_cPO	101.3 (mean) 120.6 (0.4) 109.4 (mean)	»	92
$(NCPl_2)_\infty$ (L)	plane fibres	»	1.60			NPN PNP	119 127			»	93
B. Phosphonitriles with substituents of different types at the phosphorus atoms											
$N_3P_3Ph_2F_4$ (LI)	boat (weak)	»	1.539 (0.005) 1.558 (0.004) 1.618 (0.005)	 	1.79 (0.01) 1.526 (0.005)	NPN PNP	115.5 (0.3) 120.6 (0.3) 120.5 (0.2)	CPC NPC FPF NPF	107.9 (0.3) 108.4 (0.3) 96.9 (0.2) 109.4 (0.3)	»	94
$N_3P_3Ph_2Cl_4$ (LII)	chair (weak)	»	1.555 (0.005) 1.578 (0.005) 1.615 (0.005)	 	1.788 (0.006) 1.998 (0.002)	NPN PNP	115.2 (0.3) 119.7 (0.3) 119.2 (0.3) 122.0 (0.3)	CPC ClPCl	104.4 (0.3) 100.3 (0.1)	»	95

Table 7 (continued).

Compound	Ring conformation	Endocyclic bonds: bond type	Endocyclic bonds: bond length, Å	Exocyclic bonds: bond type	Exocyclic bonds: bond length, Å	Endocyclic valence angles: angle	Endocyclic valence angles: magnitude, deg	Exocyclic valence angles: angle	Exocyclic valence angles: magnitude, deg	Method	Refs.
$N_3P_3Ph_4Cl_2$ (LIII)	boat (weak)		1.556 (0.009) 1.578 (0.008) 1.609 (0.008)	 	1.792 (0.011) 2.017 (0.005)	NPN PNP	115.5 (0.4) 120.7 (0.5) 121.1 (0.5) 124.9 (0.5)	CPC ClPCl	104.4 (0.5) 98.5 (0.2)	X-ray	96
$N_3P_3Cl_5F$ (LIV)	planar	ditto	1.563 (0.007)		1.963 (0.005) (mean)	NPN PNP	118.5 (0.5) 121.9 (0.4)	HalPHal NPHal	100.5 (0.2) 108.9 (0.4)	ditto	97
$N_4P_4Me_2F_6$ (LV)	saddle	»	1.487 (0.006) 1.532 (0.006) 1.470 (0.006) 1.584 (0.006)	 	1.481 (0.009) 1.794 (0.008)	NPN PNP	125.4 (0.5) 116.9 (0.5) 145.0 (0.5)	FPF CPC FPN CPN	93.7 (0.5) 105.7 (0.6) 107.9 (0.5) 108.4 (0.4)	»	98
$N_4P_4Me_4F_4$ (LVI)	saddle	»	1.53 (0.01) 1.59 (0.01)	 	1.52 (0.01) 1.81 (0.01)	NPN PNP	125.9 (0.9) 117.5 (0.5) 134.6 (0.7)	FPF CPC FPN CPN	96.7 (1.2) 106.9 (0.7) 108 (mean) 108 (mean)	»	99
C. Diphosphatriazines and phosphatriazines											
$NPCl_2(NSOCl)_2$ (LVII)	chair	»	1.585 (0.013)		1.957 (0.006)	NPN PNS	115.3 (0.7) 122.5 (0.8)	ClPCl NPCl	104.4 (0.3) 109.2 (0.5)	»	100
$(NPPh_2)_2NCMe$ (LVIII)	twisted boat	»	1.597 (0.003) 1.620 (0.003)		1.801 (0.002)	PNP PNP PNC	116.5 (0.2) 115.4 (0.2) 119.9 (0.2)	CPC NPC	105.4 (0.2) 108.5 (mean)	»	101
$(NPPh_2)_2NCNMe_2$ (LIX)	ditto	»	1.597 (0.002) 1.608 (0.002)	ditto	1.802 (0.002)	NPN PNP PNC	117.1 (0.1) 115.4 (0.1) 120.9 (0.1)	CPC NPC	104.1 (0.1) 108.1 (mean)	»	102
D. Structures complicated by additional covalent bonds at the nitrogen atom											
$[(NPMe_2)_4H]CuCl_3$ (LX)	boat	»	1.56 (0.02) 1.60 (0.02) 1.63 (0.02) 1.67 (0.02)		1.78 (0.03)	NPN PNP	115 (1.5) 113 (1.5) 129 (mean)	CNC	106.6 (mean)	»	103
$N_7P_6Cl_9$ (LXI)	condensed non-planar structure	 	1.572 (0.007) 1.559 (0.007) 1.723 (0.006)		1.980 (0.004) 2.004 (0.004)	N=P=N N—P=N PNP	116.9 110.7 125.5	ClPCl NPCl NPN	101.6 (0.1) 109.3 (0.3) 113.1 (0.4)	»	104

*Each ring phosphorus atom has two different substituents.

by 0.13 and 0.17 Å. Since most of the investigations were made by X-ray diffraction on crystalline materials, the deviations from the planar conformation are frequently accounted for by intermolecular interactions. This view appears to be confirmed by the vibration spectra of solutions of (XXXII) [60] and also the spectra of the tetrafluoro- and hexachloro-compounds in solutions and in liquid and gaseous phases [61,62], which agree with the D_{3h} symmetry. When the substituents at the phosphorus atoms are very bulky, the distortion of the planar conformation can also be a consequence of intramolecular steric interactions. The almost planar ring conformation in trimers and also the equivalence of the endocyclic PN bonds are sometimes quoted as evidence in support of the aromaticity of the $(R_2PN)_3$ system [63].

In the crystalline phase, the tetrameric phosphonitriles (XXXIX)–(XLVI) have significantly non-planar rings with the exception of the octafluoro-compound (XLIII), the conformation of which in the crystalline phase shows only a slight deviation from the D_{4h} symmetry. The displacement of the phosphorus atoms from the mean plane [83] varies as a function of substituents up to 0.35 Å and that of the nitrogen atom is almost constant (0.47–0.54 Å) in such structures, with the exception of (XLIII).

One should note that the vibration spectra of the octafluoro-compound in the gaseous and liquid phases [62] were interpreted on the basis of a lower symmetry (probably C_{2h}) than those of the crystalline phase ($\sim D_{4h}$). The authors [62] believe that this is an indication of a high flexibility of the phosphonitrile ring.

The importance of the role of steric interactions in the determination of the conformations of the tetrameric rings is confirmed by the existence of configurational isomers in the crystalline phase. The first known example (the octachloro-compound) has two polymorphic forms (XLIVa) and (XLIVb) with similar bond lengths and valence angles: the K-form (boat, symmetry close to S_4) and the T-form (chair, symmetry close to C_{2h}). The conformation of the

ring of (XLIV) is evidently different in the liquid and gaseous phases. The vibration spectra of the octachloro-compound in the vapour and liquid phases and in two solid modifications are interpreted according to latest data on the basis of the molecular symmetries D_{4h}, D_{2h}, S_4, and C_{2h} respectively[64], although previously the spectra of the gaseous phase were interpreted on the basis of a lower symmetry[62].

Yet another example of configurational isomerism is provided by a structure with symmetrical non-geminal substituents at the phosphorus atoms: $N_4P_4(C_6H_5)_4Cl_4$. Two crystalline modifications, (XLV) and (XLVI), are known; their molecules differ not only by the ring from (chair, close to C_{2h} symmetry, and crown with distortions resulting in a lowering to C_{2v} symmetry instead of C_{4v} symmetry) but also by the mutual orientation of the substituents at the phosphorus atoms. Whereas in (XLV) the chlorine atoms as well as the C_6H_5 groups are located alternately above and below the ring (the *trans*-isomer), in (XLVI) all the chlorine atoms lie on one side of the ring (the *cis*-isomer). Since (XLV) and (XLVI) are geometrical isomers, the differences between their ring forms are most probably due to steric factors.

Despite the fact that the ring conformations of the tetramers are mainly non-planar, a common feature of phosphonitriles is believed to be a tendency to assume a planar ring conformation. This tendency competes with steric influences of different types.

Analysis of the vibration spectra of solutions and of the liquid and gaseous phases[61,62] suggested a planar ring conformation (symmetry close to D_{5h}) of the decafluoro-pentamer and a lower, probably C_{5v}, symmetry (crown conformation) for the decachloro-pentamer. X-Ray diffraction showed that in the decachloro-pentamer (XLVII) the ring conformation is also very nearly planar: the displacement of the atoms from the plane are not more than 0.2 Å). In the case of D_{5h} symmetry, a planar ten-membered ring would require an increase of the nitrogen valence angles to about 170° (since the endocyclic phosphorus angles usually differ little from 120°). The actual planar conformation (symmetry C_{2v}) is achieved owing to the formation by two nitrogen atoms of angles directed inwards into the ring ("re-entrant" angles). As a result, the average angle of the nitrogen atom decreases to 148°. The vibration spectra of the decabromo-pentamer[65] indicate a distortion of the ring conformation with a consequent change from D_{5h} symmetry probably to a C_{2v} structure, of the type observed for the chloro-derivative. The ring system of the octamer (XLIX) consists of two symmetrical six-membered segments located in parallel planes and joined to one another via PN units. The planarity of each segment (the average deviation of the atoms from the plane is about 0.12 Å) is ensured, as in compound (XLVII), by re-entrant nitrogen atoms. The deviation of the ring atoms from the common plane is also small (0.26 Å).

A nearly planar distribution of PN bonds was found by X-ray diffraction in the structure of the high-polymer (L). This is not inconsistent with infrared spectroscopic data[66]. According to X-ray diffraction, the $[NPF_2]_\infty$ fibres also have a planar chain structure[67]. In this case two molecular conformers were found.

However, the hexamer (XLVIII) has a highly puckered ring. The displacement of the phosphorus atoms from the average plane is 0.56 Å and that of the nitrogen atoms is 0.39 Å. This is regarded as a consequence of the steric interactions of the substituents at the phosphorus atoms—$N(CH_3)_2$ groups.

2. Phosphonitriles with Different Substituents at the Nitrogen Atoms [(LI)–(LVI)]

The different exocyclic substituents at the phosphorus atoms result in the inequality of the PN bond lengths and the analogous angles in the ring. The length of the PN bond in each PNP segment depends in general on substituents at the two extreme phosphorus atoms. For example, r(PN) on the side of halogen atoms is somewhat shorter than on the side of hydrocarbon groups. This is clearly illustrated by the results of an X-ray diffraction study of trimers (in Å): (LI) (1.558 for $=PF_2-N=PF_2$; 1.539 and 1.618 for $=PF_2-N=PPh_2=$); (LII) (1.578 for $=PCl_2-N=PCl_2=$; 1.555 and 1.615 for $=PCl_2-N=PPh_2=$); (LIII) (1.556 and 1.609 for $=PPh_2-N=PPh_2=$; 1.578 for $=PCl_2-N=PPh_2=$). Similar relations were found also for the tetramers (LV) and (LVI).

An increase of the relative number of halogen substituents leads to a systematic decrease of the average PN bond length in the ring, although in the chloro-derivatives these changes are in general within the limits of experimental error; we have (in Å):

1.597 in $N_3P_3Ph_6$ (XXXI) → 1.581 in $N_3P_3Cl_2Ph_4$ (LIII) → 1.583 in $N_3P_3Cl_4Ph_2$ (LII) → 1.581 in $N_3P_3Cl_6$. (XXXVII)

However, in the fluoro-derivatives the changes are fairly explicit:

1.597 in $N_3P_3Ph_6$ (XXXI) → 1.572 in $N_3P_3F_4Ph_2$ (LI) → 1.560 in $N_3P_3F_6$; (XXXVI)

1.596 in $N_4P_4Me_8$ (XXXIX) → 1.560 in $N_4P_4F_4Me_4$ (LVI) → 1.518 in $N_4P_4F_6Me_2$ (LV) → 1.507 in $N_4P_4F_8$. (XLIII)

The conformations of the trimeric rings are nearly planar, as in the case discussed above. In compound (LII) the maximum deviation of the ring atoms from the average plane does not exceed 0.078 Å. In (LI) five P and N atoms are located approximately in one plane and the sixth atom (phosphorus), linked to two phenyl groups, is displaced from this plane by 0.20 Å. The opposite N atom is displaced from the plane of the remaining four atoms by 0.06 Å. This form of the ring may be regarded as a weak boat type of conformation. A similar conformation was found in compound (LIII).

The six-membered ring is closest to planarity in compound (LIV), where the maximum deviation of the P and N atoms from the plane is only 0.011 Å.

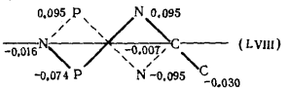
In the tetramer (LVI), the N atoms deviate from the plane of the phosphorus atoms by 0.48 Å. In (LV) the deviation is much less (0.15 Å). In this case, there is a correlation between the increase of the number of F atoms and the tendency towards the formation of a planar ring.

3. Diphosphatriazines and Phosphatriazines [(LVII)–(LIX)]

The six-membered diphosphatriazine rings N_3P_2C are intermediate between the planar triazine structures N_3C_3 and the trimeric phosphonitriles, which, apart from the hexafluoro-compounds, have incompletely planar ring conformations.

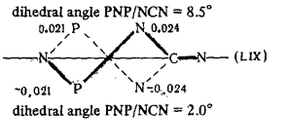
The replacement of one of the phosphorus atoms in the trimer by a carbon atom $=C\langle$ results, according to X-ray diffraction data, in a lengthening of the PN(C) bonds in the ring compared with the PN(P) bonds, to 1.620 Å in (LVIII) and to 1.608 Å in (LIX). Moreover, the endocyclic NPN and PNP angles are smaller than the corresponding angles

in the trimeric phosphonitriles. The ring conformations in both molecules were found to be non-planar, although X-ray diffraction study of the $(NPMe_2)_2NCNMe_2$ structure led to the opposite conclusion[68]. In the methyl derivative (LVIII), the displacement of the ring atoms from the average plane reaches 0.1 Å. In the amino-derivative (LIX), the degree of puckering of the ring is significantly smaller (the displacement of the atoms from the average plane is up to 0.024 Å). However, this difference has little influence on the geometrical ring parameters.



(LVIII)

dihedral angle PNP/NCN = 8.5°



(LIX)

dihedral angle PNP/NCN = 2.0°

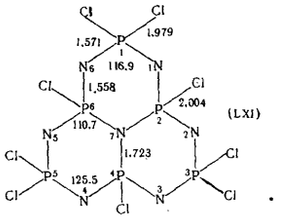
The ring in compound (LVII) also has a non-planar conformation of the chair type which is somewhat distorted owing, it is believed, to intermolecular interactions in the crystalline phase.

4. Structures Complicated by Additional Covalent Bonds at the N Atoms [(LX) and (LXI)]

In compound (LX), the proton and the $CuCl_3$ group are linked covalently to the N atoms at the opposite ends of the eight-membered ring which thus become tricoordinate§. This causes a significant increase in the length of the nearest PN endocyclic bonds. PN bonds of different lengths are located in the ring symmetrically in pairs, the effect of the proton on their length being more pronounced than that of the $CuCl_3$ group: the respective lengths are 1.67, 1.56, 1.60, and 1.63 Å. The valence angles of the P atoms differ significantly from those in the initial compound (XXXIX): the average NPN angle is 114° against 119.8° in the initial compound and the exocyclic CPC angle is 106.6° against 104°. In the absence of factors distorting their symmetry, the endocyclic NPN angles do not differ significantly from 120° in any of the phosphonitrile structures and the exocyclic XPX angles as a rule do not exceed 104°.

The conformation of the ring in compound (LX) is non-planar boat. As in other tetrameric structures (see above), the displacement of the N atoms from the average plane is somewhat greater than that of the P atoms (0.55 and 0.48 Å).

In the condensed cyclic structure of (LXI), the geometrical parameters of the central fragment with a tricoordinate central N atom are of special interest. The average length of the three PN bonds formed by this atom is 1.723 Å, i.e. greater than the average length of the exocyclic PN bonds in phosphonitriles and also of the endocyclic bonds in cyclophosphazanes with tetracoordinate phosphorus (see below). The central N atom is almost coplanar with the neighbouring P atoms (its deviation from their plane amounts to only 0.04 Å), while in the last two cases the N atoms have less planar bond configurations. The increase of the PN bond length with retention of a nearly planar configuration of the N bonds was noted also in the review of the molecular structures of acyclic phosphorus compounds[11].



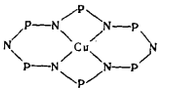
(LXI)

The three penta-atomic segments in compound (LXI) (without the $N_{(7)}$ atom) are almost planar (the average deviation is 0.06 Å) but on the whole the molecule is non-planar; the average dihedral angle of the type $N_{(1)}P_{(2)}N_{(2)}/P_{(2)}P_{(4)}P_{(6)}$ is 49°.

§ In contrast to compound (LX), the complex $[(NPMe_2)_4H^+]_2CoCl_4^{2-}$ has an ionic structure[69]. In each of the two cyclic cations, the only perturbing factor is the proton linked to one of the N atoms. It is interesting to note that the rings have different conformations. One of them has the same boat conformation as (LX), the displacement of the N atoms from the average plane being greater than that of the P atoms (0.59 and 0.40 Å). The other has a conformation of the saddle type, where the P atoms are in one plane to within 0.02 Å and the N atoms are located alternately above and below this plane at a distance of about 0.61 Å. Despite this, the variation of the PN bond length in the two rings is the same: the average length of each pair of bonds is independent of the conformation. Starting with the protonated N atom, the longest of the PN bonds is followed by the shortest bond, after which a long bond is followed by a shorter bond: 1.695, 1.538, 1.614, and 1.582 (±0.015) Å. The remaining parameters are close to those found for compound (LX).

In the trimeric cation $N_3P_3Cl_2(iso\text{-}C_3H_7NH)_4H^+$,[70] the protonation of the ring also has an appreciable influence on the endocyclic bonds and angles. The variation of the PN bond in the ring, starting with the protonated N atom, is as follows: 1.666, 1.583, and 1.558 (±0.005) Å. The shortest bond is near the PCl_2 group, i.e. the differences between the substituents at the P atoms also affect the ring parameters. The lengths of the exocyclic bonds are $r(PN) = 1.609(5)$ and $r(PCl) = 2.000(3)$ Å. The ring has a distorted boat conformation with deviations of the N and P atoms from the average plane up to 0.09 Å.

In the hexameric cyclic cation $[N_6P_6(NMe)_2]_{12}CuCl^+$,[71] the copper atom is linked covalently to four ring N atoms as well as to the Cl atom (overall symmetry $\sim C_2$). As a result there are two types of PN bonds in the ring system



with di- and tri-coordinate N atoms: bond lengths of 1.55 and 1.62 (±0.02) Å. The average endocyclic N and P angles are reduced, compared with those found in the initial structure of (XLVIII), to 133.6(1.3)° and 107.5(1.1)° against 147.5° and 120.0°.

Table 8. Cyclophosphazanes.

Compound	Ring conformation	Endocyclic bonds		Exocyclic bonds		Endocyclic valence angles		Exocyclic valence angles		Method	Refs.
		bond type	bond length, Å	bond type	bond length, Å	angle	magnitude, deg	angle	magnitude, deg		
$[ClP(=S)NMe]_2$ (LXII)	planar	$=P_c-N_c<$	1.67	$=P_c-Cl$	1.93	NPN	84.0	NPCl=NP= =S	114.7	X-ray	118
				$-P_c=S$	1.93	PNP	96.0	ClP=S	111.5		
$[MeOP(=O)NMe]_3$ (LXIII)	twisted boat	ditto	1.664 (0.011)	$=P_c-O-$	1.564 (0.011)	NPN	105.2(0.6)	NP=O OP=O	113.5 (0.7) 116.1 (0.7)	ditto	119
				$-P_c=O$	1.453 (0.012)	PNP	121.7(0.6)	OPN POC	103.7 (0.7) 119.3 (1.0)		
$(F_3PNMe)_2$ (LXIV)	planar	$(P_cN_c)_a$	1.735	$(P_cF)_a$	1.605	NPN	77.9	F_aPN_e F_aPF_e	99.1 88.5	el. dif.	120
		$(P_cN_c)_e$	1.595	$(P_cF)_e$	1.570	PNP	102.1	N_aPN_e F_aPF_e N_aPF_e	92.0 103.9 127.5		
$(PhF_2PNMe)_2$ (LXV)	ditto	$(P_cN_c)_a$	1.78 (0.02)	$(P_cF)_a$	1.62 (0.02)	NPN	80.6	F_aPN_e F_aPF_e	92.5 87.0	X-ray	121
		$(P_cN_c)_e$	1.64 (0.02)	$(P_cF)_e$ $(P_cC)_e$	1.57 (0.02) 1.79 (0.02)	PNP	99.4	F_aPC_e N_aPF_e N_aPC_e N_ePF_e N_ePC_e F_ePC_e	91.8 91.7 97.9 128 122 109		
$(Cl_3PNMe)_2$ (LXVIa)	»	$(P_cN_c)_a$ $(P_cN_c)_e$	1.769 (0.007) 1.635 (0.007)	$(P_cCl)_a$ $(P_cCl)_e$	2.133 (0.003) 2.026 (0.004)	NPN PNP	80.5 (0.4) 99.5 (0.4)	Cl_ePCl_e Cl_aPN_e X_aPX_e	110 (0.2) 124.8 (0.3) 90.2–94.5	ditto	122
$(Cl_3PNMe)_2$ (LXVIb)	»	$(P_cN_c)_a$ $(P_cN_c)_e$	1.776 (0.01) 1.629 (0.01)	$(P_cCl)_a$ $(P_cCl)_e$	2.152 (0.005) 2.020 (0.005)	NPN PNP	81.7 (0.5) 98.3 (0.5)	Cl_aPN_e Cl_aPCl_e N_aPCl_e Cl_ePCl_e N_ePCl_e	93.8 (0.4) 90.5 (0.3) 92.0 (0.4) 109.8 (0.3) 124.9 (0.4)	»	123
$P_3Cl_3(NMe)_6$ (LXVII)	»	$(P_cN_c)_a$ $(P_cN_c)_e$	1.74 (mean) 1.66 (mean)	$(P_cCl)_a$ $(P_cCl)_e$	2.16 2.05 2.10	NPN PNP	80.6 99.4			»	124

*The subscripts a and e correspond to the axial and equatorial bonds in the trigonal bipyramidal structure.

VIII. CYCLOPHOSPHAZANES [(LXII)–(LXVII)]

In contrast to phosphonitriles, the phosphazane ring systems contain tricoordinate nitrogen and are saturated. Among compounds of this class, the structures with tetra- and penta-coordinate phosphorus have been investigated (Table 8).

In the first case, there are X-ray diffraction data for the dimer (LXII) and the trimer (LXIII)¶. The endocyclic PN bonds in each molecule are equivalent. Their average length (1.67 Å) is greater by about 0.1 Å than in phosphonitriles, where the terminal PN bonds have the same length only in structures complicated by additional bonds formed by the N atoms (see above). This length is comparable to that of single PN bonds formed by tetracoordinate phosphorus in acyclic structures (1.60–1.71 Å).[11] The configuration of the bonds involving the nitrogen atom is planar.

It is also striking that the endocyclic angles of the phosphorus atom in compound (LXIII) (105.2°) are significantly

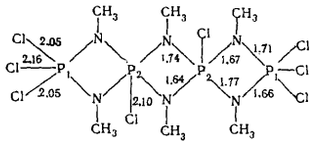
¶ In addition there are data for the structures of the cyclic phosphazane anions $(HNPO_2)_n^{n-}$, where $n = 3$ or 4. These structures differ from those of the non-ionised phosphazanes by the fact that their exocyclic PO bonds are equivalent. It has been shown by X-ray diffraction[105–107] that the endocyclic PN bonds in phosphazane anions are also equivalent (1.66–1.68 Å). The endocyclic angles NPN (104.5° in the trimer[106] and 107–108° in the tetramers[106,107]) are much smaller than in phosphonitriles.

The six-membered ring of the trimer has C_{3v} symmetry (chair conformation), which is confirmed by the vibration spectra of the crystalline structures and solutions[108,109]. The conformational isomerism of eight-membered rings is extremely interesting. X-Ray diffraction data[106,107] and the vibration spectra of the crystalline structures[110,111] showed that the tetrameric anions have conformations of the chair (C_{2h}), boat (S_4), and saddle (D_{2d}) types, the difference between the conformations not affecting the geometrical parameters. The non-planarity of the ring in the tetrameric phosphazane anions is probably greater than in the tetrameric phosphonitriles. In one of the structures with the boat conformation[106], the displacement of the phosphorus atoms from the mean plane[83] is $\Delta P = 0.42$ Å and that of nitrogen atoms $\Delta N = 0.71$ Å, which is greater than in the tetrameric phosphonitriles (see above).

smaller than the exocyclic OP=O angles (116.1°), while in phosphonitriles the opposite relation obtains between the endocyclic NPN angles (115–122°) and the exocyclic XPX angles (97–108°). The ring system of the dimer (LXII) is planar. However, in the molecule of the trimer (LXIII) the ring has a non-planar boat conformation with a symmetry approaching C_s. The N and P atoms located at the opposite ends of the molecule are displaced from the plane of the remaining four ring atoms by about 0.54 Å. Two of the exocyclic MeO groups are located on one side of the ring and the third is on the other. The study of the dipole moments of the dimers with tetracoordinate phosphorus showed that there is a possibility of geometrical (*cis–trans*) isomerism, depending on the relative positions of the exocyclic substituents at the P atom [112].

In dimeric cyclophosphazanes with pentacoordinate phosphorus [compound (LXIV–(LXVII)], the immediate environment of each phosphorus atom gives rise to a distorted trigonal bipyramid. According to X-ray diffraction and electron diffraction data, the endocyclic PN bonds are not equivalent: one of the N atoms is axial and the other is equatorial. The equatorial PN bonds (~1.63 Å) are shorter than the PN bonds in phosphazanes with tetracoordinate phosphorus. The average length of the axial PN bonds (1.74–1.78 Å) is somewhat greater than the sum of the covalent radii corrected for heteropolarity by the Shoemaker–Stevenson method (1.75 Å). The configuration of the bonds involving the N atoms is planar. It is interesting to note that the empirical rule according to which the axial positions in the trigonal bipyramidal structure of substituted fluorophosphoranes should contain F atoms does not hold for the fluoro-derivatives (LXIV) and (LXV). [113,114]

The conformation of the four-membered ring in the dimers with pentacoordinate phosphorus is planar. This is confirmed for (LXIV) by the vibration spectra of solutions [115,116] and also of the liquid and vapour phases [117]. It is striking that the endocyclic NPN angle is smaller than the PNP angle. The condensed structure of (LXVII) contains three planar four-membered rings. The interatomic distances and the angles around $P_{(1)}$ are largely consistent with those found in (LXVI). The trigonal bipyramid around $P_{(2)}$ is distorted much more, since the $P_{(2)}$ atom is involved simultaneously in two rings.



(LXVII)

IX. CYCLIC PHOSPHITES [(LXVIII)–(LXXI)] AND PHOSPHATES [(LXXII)–(LXXXIV)]

In cyclic phosphites, the PO bond length is greater and the OPO bond angles are smaller than the corresponding ring parameters of cyclic phosphates (Table 9), as in the open-chain compounds [11].

However, in the cyclic structures, the geometrical parameters depend on the dimensions of the ring system. In the five-membered rings of (LXVIII)–(LXX) and (LXXII)–(LXXIV), the endocyclic OPO and POC angles

Table 9. Cyclic phosphites and phosphates.

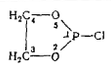
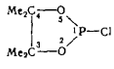
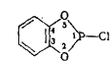
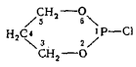
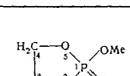
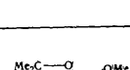
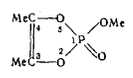
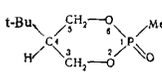
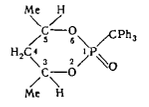
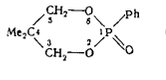
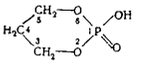
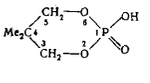
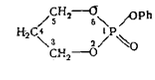
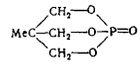
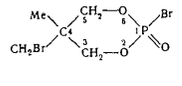
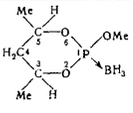
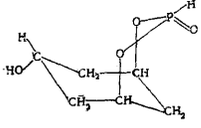
Compound	Ring conformation	Endocyclic bonds		Exocyclic bonds		Endocyclic valence angles		Exocyclic valence angles		Method	Refs.
		bond type	bond length, Å	bond type	bond length, Å	angle	magnitude, deg	angle	magnitude, deg		
 (LXVIII)	envelope	$>P_c-O_c-$	1.631(0.007)	$>P_c-Cl$	2.105 (0.007)	OPO POC	95.7 110.6	OPCl	99.6(0.5)	el. dif	125
 (LXIX)	half-chair	ditto	1.630(0.01)	ditto	2.093 (0.009)	OPO POC	95.9(2.0) 112.0	ditto	103.2 (0.6)	ditto	126
 (LXX)	envelope	»	1.65(0.03)	»	2.106 (0.008)	OPO POC	99.0(1.0) 104.6(1.0)	»	101.6(2.0)	»	127
 (LXXI)	chair	»	1.63 (assumed)	»	2.128 (0.008)	OPO POC	102.6(3.0) 120.1(1.0)	»	100.8(1.8)	»	128
 (LXXII)	envelope (distorted)	$\begin{array}{c}\vert\\ =P_c-O_c-\\ \vert\end{array}$	1.585(0.01)	$\begin{array}{c}\vert\\ =P_c-O\\ \vert\\ -P_c=O\\ \vert\end{array}$	1.54(0.01) 1.45(0.01)	OPO POC	98.1(0.5) 113.4(0.8)	POC $O_cP=O$ $OP=O$ O_cPO	119.7(1.1) 116.5(0.8) 108.6(0.9) 108.3 ((mean)	X-ray	129, 130
 (LXXIII)	half chair	ditto	1.58(0.01)	$\begin{array}{c}\vert\\ =P_c-O\\ \vert\\ -P_c=O\\ \vert\end{array}$	1.56(0.01) 1.44(0.01)	OPO POC	98.4(0.5) 112.1(0.8)	POC $O_cP=O$ $OP=O$ O_cPO	123.4(0.9) 116.6(0.6) 112.6(0.6) 105.6(0.7)	ditto	131

Table 9 (continued).

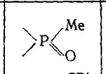
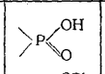
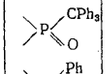
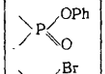
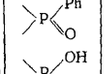
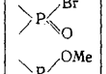
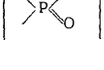
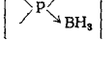
Compound	Ring conformation	Endocyclic bonds: bond type	Endocyclic bonds: bond length, Å	Exocyclic bonds: bond type	Exocyclic bonds: bond length, Å	Endocyclic valence angles: angle	Endocyclic valence angles: magnitude, deg	Exocyclic valence angles: angle	Exocyclic valence angles: magnitude, deg	Method	Refs.
 (LXXIV)	planar		1.58(0.02)		1.53(0.02) 1.38(0.03)	OPO POC	98.5(0.6) 108.0(1.5)	POC $O_cP{=}O$ $OP{=}O$ O_cPO	122.9(0.9) 116.2(0.7) 109.5(0.8) 107.9(0.7)	X-ray	132
 (LXXV)	chair	»	1.57(0.01)		1.81(0.03) 1.48(0.01)	OPO POC	104.4(0.4) 120.0(0.8)	$C_cP{=}O$ $CP{=}O$ O_cPC	113.1(0.5) 108.7(0.5) 108.7(0.5)	ditto	133
 (LXXVI)	ditto	»	1.579(0.015)		1.860 (0.025) 1.469 (0.021)	OPO POC	104.6(0.8) 127.7(1.2)	$O_cP{=}O$ $CP{=}O$ O_cPC	113.2(1.1) 113.1(1.1) 106.0(0.9)	»	134
 (LXXVII)	»	»	1.55(0.02)		1.82(0.02) 1.47(0.02)	OPO POC	106.2(0.8) 119.9(1.5)	$O_cP{=}O$ $CP{=}O$ O_cPC	112.5(0.9) 111.7(0.9) 107.2(0.9)	»	135
 (LXXVIII)	»	ditto	1.57(0.03)		1.55(0.03) 1.51(0.03)	OPO POC	104.6(0.5) 118.9(1.1)	$O_cP{=}O$ $OP{=}O$ O_cPO	110.2(0.6) 116.6(0.7) 107.3(0.7)	»	136
 (LXXIX)	»	»	1.581(0.012)		1.542 (0.011) 1.457 (0.014)	OPO POC	106.1(0.8) 116.0(1.2)	$O_cP{=}O$ $OP{=}O$ O_cPO	111.3(0.8) 117.8(0.8) 104.7 (mean)	»	137
 (LXXX)	»	»	1.565(0.01)		1.59(0.01) 1.48(0.01)	OPO POC	106.6(0.6) 117.6(0.9)	POC $O_cP{=}O$ $OP{=}O$ O_cPO	121.3(0.9) 114 114 104.5	»	138
 (LXXXI)	bicyclic, boat	»	1.57(0.02)		1.46(0.02)	OPO POC	103.7(0.6) 115.2(1.1)	$O_cP{=}O$	115.0(1.1)	»	139
 (LXXXII)	chair	»	1.555(0.013)		2.171 (0.06) 1.443 (0.016)	OPO POC	104.9(0.7) 120.5(1.2)	$O_cP{=}O$ $BrP{=}O$ O_cPBr	115.0(1.0) 111.5(0.7) 104.8(0.5)	»	140
 (LXXXIII)	»		1.562(0.01)		1.562 (0.01) 1.879 (0.017)	OPO POC	105.1(0.6) 119.3(0.9)	O_cPB OPB O_cPO POC	113.6(0.7) 115.5(0.7) 104 (mean) 119.9(1.1)	»	141
 (LXXXIV)	boat		1.550(0.005)		1.430 (0.006)	OPO POC	107.5(0.2) 121.7(0.4)	$O_cP{=}O$	114.5 (0.3)	»	142

are significantly smaller (by 5–10°) than in the open-chain analogues. Conversely, the magnitude of the exocyclic OPO and POC angles in (LXXII)–(LXXIV) is characteristic also of acyclic esters. The six-membered rings of (LXXI) and (LXXV)–(LXXXIV) are very similar to the acyclic structures as regards the parameters under consideration. It is also noteworthy that the exocyclic PCl bonds in cyclic phosphites are significantly longer than in the PCl_3 or $MeOPCl_2$ molecules (by 0.05–0.08 Å),[11] but not to the same extent as in the oxaphosphadiazole,

etc. structures discussed above. The length of the PBr bond in the six-membered cyclic phosphate is greater by 0.03 Å than in $POBr_3$.[11]

According to electron and X-ray diffraction data, cyclic phosphites and phosphates have as a rule non-planar ring conformations. The only exception is compound (LXXIV), where the five-membered ring with tetracoordinate phosphorus and one multiple bond was found to be planar. Five-membered cyclic phosphites have conformations of the envelope (with an axial exocyclic PCl bond) or twisted envelope (half-chair) types. The OPO/OCCO dihedral angle, characterising in the case of envelope conformation the displacement of the P atom from the plane of the remaining ring atoms, is 26° in (LXVIII) and 24.3° in (LXX). In non-planar five-membered cyclic phosphates, the dihedral angles $O_{(2)}PO_{(5)}/O_{(2)}C_{(3)}O_{(5)}$ and $O_{(2)}PO_{(5)}/O_{(2)}C_{(4)}O_{(5)}$ were found to be respectively 10.9° and 1.8° in (LXXII) (distorted enveloped conformation) and 12.2° and 12.1° in (LXXIII) (half-chair conformation). The only study so far of the six-membered cyclic phosphite (LXXI) showed that in the gas phase its ring has a chair conformation (with an axial exocyclic PCl bond). The chair conformation (with an equatorial P=O phosphoryl bond) is also most characteristic of six-membered cyclic phosphates in the crystalline phase. The phosphorus end of the ring in these compounds is more planar than the carbon end (Table 10).

Table 10.

Compound	Exocyclic substituents at P atom	Dihedral angles, deg		Compound	Exocyclic substituents at P atom	Dihedral angles, deg	
		$O_{(2)}PO_{(6)}/O_{(2)}C_{(3)}C_{(5)}O_{(6)}$	$C_{(3)}C_{(4)}C_{(5)}/O_{(2)}C_{(3)}C_{(5)}O_{(6)}$			$O_{(2)}PO_{(6)}/O_{(2)}C_{(3)}C_{(5)}O_{(6)}$	$C_{(3)}C_{(4)}C_{(5)}/O_{(2)}C_{(3)}C_{(5)}O_{(6)}$
(LXXV)		33.5	54.9	(LXXIX)		41.8	54.7
(LXXVI)		3.7	53.3	(LXXX)		36.5	53.1
(LXXVII)		32.6	51.2	(LXXXII)		36.7	52.5
(LXXVIII)		40.4	54.2	(LXXXIII)		38.3	54.0

The degree of smoothing of the conformation on the side of phosphate group is evidently determined by the nature of the exocyclic substituents at the phosphorus atom, since the $C_{(3)}C_{(4)}C_{(5)}/O_{(2)}C_{(3)}C_{(5)}O_{(6)}$ dihedral angle hardly changes on passing from one structure to the other. Boat conformations occur only in the bicyclic structures of (LXXXI) and (LXXXIV). Numerous studies dealing with the problems of conformational equilibrium and the geometrical isomerism and stereochemistry of cyclic phosphites[143–172] and phosphates[173–193] have been carried out by NMR, by determining the dipole moments, etc. However, as pointed out, in particular, by White et al.[166], the interpretation of the results of these studies is frequently ambiguous and contradictory. Further studies by structural methods are necessary for the solution of the above problems.

X. CYCLIC OXYPHOSPHORANES [(LXXXV)–(LXXXVII)]

1. Characteristics of the Geometrical Structure

Cyclic oxyphosphoranes are a new class of compounds in which a pentacoordinate phosphorus atom is located at the centre of a distorted trigonal bipyramid. The distortion may be due to the presence of a ring system and of different substituents at the phosphorus atom.

In compound (LXXXV), which was investigated by X-ray diffraction, two ester groups in the axial and equatorial positions are linked to a five-membered ring. Two tendencies (Table 11) may be noted: (1) the length of the axial bonds is greater than that of the equatorial bonds, as in other trigonal bipyramidal structures; (2) the PO bonds in the five-membered ring are much longer than the corresponding exocyclic bonds (by 0.05 Å for the equatorial bonds and by 0.1 Å for the axial bonds). The OPO angle in this ring (89.3° ± 0.3°) is smaller than in five-membered cyclic phosphates and phosphites and corresponds to the angle between the axial and equatorial bonds. The POC endocyclic bonds are smaller than the exocyclic bonds and close to the analogous angles in the five-membered cyclic phosphites and phosphates.

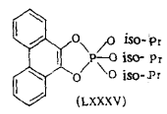
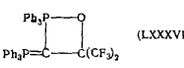
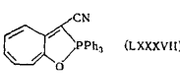
In contrast to compound (LXXXV), in compounds (LXXXVI) and (LXXXVII) the phosphorus atom can be regarded as the centre of a trigonal bipyramid only by convention. The endocyclic axial PO bonds in the last two compounds are significantly longer than in (LXXXV) (by 0.25 and 0.6 Å respectively). On the other hand, the endocyclic PC bonds, which are formally equatorial in the trigonal bipyramid, are unusually short. In the four-membered ring of (LXXXVI), this bond (1.76 ± 0.02 Å) is of the same length as the exocyclic P=C bond (1.75 ± 0.02 Å) within the limits of experimental error. The investigators who studied the structure of (LXXXVI) suggest a delocalisation of electrons in the P=C=P system and explain thereby the stability of the ring. It is noteworthy that the CPO angle in the ring is only 71.3° ± 1.0°, which is smaller by 10° than in four-membered phosphorus–carbon heterocycles, while the POC angle is 94.1° ± 1.0°. In the five-membered ring of (LXXXVII), the equatorial PC bond is even shorter (1.70 Å) than in (LXXXVI). The ring conformations in the above structures are planar to within 0.07–0.10 Å.

2. Pseudorotation

The study of the NMR spectra of oxyphosphoranes with four-, five-, and six-membered rings[198–208] showed that, as in acyclic fluorophosphoranes[11], they undergo an intramolecular rearrangement which is usually described as "pseudorotation". This process involves a deformation of the valence angles and as a result two axial groups of the trigonal bipyramid move to the equatorial positions and correspondingly two equatorial groups move to the axial positions. This mechanism was proposed by Berry[209]. However, it is noteworthy that Berry's mechanism does not always provide a sufficiently complete explanation of the characteristics of the spectra[202,207]. The possible mechanisms of pseudorotation are also discussed in other reports[210–215].

It is assumed that in ring structures pseudorotation is hindered by two principal factors characterised by the polarity[216] and strain rules[217,218]. According to the former, alkyl groups occupy preferentially equatorial

Table 11. Cyclo-oxyphosphoranes*.

Compound	Ring conformation	Endocyclic bonds: bond type	Endocyclic bonds: bond length, Å	Exocyclic bonds: bond type	Exocyclic bonds: bond length, Å	Endocyclic valence angles: angle	Endocyclic valence angles: magnitude, deg	Exocyclic valence angles: angle	Exocyclic valence angles: magnitude, deg	Method	Refs.
 (LXXXV)	planar	$(P_cO_c)_a$ $(P_cO_c)_e$	1.752 (0.007) 1.633 (0.007)	$(P_cO)_a$ $(P_cO)_e$	1.638 (0.006) 1.581 (0.008)	O_aPO_e PO_aC PO_eC	89.3 (0.3) 111.9 (0.6) 114.2 (0.6)	PO_aC PO_eC	121.8 (0.6) 128.7 (mean) distortion of trigonal bipyramid within the limits of experimental error	X-ray	194, 195
 (LXXXVI)	ditto	$(P_cO_c)_a$ $(P_cO_c)_e$	2.01 (0.02) 1.76 (0.02)	$(P_cC)_{av}$ $C_c=P$	1.848 (0.02) 1.745 (0.02)	O_aPC_e PO_aC PC_eC	71.3 (1.0) 94.1 (1.0) 98.5 (1.0)	C_aPO C_ePO C_aPC_e C_ePC_e	172.4 (0.8) 86.1 (mean) 99.3 (mean) 106.8 (0.9) 122.6 (mean)	ditto	196
 (LXXXVII)	»	$(P_cO_c)_a$ $(P_cC_c)_e$	2.36 1.70	$(P_cC)_a$ $(P_cC)_e$	1.83 1.775			C_aPO C_aPC C_ePC_e	177.8 102.6 (mean) 112 116 119	»	197

*The subscripts a and e correspond to axial and equatorial bonds in the trigonal-bipyramidal structure.

positions, while O atoms occupy preferentially axial positions. According to the second rule, the pentacoordinate phosphorus atom is bound to the adjacent ring atoms mainly via one axial and one equatorial bond. This reduces ring strain to a minimum, as a result of which the angle between the axial and the equatorial bonds involving the phosphorus atom is smaller than, for example, that between two equatorial bonds. Pseudorotation requires an energy sufficient to overcome the barrier due to one of these factors or to both at the same time. According to the available data, the potential barrier caused by the polarity rule in alkoxyphosphoranes containing at least one PO bond in a five-membered ring is 10–17 kcal mole^{-1}.[203] The barrier due to the strain rule has been estimated as higher—up to 22 kcal mole^{-1}.[203] In such structures at a temperature ≤140°C, an axial–equatorial arrangement of the ring is greatly preferred[202,203]. In alkoxyphosphoranes with a four-membered phosphetane ring (i.e. having only PC bonds in the ring), an axial–equatorial arrangement of the ring is also preferred, at least at a temperature ≤30°C.[207] The barrier to the transition of the ring to a diequatorial arrangement is estimated in this case as 20 kcal mole^{-1}.[204] Six-membered rings with two oxygen atoms linked to a phosphorus atom can assume a diequatorial arrangement[208]. It is interesting that in the $C_5H_{10}PF_3$ molecule, containing a six-membered phosphorus–carbon ring, there is no pseudorotation at room temperature and the ring assumes a diequatorial arrangement[216].

XI. CYCLIC POLYPHOSPHATES [(LXXXVIII)–(LXXXIX)] AND PHOSPHORUS OXIDES [(XC)–(XCVI)]

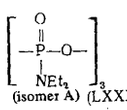
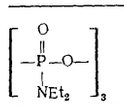
The cyclic skeletons of the molecules of these compounds consist of alternating P and O atoms. Among the unionised polyphosphates, only two geometrical isomers of the trimeric diethylamide of metaphosphoric acid, (LXXXVIII) and (LXXXIX), have been investigated. In the first of these, the six-membered ring has the chair conformation, two atoms (phosphorus and oxygen) deviating from the plane of the remaining four by +0.61 and −0.53 Å. Overall, the molecule has the ~C_{3v} symmetry: all three endocyclic P=O bonds lie on one side of the ring (axial bonds) and all three PN bonds are on the other side (equatorial bonds). In the second structure the ring has an unusual conformation: three oxygen atoms and two phosphorus atoms lie approximately in one plane (to within 0.1 Å) and the third phosphorus atom deviates from this plane by 0.54 Å. Two PN bonds are located on one side of the ring and the third on the other. The PO bonds in the ring were found to have the same length (Table 12)†, which however is greater by about 0.05 Å than the length of the analogous bonds in six-membered cyclic phosphates and also in acyclic structures[11]. On the other hand, the OPO endocyclic angles were found to be somewhat smaller than in cyclic phosphates. The configuration of the bonds involving the exocyclic N atoms is almost planar in both structures.

Phosphorus oxides form three-dimensional polycyclic structures. In the simplest of these (the trioxide P_4O_6), tervalent phosphorus atoms are located at the vertices of a tetrahedron and O atoms form bridging bonds along the edges of the tetrahedron. The pentoxide molecules P_4O_{10} consist, as it were, of a P_4O_6 nucleus and four terminal oxygen atoms completing the tetrahedron around each

† Until recently, X-ray diffraction data could not yield an unambiguous answer concerning the identity or non-identity of the PO endocyclic bond lengths in trimeric and tetrameric cyclic polyphosphate anions[4,219]. The identity of the bond lengths has now been demonstrated. In the $Na_3P_3O_9$ crystal structure, the $P_3O_9^{3-}$ anions (the chair conformation) have the following geometrical parameters[220]: $r(P_c-O_c)$ = 1.615(0.004) Å, $r(-P_c=O)$ = 1.484(0.004) Å, ∠POP = 126.9(0.2)°, and ∠OPO = 101.1(0.3)°.

In the $(NH_4)_4P_4O_{12}$ structure, these parameters for the $P_4O_{12}^{4-}$ anion (the chair conformation) have the following values[221]: 1.607(0.004) Å, 1.479(0.004) Å, 131.2(0.0)°, and two different OPO angles—98.7(0.02)° and 104.5(0.2)°.

Table 12. Cyclic polyphosphates and phosphorus oxides*.

Compound	Ring conformation	Endocyclic bonds		Exocyclic bonds		Endocyclic valence angles		Exocyclic valence angles		Method	Refs.
		bond type	bond length, Å	bond type	bond length, Å	angle	magnitude, deg	angle	magnitude, deg		
 (isomer A) (LXXXVIII)	chair		1.62 (0.03)		1.44 (0.03) 1.67 (0.04)	OPO POP	104 (2) 124 (2)	OP=O NP=O NPO PNC CNC	115 (2) 116 (2) 102 (2) 121 (3) 117 (3)	X-ray	222
 (isomer B) (LXXXIX)	non-planar	ditto	1.62 (0.02)		1.49 (0.02) 1.62 (0.02)	OPO POP	102 (0.5) 132 (1)	OP=O NP=O NPO PNC CNC	112 (1) 117 (1) 104 (1) 121 (3) 115 (3)	ditto	223
$(P_2O_5)_\infty$ (XC)	three dimensional network of rings formed by six PO_4 tetrahedra	»	1.56 (0.015)		1.49 (0.015)	OPO POP	103 145	OP=O	116	»	224
P_4O_{10} (XCI a)*	tricyclic structure	»	1.58 (mean)	ditto	1.43 (mean)	OPO POP	101 124	ditto	117	»	225
$P_4O_6S_4$ (XCII a)	ditto	»	1.61 (0.02)		1.862 (0.02)	OPO POP	100.8 (0.9) 124.5 (0.6)	OP-S	117.2 (0.8)	»	226
$P_4O_6S_4$ (XCII b)	»	»	[1.85 (0.02)]	ditto	1.85 (0.02)	OPO POP	101.5 (1.0) 123.5 (1.0)	ditto	116.5 (1.0)	el.dif.	227

*See also Table 13.

Table 13. Bond lengths and valence angles in phosphorus oxides.

Compound	Bond lengths, Å*					Valence angles, deg*							Method	Refs.
	$P^{III}-O P^{III}$	$P^{III}-O P^{V}$	$P^{V}-O P^{III}$	$P^{V}-O P^{V}$	$P^{V}=O$	$P^{III}O P^{III}$	$P^{III}O P^{V}$	$P^{V}O P^{V}$	$O P^{III}O$	$O P^{V}O$	(P^{III}) OP=O	(P^{V}) OP=O		
P_4O_6 (XCI II)	1.638 (0.003)	—	—	—	—	126.4 (0.7)	—	—	99.8 (0.8)	—	—	—	el. dif.	228
P_4O_7 (XCIV)	1.637	1.67	1.59	—	1.424	128	125	—	99.5	105	117	—	estimate	228
P_4O_8 (XCV)	1.633 (0.014)	1.668 (0.014)	1.556** 1.596 (0.014)	1.596 (0.014)	1.414 (0.014)	130.1 (0.9)	124.4 (0.9)	121.2 (0.9)	98.0 (mean)	104 (mean)	115.6 (1.0)	113.6 (0.8)	X-ray	228
P_4O_9 (XCVI)	—	1.661 (0.014)	1.605 (0.014)	1.590 (0.014)	1.418 (0.014)	—	126.8 (0.7)	122.8 (0.7)	96.7 (0.7)	102 (mean)	118.8 (0.7)	114.6 (0.7)	X-ray	229
P_4O_{10} (XCI b)	—	—	—	1.604 (0.004)	1.429 (0.004)	—	—	123.5 (0.7)	—	101.6 (0.8)	—	116.5 (0.3)	el. dif.	229
Weighted mean values	1.637 (0.004)	1.666 (0.008)	1.586 (0.010)	1.598 (0.004)	1.424 (0.004)	128.0 (0.6)	125.3 (0.5)	122.6 (0.5)	98.4 (0.8)	103.0 (0.8)	117.0 (0.5)	115.3 (0.3)	—	—

*The symbols P^{III} and P^{V} denote tervalent and quinquevalent phosphorus respectively.
**Beagley et al.[228] believe that the length 1.556 Å is due to an unusual error in the X-ray diffraction data.

quinquevalent phosphorus atom. The remaining oxides differ from these by the number of terminal oxygen atoms (and correspondingly by the number of tervalent and quinquevalent phosphorus atoms). The replacement of P=O by P=S bonds in $P_4O_6S_4$ leaves the overall structure the same as before.

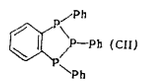
Table 13, which we took from Stosick[227], lists the bond lengths and the valence angles of all the phosphorus oxides. The $P^{III}-O$ bridging bonds are not the same for both types of oxygen atoms (the difference is 0.029 ± 0.009 Å). This is evidence that the intermediate oxides P_4O_7, P_4O_8, and P_4O_9 cannot be regarded as comprising simply fragments of the terminal members of the series (P_4O_6 and P_4O_{10}).

The $P^{III}-O$ bridging bonds are longer than the $P^{V}-O$ bonds and the corresponding bonds in the acyclic structures (1.60 Å).[11]

XII. CYCLIC POLYPHOSPHINES AND ELEMENTAL PHOSPHORUS

An interesting feature of the PP bond in acyclic structures is the low sensitivity of its length to changes in the valence state of the phosphorus atom and in the nature of the attached groups (2.18–2.22 Å).[11] In the ring systems

Table 14. Cyclic polyphosphines and elemental phosphorus.

Compound	Ring conformation	Endocyclic bonds		Exocyclic bonds		Endocyclic valence angles		Exocyclic valence angles		Method	Refs.
		bond type	bond length, Å	bond type	bond length, Å	angle	magnitude, deg	angle	magnitude, deg		
$(PCF_3)_4$ (XCVII)	non-planar	$>P_c-P_c<$	2.213 (0.005)	$>P_c-C-$	1.867 (0.014)	PPP	84.7	PPC	97.8	X-ray	230,231
$(PC_4H_{11})_4$ (XCVIII)	ditto	ditto	2.224 (0.002)	ditto	1.874 (0.002)	ditto	85.5 (0.06)	ditto	102.7 (0.2)	ditto	232
$(PC_6F_5)_4$ (XCIX)	»	»	2.236 (0.002)	$>P_c-C<$	1.838 (0.003)	»	85.24 (0.04)	»	101.05 (0.1)	»	233
$(PCF_3)_5$ (C)	envelope	»	2.223 (0.017)	$>P_c-C-$	1.906 (0.020)	»	101.3 (mean)	»	97.6 (mean)	»	234,235
$(PPh)_5$ (CI)	ditto	»	2.217 (0.006)	$=P_c-C<$	1.843 (0.01)	»	100 (mean)	»	102	»	236
 (CII)	planar bicyclic ring system	»	2.209 (0.003)	ditto	1.825 (0.01)	» PPC PCC	97.3 (0.1) 99.7 (0.2) 120.5 (mean)	»	101.8 (mean)	»	237
$(PPh)_6$ (CII)	chair	»	2.235 (0.005)	»	1.843 (0.01)	PPP	95.0 (0.5)	»	98.5 (0.5)	»	238,239
P_4 (vapour)(CIV)	tricyclic structure (tetrahedron)	»	2.21 (0.02)	—		ditto	60	—		el. dif.	240
Black orthorhombic phosphorus $(P_6)_\infty$ (CV)	chair	»	2.234 (mean)	—		»	100	—		X-ray	241
Violet phosphorus (eight-, nine-membered groups) (CVI)	non-planar	»	2.219 (0.01)	—		»	101.0 (0.3)	—		ditto	242

considered (Table 14), the length of the $>P-P<$ bond is apparently somewhat greater, although the range of its variation remains fairly narrow (2.21–2.24 Å)‡. Within the limits of each structure the PP bonds are almost equal. The valence angles of the phosphorus atoms vary with the complexity of the ring.

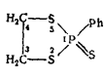
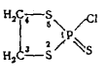
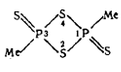
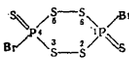
The conformation of the cyclic polyphosphines investigated in the crystal phase is as a rule non-planar. The only exception is compound (CII), where the average torsion angle is only 5° within the limits of the bicyclic ring system. The tetramers (XCVII)–(XCIX) have the molecular symmetry ~D_{2d} with equatorial orientation of the exocyclic substituents. Their PPPP torsion angles are respectively 34°, 31.4°, and 32.2°. The Raman spectra of liquid cyclic polyphosphines $(PR)_4$ have also been interpreted in terms of D_{2d} symmetry [243]. In the pentamers (C) and (CI), the PPPP torsion angles vary in the ranges 18–58° and 2–61° (the envelope conformation), the average in both structures being 38°. In these molecules, the exocyclic substituents at the two adjacent phosphorus atoms lie on one side of the ring, since, in contrast to the tetramers, a regular alternation of the directions in which the substituents are oriented relative to the average plane is in this case impossible. The ring system of the hexamer (CIII) has a chair conformation characterised by an average torsion angle of 84° with equatorial orientation of the exocyclic phenyl groups.

The possibility that the cyclicpolyphosphine ring systems $(PR)_n$ ($n = 4$, 5, or 6) are aromatic was discussed recently [7,29,244]. This hypothesis arose in connection with certain characteristics of the ultraviolet spectra of these compounds [245,246]. One must emphasise that there are no grounds for such a conclusion from the standpointof the structure of cyclic polyphosphines. In particular the absence of electron delocalisation is indicated by the invariance of the PP bond lengths.

The tetrahedral molecules of elemental phosphorus (CIV) in the vapour phase may be regarded as a tricyclic phosphine. The valence angles of the phosphorus atoms are in this case only 60°. It has been suggested that white (crystalline) phosphorus has a similar structure [247,248]. Red phosphorus is formed from white phosphorus when one of the bonds in the tetrahedra is cleaved and the tetrahedra are joined together to form chains or rings [249]. This hypothesis is consistent with the variation spectra of amorphous red phosphorus [250], which agrees best with a polymeric structure consisting of puckered four-membered rings with the D_{2d} (or C_{2v}) symmetry which is the same as (or similar to) the symmetry of the molecules of tetrameric cyclicpolyphosphines (XCVII)–(XCIX). None of the crystalline modifications of red phosphorus, the existence of which has been demonstrated by X-ray diffraction [251], has been subjected to a detailed structural analysis. The different modifications of black phosphorus (CV) and (CVI) contain more complex rings as repeating structural units.

‡ Anomalous $>P-P<$ (2.26–2.33 Å) bond lengths were found in the crystal structures of phosphorus sulphides and selenides (see below).

Table 15. Cyclic phosphonothioates, phosphorohalidothioates, polyphosphonothioates, and polyphosphorohalidothioates.

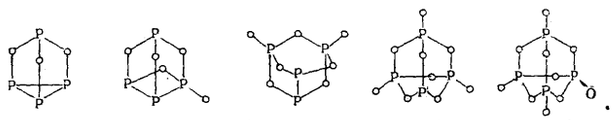
Compound	Ring conformation	Endocyclic bonds		Exocyclic bonds		Endocyclic valence angles		Exocyclic valence angles		Method	Refs.
		bond type	bond length, Å	bond type	bond length, Å	angle	magnitude, deg	angle	magnitude, deg		
 (CVII)	envelope»		2.087 (0.002)		1.801 (0.006)	SPS	98.5 (0.1)	$S_cP{=}S$	115.1 (0.1)	X-ray	252
					1.936	PSC	99.4	$CP{=}S$	113.9 (0.2)		
					(0.002)		(0.4)	S_cPC	106.4 (0.2)		
 (CVIII)	half-chair	ditto	2.051 (0.005)		2.059 (0.004)	SPS	100.5 (0.2)	$S_cP{=}S$	117.3 (0.2)	ditto	253
					1.910 (0.005)	PSC	96.1 (0.5)	$ClP{=}S$	111.4 (0.2)		
								S_cPCl	104.5		
 (CIX)	Planar	»	2.141 (0.006)		1.830 (0.015)	SPS	94.54 (0.22)	$S_cP{=}S$	116.56 (0.18)	»	254, 255
					1.945 (0.005)	PSP	85.46 (0.23)	$CP{=}S$	113.54 (0.51)	–	
								S_cPC	106.81 (0.18)		
 (CX)	boat	»	2.10 (0.02)		2.07 (0.02)	SPS	106			»	256
					1.98 (0.02)	PSS	100				

XIII. CYCLIC PHOSPHONOTHIOATES (CVII), PHOSPHOROHALIDOTHIOATES (CVIII), POLYPHOSPHONOTHIOATES (CIX), AND POLYPHOSPHOROHALIDOTHIOATES (CX)

The length of the $=\overset{|}{P}-S-$ endocyclic bonds in five-membered phosphonothioates and phosphorohalidothioates (Table 15) has been shown by the first studies of these structures in the crystalline phase not to differ from that in the acyclic structures (2.07–2.09 Å) within the limits of error [11]. The SPS endocyclic angles are similar to the OPO angles in five-membered cyclic phosphates (98–99°) (see above), but the PSC angles are significantly smaller than the POC angles. The conformations of five-membered rings in phosphonothioates and phosphorohalidothioates are non-planar, as for cyclic phosphates. In structure (CVII), the phosphorus and sulphur atoms deviate from the mean-square plane by 0.15 Å in the opposite directions (the envelope conformation); in structure (CVIII) the deviations of the ring atoms from the best plane are −0.194 Å for P, 0.299 Å for $S_{(2)}$, −0.336 Å for $C_{(3)}$, 0.161 Å for $C_{(4)}$, and 0.071 Å for $S_{(5)}$ (the conformation is close to that of the half-chair form). The conformation of the four-membered ring of the polyphosphonothioate (CIX) is planar (C_{2h} symmetry), like that found for the diphosphazane molecule with tetracoordinate phosphorus [compound (LXII)]. The six-membered ring in compound (CX) has a boat conformation with a PSSP torsion angle of 86°.

XIV. PHOSPHORUS SULPHIDES [(CXI)–(CXVII)] AND SELENIDES [(CXVIII)–(CXX)]

Phosphorus sulphides and selenides (Table 16) consist of large polycyclic molecules P_4S_n or P_4Se_n (n = 3, 5, 7, 9, or 10):



(CXI, CXVIII) (C_{3v}) (CXIV, CXX) (C_1) (CXV *a* and *b*) (C_s) (CXVI) (C_s) (CXVII) (C_{3v})

In contrast to phosphorus oxides, among phosphorus sulphides and selenides there are structures without symmetry elements. The isomeric di-iodo-derivatives resemble closely this series of compounds:

The polycyclic systems contain three-, four-, five-, and six-membered rings. The conformation of the four-membered rings in (CXIV) and (CXX) is close to that of the rings of tetrameric cyclic polyphosphines (see above). The five-membered rings in each of the sulphides [except (CXVI) and (CXVII)] and selenides show a considerable geometrical similarity to the rings of the five-membered polyphosphines (C) and (CI) (the envelope conformation).

Table 16. Phosphorus sulphides and selenides.

Compound	Endocyclic PE bonds (E = S, Se)					Exocyclic bonds, Å	Endocyclic valence angles (E = S, Se, or P)					Exocyclic bonds		Method	Refs.
	$P^{III}-EP^{III}$	$P^{III}-EP^{V}$	$P^{V}-EP^{III}$	$P^{V}-EP^{V}$	$P^{III}-P^{III}$		$EP^{III}E$	$EP^{V}E$	$P^{III}EP^{III}$	$P^{III}EP^{V}$	$P^{V}EP^{V}$	angle	magnitude, deg		
P_4S_3 (CXI a)	2.090 (0.005)	—	—	—	2.235 (0.005)	—	60** 99.4 103.1	—	103.0	—	—		—	X-ray	257
P_4S_3 (CXI b)	2.17 (0.02)	—	—	—	2.21 (0.02)	—	—	—	105(3)		—		—	el. dif.	258
α-$P_4S_3I_2$ (CXII)	2.10 (0.04)	—	—	—	2.20 (0.04)	2.48(0.03) (>P_c—I)	102—105	—	104		—	PPI SPI	98 104	X-ray	259
β-$P_4S_3I_2$ (CXIII)	2.095 (0.016) 2.13 (0.01)	—	—	—	2.21 (0.01)	2.471(0.008) (>P_c—I)	101.6 (0.3)	—	99.6(0.3) 106(0.3)		—	PPI SPI	94.5(0.2) 103.0(0.4)	ditto	260
P_4S_5 (CXIV)	2.11 (mean)	2.14 (mean)	2.085 (0.01)	—	2.26 (0.01) 2.24 (P^V-P^{III})	1.94 (0.01) (—P_c=S)	85** 102.5 (mean)	89.6*** 108.4	103.8 (mean)	88.7*** 103.4	—	PP=S SP=S	125.5 112 (mean)	»	261, 262
α-P_4S_7 (CXV a)	—	2.108 (0.007)	2.079 (0.007)	2.114 (0.007)	2.326 (0.007)	1.918(0.007) (—P_c=S)	103.5 (mean)	107 (mean)	—	102.4	110.1	SP=S	112 (mean)	»	262, 263
β-P_4S_7 (CXV b)	—	2.11 (0.045)	2.07 (0.04)	2.12 (0.04)	2.26 (0.02)	1.89(0.045) (—P_c=S)	103 (mean)	107 (mean)	—	102.5	110	SP=S	112	»	264
P_4S_9 (CXVI)	—	2.11 (0.01)	2.12 (0.01)	2.12 (0.01)	—	1.93 (0.01) (—P_c=S)	108.4	109.6	—	110.8	108.7	SP=S	109.3	»	265
P_4S_{10} (CXVII)	—	—	—	2.097 (0.015)	—	1.908(0.015) (—P_c=S)	—	109.3 (0.7)	—	—	109.8 (0.7)	SP=S	109.6(0.7)	»	262, 263
P_4Se_3 (CXVIII)	2.24 (0.03)	—	—	—	2.25 (0.03)	—	60** 100 105	—	100	—	—	—	—	»	266
β-$P_4Se_3I_2$ (CXIX)	2.25 (0.04)	—	—	—	2.22 (0.03)	2.47 (0.02) (>P_c—I)	102.7 (1.2)	—	97.1(1.5) 103.6(1.1)	—	—	PPI SePI	94.6(1.0) 101.4(0.8)	»	267
P_4Se_5 (CXX)	2.25 (mean)	2.285 (mean)	2.245 (0.015)	—	2.294 (0.019) 2.237 (0.016) (P^V-P^{III})	2.123(0.013) (—P_c=Se)	86.5(0.5)*** 103.2 (mean)	89.6(0.6)*** 109.3 (mean)	102 (mean)	85.4(0.4)*** 99.7(0.4)	—	PP=Se SeP=Se	121.9(0.6) 112 (mean)	»	268

*The symbols P^{III} and P^{V} denote tervalent and quinquevalent phosphorus respectively.
**In a tervalent (three-membered?) ring.
***In a quadrivalent (four-membered?) ring.

The six-membered rings in compounds (CXVI) and (CXVII), which include tri- and tetra-coordinate phosphorus, have a chair conformation—the same as in (CIII) and (CV). In the molecules of the di-iodides (CXII), (CXIII), and (CXIX), two five-membered rings are joined by a common PXP fragment.

In turn, the remaining endocyclic bonds form a common six-membered ring in the boat form with the following endocyclic angles:

(CXII)	(CXIII)	(CXIX)
PPS 91° (mean)	PPP 96.5±0.5° SPS 103.2±0.5°	PPP 97.8±1.5° SePSe 103.6±1.3°

It is interesting that the PPP bonds considered are much smaller than in the six-membered rings of black phosphorus (102°). As already noted, the PP bonds in the sulphides and selenides are significantly longer in many cases than the usual bond. The lengths of the PS(PSe) bonds are on average little different from those found in the acyclic compounds[11]. The difference between the bonds of tervalent and quinquevalent phosphorus are not as pronounced as in the oxides. On the other hand, in certain structures [for example, in (CXIV) and (CXX)] the lengths of the single PS and PSe bonds are different, the differences reaching about 0.1 Å.

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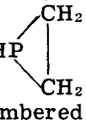
The above discussion of the molecular structures of cyclic organophosphorus compounds shows that their geometrical structures have certain definitely unusual features.

In small rings with $n = 3-5$ atoms, the valence angles involving the phosphorus atom are apparently largely determined by the dimensions of the ring system. The smallest of the known valence angles of the phosphorus atom—the CPC angle in the  molecule—is only 47.4°. In four- and five-membered rings, the valence angles of the phosphorus atoms are still significantly

smaller than the analogous angles in the acyclic structures. In small rings, the single phosphorus–element bonds are as a rule longer than the bonds in the acyclic structures.

In the case of six-membered rings (excluding, of course, phosphonitriles and similar formally unsaturated structures), there is usually considerable similarity with acyclic structures as regards the above parameters. The main reason for such differences is frequently believed to be the existence of ring strain in small ring systems. However, an appreciable increase in the length of PO bridge bonds occurs also in six-membered rings in the structure of phosphorus oxides.

The effect of exocyclic substituents on the geometrical parameters of the ring system is shown, in particular, in phosphonitriles, where the inhomogeneity of these substituents leads to different lengths of endocyclic bonds and a decrease of the symmetry of the ring system.

It is as a rule impossible to establish significant differences between the parameters of endocyclic bonds and those of acyclic compounds. However, the length of the PCl bonds in phosphadiazoles (2.17–2.19 Å for tricoordinate phosphorus and 2.07 Å for tetracoordinate phosphorus) is much greater (by up to 0.20 Å) than in other phosphorus compounds. In most of the structures investigated, the PCl bonds are shorter than the sum of the covalent radii (2.09 Å). This factor was interpreted as an increase in the multiplicity of the PCl bonds. The greater length of the PCl bond found in phosphadiazoles compared with the sum of the covalent radii gives rise to new theoretical problems.

Ring structures with pentacoordinate phosphorus (cyclophosphazanes) constitute the first case to which the empirical rule of the preferential axial location of fluorine atoms in the trigonal-bipyramidal environment of the phosphorus atom is inapplicable.

The simplest cyclic systems (three-membered systems) do not present any conformational problems, since in such cases only planar structures are possible. Examination of the complete set of the available data shows that in more complex rings the conformation is non-planar when tricoordinate phosphorus is present. The only exception is the five-membered ring in compound (CII), where the average torsion angle is only 5°. Planar conformations are apparently characteristic of ring systems containing di- and penta-coordinate phosphorus. Structures containing tetracoordinate phosphorus can have both planar and non-planar conformations. The non-planarity of the phosphole ring merits particular attention. It implies the non-planarity of ethylene systems, which is difficult to expect in view of the high barrier to rotation about the C=C bond.

It is believed that the ring conformations are due to the operation of forces associated with angular deformations and torsional interactions in relation to bonds. Thus the replacement of hydrogen atoms linked to terminal carbon atoms in five-membered cyclic phosphites and phosphates by methyl groups leads to an increase of torsional interactions and a change in conformation from envelope to half-chair. On the other hand, the envelope conformation is difficult to expect for a ring of this type on the basis of the hypothesis concerning the twisting moments about different bonds, since in this case there is an eclipsed configuration relative to the C–C bond, although it is known that the barrier to rotation relative to this bond is greater than that relative to the C–O and P–O bonds.

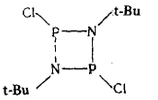
The axial disposition of the P–Cl bonds in the molecules of five- and six-membered ring phosphites and phosphates may be regarded as analogous to the *gauche*-conformation of such bonds about the P–O bonds in the acyclic derivatives.

The valence angles involving the exocyclic N and O atoms are appreciably greater, as in the acyclic compounds, than the values found in trimethylamine and in methyl ether: the nitrogen atom has a planar bond configuration and the POC valence angles are about 120°, exceeding the COC valence angle by 10°.

On the whole, analysis of the structures investigated makes it possible so far to elucidate only the general trends, which require further confirmation and refinement. The inadequacy of the available data is caused not only by the small number of studies but to a greater extent by the insufficient accuracy of their results.

ADDENDUM

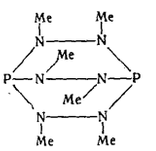
The structure of the dimeric molecule of a cyclophosphazane (CXXI) with tricoordinate phosphorus was investigated for the first time by Muir and Nixon[269]. It was shown by X-ray diffraction that the four-membered ring of this molecule is slightly non-planar: the P and N atoms are alternately 0.045 Å above and below the average plane (a dihedral angle of 6°). Both Cl atoms linked to the P atoms occupy equatorial positions, i.e. they are located on the same side of the ring as the N atoms. However, the substituents at the N atoms are not equivalent in this respect: one of them is in the *cis*-position relative to the Cl atoms and the other in the *trans*-position:



(CXXI).

The molecule of compound (CXXI) has the following geometrical parameters: $r(\rangle P_c-Cl) = 2.105(0.009)$ Å; $r(\rangle P_c-N_c\langle) = 1.689(0.005)$ Å; $\angle NPN = 82.5(0.3)°$; $\angle PNP = 97.3(0.4)°$; $\angle NPCl = 103.3(0.4)°$; $\angle PNC = 129.5°$ (on average). Evidently the bond lengths and valence angles in the ring are very close to the values of the corresponding parameters for the dimeric molecule of a cyclophosphazane with tetracoordinate phosphorus (LXII). However, the PCl bond length in (CXXI) is much greater. A correction for thermal motion increases the length of this bond to 2.149(0.009)Å.

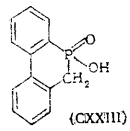
According to an X-ray diffraction study[270], the fundamental geometrical parameters of the bicyclic molecule of (CXXII) have the following values: $r(\rangle P_c-N_c\langle) = 1.68(0.03)$ Å; $\angle NPN = 100(3)°$; $\angle PNN = 117(4)°$; the sum of the valence angles of the nitrogen atom $\alpha_N = 345(2)°$. The PNNP chain in (CXXII) was found to be planar to within 0.06(0.02) Å.



(CXXII).

Two X-ray diffraction studies of cyclic structures with tetracoordinate phosphorus, carried out at the beginning of the 1960's but not mentioned in earlier reviews, are of interest. In one of

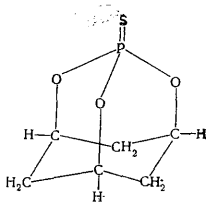
these investigations [271], it was found that in the molecule of compound (CXXIII) the P atom and the C atom of the methylene group are located in the planes of the closest benzene rings, the angle between these planes being 22°.



(CXXIII)

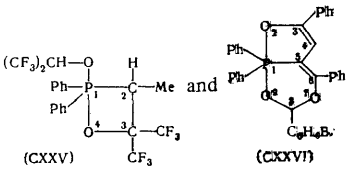
The geometrical parameters of the phosphorus fragment in (CXXIII) are are follows: $r(=P_c-C_c<) = 1.80$ Å; $r(=P_c-C_c-) = 1.79$ Å; $r(-P_c=O)_1 = 1.47$ Å; $r(-P_c=O)_2 = 1.57$ Å; $\angle OP{=}O = 115°$; $\angle CPO = 107°$; $\angle CP{=}O = 114°$; $\angle(CPC)_c = 101°$.

In the second of the above two investigations [272], the following parameters were found for the (CXXIV) molecule: $r(-P_c=S) = 1.90(0.01)$ Å; $r(=P_c-O_c-) = 1.58(0.002)$ Å; $\angle OP{=}S = 113.7(0.9)°$; $\angle OPO = 104.7(1.1)°$; $POC = 113.3(1.7)°$. All three oxygen atoms in the (CXXIV) molecule occupy axial positions in relation to the cyclohexane ring.



(CXXIV)

A further two X-ray diffraction studies have been made on the structure of the cyclicoxyphosphoranes (CXXV) and (CXXVI):



(CXXV) (CXXVI)

In both molecules the oxygen atoms occupy axial positions. In (CXXV), [237] the P atom is in the centre of a distorted trigonal bipyramid with a four-membered ring in the axial-equatorial plane. The ring is non-planar but has a relatively small $C_{(2)}PO_{(4)}/C_{(2)}C_{(3)}O_{(4)} = 11°$ dihedral angle, which corresponds to a displacement of the atoms from the average ring plane by not more than 0.06 Å. The (CXXV) molecule has the following fundamental geometrical parameters: $r(P_cO_c)_a = 1.79(0.01)$ Å; $r(P_cO)_a = 1.71(0.01)$ Å; $r(P_cC_c)_e = 1.83(0.02)$ Å; $r(P_cC)_e = 1.79$ Å (mean); $C_{(2)}PO_{(4)} = 75.5(0.6)°$; $\angle PO_{(4)}C_{(3)} = 94.8(1.0)°$; $\angle PC_{(2)}C_{(3)} = 94.8(1.0)°$.

In the (CXXVI) molecule [274], the P atom is in the centre of an almost regular trigonal bipyramid. Both rings occupy axial-equatorial positions. The five-membered ring is planar, with the parameters $r(P_cO_c)_a = 1.786(0.006)$ Å; $r(P_cC_c)_e = 1.815(0.006)$ Å; $\angle OPC = 87.3(0.2)°$; $\angle POC = 113.8(0.2)°$.

The non-planar six-membered ring has the following parameters: $r(P_cO_c)_a = 1.737(0.006)$ Å; $\angle OPC = 92.7(0.2)°$; $\angle POC = 113.3(0.2)°$.

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Thin-layer Electrochemistry

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This review deals with the theoretical foundations of the methods of thin-layer electrochemistry (chronopotentiometry, voltammetry, and the steady-state current method), and with the application of these methods to the measurement of rate constants of electrochemical reactions, to the study of adsorption, and to the determination of diffusion coefficients, number of electrons involved in the reaction, etc. The scope of the methods of thin-layer electrochemistry, and their advantages in specific cases over alternative methods of studying electrode processes, are discussed. 53 references.

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I. INTRODUCTION

The most important recent advances in electrochemistry have been concerned with the development of the theory of electrode processes, which is relevant not only to electrochemistry itself but also to related branches of science and technology. Electrochemical concepts and techniques are used, for example, in studies of biological processes, in studies of the electrochemical and adsorption properties of the semiconductor–electrolyte interface, etc.

Electrochemical processes often need to be studied not only on macroscopic samples but also on small (and even very small) samples. Measurements with small volumes of solution have long been carried out in polarography with the dropping mercury electrode, but the smallest practical volume of solution in cells of conventional design has been 0.2–0.3 ml. The first papers on thin-layer electrochemistry appeared in the early 1960's, and laid the foundations for the solution of the theoretical and the practical problems inherent in studies of the electrolysis of solutions held in a narrow gap between two electrodes. During the last decade there have been significant developments in this area of electrochemistry. Depending on the method used to display the infromation, we can classify this work into thin-layer chronopotentiometry, oscillographic voltammetry, and the steady-state current method. The methods of thin-layer electrochemistry have some definite advantages over the corresponding methods which rely on large volumes of solution. These advantages stem from the fact that the convective transfer of electrochemically active material is practically negligible in thin layers of electrolyte, and therefore the mathematical description of the electrode processes is greatly simplified. Hence, important kinetic parameters such as the rate constants k, the diffusion coefficients D, and the number of electrons n can be evaluated without difficulty. Thin-layer methods using solution volumes as small as 10^{-3} ml are also convenient for the analysis of strongly radioactive solutions which cannot be safely handled in large volumes. Insufficient attention has been paid to thin-layer electrochemistry in the Soviet literature: this review aims to rectify the omission in some measure.

II. THEORY OF THIN-LAYER ELECTROCHEMISTRY

We shall discuss the theory of thin-layer electrochemistry by considering the electrode processes in a thin cylindrical layer of solution of thickness l held between two plane-parallel coaxial electrodes of area A and radius r. The thickness of the layer can be controlled, for example, by using a micrometer as shown in Fig. 1. The volume of solution between the electrodes is $lA \simeq 10^{-3}$ ml. In order to monitor the electrode potential, the experimental solution can be held in contact with a large volume of the same solution through the cylindrical face of the thin layer (of area $2\pi rl$).

Fig. 2 shows the circuit diagram for a thin-layer cell consisting of a pair of plane-parallel electrodes, an auxiliary electrode, and a standard electrode, with suitable connections. Several methods of connection can be used. If the potentials of the working electrodes W_1 and W_2 are controlled independently by means of a standard and an auxiliary electrode, as shown in Fig. 2, we have a coupled thin-layer cell. If the electrode potentials E_1 and E_2 are equal, the cell has effectively one working electrode of total area $2A$ and solution thickness $l/2$. If one of the electrodes is left open-circuited, it acts as an inert plate. Lastly, if the standard and the auxiliary electrode are omitted we have a simple two-electrode thin-layer cell.

As an alternative to the plane-parallel electrodes[1-4], the electrodes for thin-layer electrochemical cells can be in the form of thin wires in a narrow glass or plastic tube[5,6]. A cell of this type is shown in Fig. 3. The thickness of the layer of solution can be varied by suitable choice of wire diameter and channel bore. The electrode

material can be graphite, platinum, mercury, or other metals; for combined electrochemical and spectrophotometric measurements glass plates coated with a conducting layer have been used [1,7-11].

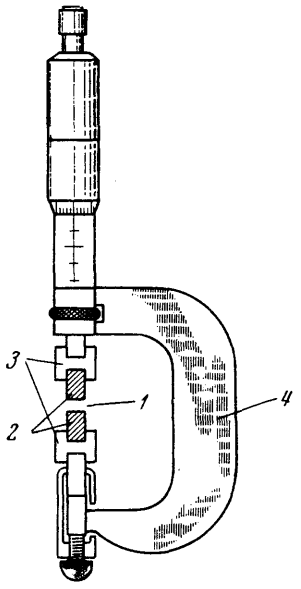

Figure 1. Plane-parallel micrometric electrodes: *1*) gap, *2*) platinum electrodes, *3*) insulating collars, *4*) micrometer.

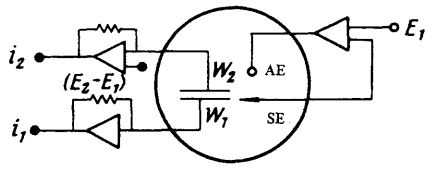

Figure 2. Circuit diagram of a two-electrode thin-layer cell: W_1 and W_2 are the working electrodes, AE is the auxiliary electrode, SE is the standard electrode.

1. Chronopotentiometry

We shall consider a solution containing an electrochemically active material in a thin-layer cell, confined between the boundaries 0 and l, so that $0 < x < l$. Only one of the two close-spaced electrodes is working, and the second electrode behaves as the wall of the cell.

If the material O is reduced at a constant current density i (galvanostatic conditions), and if the edge effect can be neglected†, the concentration of O at the electrode at any instant $c_O(0, t)$ can be calculated by the Laplace transform [12].

†See p. 1098.

Christensen and Anson [2] have shown that

$$c_O(0,t) = c_O^0 - \frac{il}{nFAD}\left[\frac{Dt}{l^2} + \frac{1}{3} - \frac{2}{\pi^2}\sum_{k=1}^{\infty}\frac{1}{k^2}\exp\left(-\frac{\pi^2 k^2 Dt}{l^2}\right)\right] \quad (1)$$

where c_O^0 is the initial concentration of O.

For large l, Eqn. (1) reduces to the familiar chronopotentiometric equation.

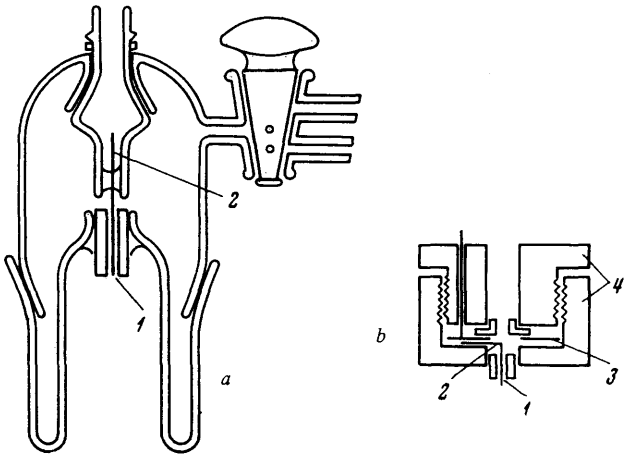

Figure 3. Types of capillary-filament electrode: *1*) gap, *2*) working electrode, *3*) Pt contact disk, *4*) Teflon body.

The time for complete removal of the depolariser from the layer adjacent to the electrode, when $c_O(0, t) = 0$, is called the transient time τ.

If τ is so large that $l^2 < \tau D$, the exponential terms in Eqn. (1) can be ignored, and the following expression for τ is obtained:

$$\tau = \frac{nFAlc_O^0}{i} - \frac{l^2}{3D}. \quad (2)$$

If the Nernst equation applies, the variation of potential with time $[E = f(t)]$ for the reversible redox couple O–R is given by the expression

$$E = E^0 + \frac{RT}{nF}\ln\frac{\tau - t + \frac{2l^2}{\pi^2 D}\sum_{k=1}^{\infty}\frac{1}{k^2}\exp\left(-\frac{\pi^2 k^2 Dt}{l^2}\right)}{t + \frac{l^2}{3D} - \frac{2l^2}{\pi^2 D}\sum_{k=1}^{\infty}\frac{1}{k^2}\exp\left(-\frac{\pi^2 k^2 Dt}{l^2}\right)} \quad (3)$$

where E^0 is the normal potential of the couple O–R. Eqn. (3) assumes equality of the diffusion coefficients of the oxidised and the reduced form of the material. The quantity $l^2/3D$ and the exponential terms of Eqn. (3) can be made small in comparison with t. In this case $E = E^0$ at $t = \tau/2$. The second term in the right-hand side of Eqn. (2) can be ignored when l is small and the concentration of O in solution is large enough. Thus, for $l = 10^{-3}$ cm and $D = 10^{-5}$ cm^2 s^{-1}, we have $l^2/3D \simeq 3 \times 10^{-2}$ s, and the second term in Eqn. (2) can be neglected under these

conditions if $\tau > 3$ s. Eqn. (3) then reduces to Faraday's law in the form used in constant-current coulometry:

$$\tau = \frac{nFAlc_0}{i} \quad (4)$$

or

$$Q = nFAlc_0 . \quad (5)$$

(*a*) Determination of the number of electrons in the reaction

Eqn. (4) can be used to evaluate n when the diffusion coefficients of the species being studied are not known. The cell used for this purpose has very closely spaced electrodes, to make $l^2/3D$ much smaller than the transient time. Thin-layer chronopotentiometry has been used to determine the number of electrons involved in the oxidation of *N,N*-dimethyl-*p*-phenylenediamine. The reaction goes through the steps

$$H_2N{-}C_6H_4{-}N(CH_3)_2 - e \rightleftarrows [H_2N{-}C_6H_4{-}N(CH_3)_2]^+ ,$$

$$[H_2N{-}C_6H_4{-}N(CH_3)_2]^+ - e \rightleftarrows NH{=}C_6H_4{=}N(CH_3)_2^+ + H^+ .$$

Conventional chronopotentiometric measurements[13] on platinum electrodes in acid solutions indicate a two-electron transition, but the interpretation of the results is complicated by subsequent chemical changes of the reaction products. The mean of the experimental values (n = 1.97) obtained in thin-layer experiments is in very good agreement with the value (n = 2) proposed for the oxidation of *N,N*-dimethyl-*p*-phenylenediamine to the di-imine. The thin-layer experiment gives more accurate values than conventional controlled-potential electrolysis[2,14]. Sharper chronopotentiograms are obtained in the thin-layer cell than in a conventional cell, as shown by the curves in Fig. 4 for the oxidation of *p*-phenylenediamine.

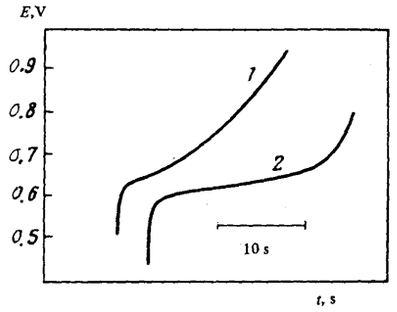

Figure 4. Chronopotentiograms for the oxidation of *p*-phenylenediamine: *1*) diffusion cell (c = 4.72 mM, current density 0.6 μA cm^{-2}); *2*) thin-layer cell (c = 4.99 mM, current density 0.09 μA cm^{-2}). In both cases the supporting electrolyte is 1 M H_2SO_4.

This is because a sharp transition to the next reaction (for example, the oxidation of water) sets in as soon as the whole of the material in the thin layer between the electrodes has been oxidised. In contrast, a significant fraction of the current in diffusion chronopotentiometry is carried by the oxidation of the experimental material which diffuses from the more remote layers of solution when the layer adjacent to the electrode has been depleted: as a result, the potential changes more gradually with time.

(*b*) Determination of diffusion coefficients

Oglesby and coworkers[15] have shown, by analysing Eqn. (2), that the diffusion coefficient of the experimental material can be determined even if the concentration of the solution and the surface area of the working electrode are not known. Thus, a plot of τ against $1/i$ is a straight line whose intercept on the τ axis gives $-l^2/3D$ (Fig. 5).

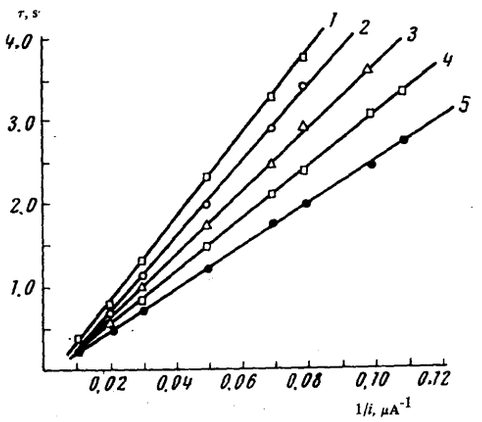

Figure 5. Plots of τ against $1/i$ for different thicknesses of solution: *1*) 1.88×10^{-3}, *2*) 1.62×10^{-3}, *3*) 1.37×10^{-3}, *4*) 1.12×10^{-3}, *5*) 0.864×10^{-3} cm. Area of working electrode 0.27 cm^2. Experimental solution $K_3Fe(CN)_6$ in 0.5 M Na_2SO_4.

Knowing l, the diffusion coefficient of the electrochemically active species can be calculated. Table 1 shows the diffusion coefficients for $Fe(CN)_6^{3-}$ in 0.5 M Na_2SO_4 obtained for different values of the layer thickness l.

Table 1. Diffusion coefficient of $Fe(CN)_6^{3-}$ in 0.5 M Na_2SO_4.

$10^3 l$, cm	$l^{2/3}D$, s	$10^5 D$, cm^2 s^{-1}
0.864	0.0502	0.49
1.12	0.0883	0.47
1.37	0.140	0.45
1.62	0.236	0.37
1.88	0.252	0.47

Average $D = 0.45 \times 10^{-5}$ cm^2 s^{-1}

(*c*) Determination of the rate constants of chemical reactions

Thin-layer chronopotentiometry is a very convenient technique for measuring the rate constants of slow chemical reactions involving the electrolysis products. As an

example, we shall consider the hydrolysis of *p*-benzoquinoneimine, formed by the anodic oxidation of *p*-aminophenol on a Pt electrode (Christensen and Anson [16]).

The anodic oxidation of *p*-aminophenol in aqueous solutions proceeds by the following mechanism [17–19]:

$$HO{-}C_6H_4{-}NH_2 - 2e \rightleftarrows O{=}C_6H_4{=}NH + 2H^+ ,$$
$$O{=}C_6H_4{=}NH + H_2O \rightarrow O{=}C_6H_4{=}O + NH_3 .$$

Fig. 6 shows a thin-layer chronopotentiogram of the oxidation of *p*-aminophenol followed by the reduction of *p*-benzoquinoneimine and *p*-benzoquinone.

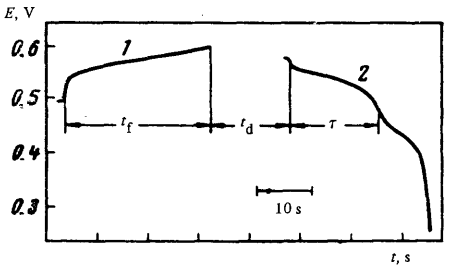

Figure 6. Thin-layer chronopotentiogram: *1*) oxidation of *p*-aminophenol, *2*) reduction of *p*-benzoquinoneimine and *p*-benzoquinone. t_d = 45.4 s.

p-Aminophenol (R) is oxidised during time t_f to *p*-benzoquinoneimine (O), which is then hydrolysed to *p*-benzoquinone (Z) by an irreversible first-order reaction. Since the reduction of *p*-benzoquinone occurs in a different region of potentials, this compound can be treated as electrochemically inert. The current is interrupted during the interval t_d, and the hydrolysis of *p*-benzoquinoneimine is the only possible reaction during this time. The polarity of the current is then reversed, and any unchanged *p*-benzoquinoneimine is reduced back to *p*-aminophenol (R). The hydrolysis reaction continues, in parallel with the reduction of *p*-benzoquinoneimine.

We shall calculate first of all the concentration of O in the thin layer of solution at time t ($0 < t < t_f$). We can write

$$\frac{dc_O}{dt} = \beta - kc_O \qquad (6)$$

where $\beta = i/nFAl$ (see Eqn. (1)). The first term in the right-hand side of Eqn. (6) describes the production of O, the second term describes its removal by the hydrolysis reaction.

Since $c_O = 0$ at $t = 0$, the solution of Eqn. (6) is

$$c_O = \frac{\beta}{k}(1 - e^{-kt}) . \qquad (7)$$

During the period when $i = 0$, i.e. for $t_f < t < t_f + t_d$, we can write

$$\frac{dc_O}{dt} = -kc_O . \qquad (8)$$

Solving Eqn. (8) and substituting for c_O from Eqn. (7), the following expression applies for $t' = t - t_f = 0$ (i.e. at the instant t_f):

$$c_O = \frac{\beta}{k} e^{-kt'}(1 - e^{kt_f}) . \qquad (9)$$

During the period of reduction of O, i.e. for $t_f + t_d < t < t_f + t_d + \tau$, we have

$$\frac{dc_O}{dt} = -\theta\beta - kc_O \qquad (10)$$

where θ is the ratio of cathodic to anodic current.

Solving Eqn. (10) and taking c_O from Eqn. (9) with $t'' = t - (t_f + t_d) = 0$ (i.e. at the instant t_d) we obtain

$$c_O = \frac{\beta}{k}\{e^{-kt''}[\theta + e^{-kt_d}(1 - e^{-kt_f})] - \theta\} . \qquad (11)$$

The transient time is determined by the condition $c_O = 0$, $t'' = \tau$. Hence, from Eqn. (11),

$$\tau = \frac{1}{k}\ln\left[1 + \frac{1}{\theta}e^{-kt_d}(1 - e^{-kt_f})\right] , \qquad (12)$$

and for $\theta = 1$

$$\tau = \frac{1}{k}\ln[1 + e^{-kt_d}(1 - e^{-kt_f})] . \qquad (13)$$

The theory for an analogous electrode process but in the usual chronopotentiometric model is much more complicated. The correctness of Eqn. (13) has been confirmed experimentally: Table 2 shows the results of measurements of the rate constant for the hydrolysis of *p*-benzoquinoneimine in 1.017 M H_2SO_4 at 25°C. The concentration of the starting material, *p*-aminophenol, was 1.01×10^{-2} M.

Table 2. Rate constant for the hydrolysis of *p*-benzoquinoneimine.

t_f, s	t_d, s	τ, s	10^3k, s^{-1}
32.1	9.9	23.9	7.8
41.8	19.9	28.1	7.3
19.0	42.2	12.7	7.0
27.4	45.4	16.6	7.5
36.0	50.4	20.3	7.3
16.6	51.1	10.3	7.4

Average $k = 7.4 \times 10^3$ s^{-1}

The equation for the rate constants of slow chemical reactions is greatly simplified by using the thin-layer cyclic potentiostatic method instead of the chronopotentiometric method. In that method, the unstable form is obtained under potentiostatic conditions, and the current (or the quantity of electricity) is plotted against time. After a certain time the potential is changed to a value at which the unstable product which has not yet reacted is converted back into the original form by the reverse electrochemical reaction. Oglesby and coworkers [20] used this method to study the acid-catalysed rearrangement of hydrazobenzene. The starting compound was the stable azo-form, and the unstable hydrazo-form was produced at the surface of the working electrode. The reaction mechanism is

$$C_6H_5{-}N{=}N{-}C_6H_5 + 2e + 2H^+ \rightleftarrows C_6H_5{-}NH{-}NH{-}C_6H_5 \xrightarrow{k} H_2N{-}C_6H_4{-}C_6H_4{-}NH_2 .$$

Theoretically, the time for complete exhaustion of a layer of solution 2×10^{-3} cm thick is less than one second[21]. If the reaction of interest is sufficiently slow, the unstable product may be formed rapidly in the potentiostatic experiment and allowed to react at the same potential during a much longer time (t_r) than the time required to generate it. The ratio of the quantities of electricity passed in the reverse and the forward electrolysis (h_r/h_b) is equivalent to the ratio of the initial concentration of reactant (e.g. azobenzene) to the final concentration of the product (e.g. hydrazobenzene). The plot of $\ln(h_r/h_b)$ against t_r for a first-order reaction should be a straight line of slope k.

When one-half of the product has reacted, $h_r/h_b = 2$. If we denote the time for half-reaction by $t_{1/2}$, the rate constant can be expressed in the form

$$k=\frac{\ln 2}{t_{1/2}}=\frac{0.693}{t_{1/2}}\ . \qquad (14)$$

The rate constants for the rearrangement of hydrazobenzene obtained by thin-layer methods agree satisfactorily with the values given by other electrochemical methods. Thus, the cyclic galvanostatic method gives 10.2×10^{-3} s^{-1}, the potential jump reversal method gives 10.7×10^{-3} s^{-1}, whereas the thin-layer chronopotentiometric and potentiostatic methods give 18.6×10^{-3} and 11.7×10^{-3} s^{-1} respectively. The concentration of $HClO_4$ was 0.075 M in every case.

(*d*) Study of adsorption

By virtue of its large ratio of electrode surface area to volume of solution, the thin-layer electrochemical cell can be used to study surface phenomena such as adsorption processes. Hubbard and Anson[3] have suggested a simple and convenient method for the quantitative determination of adsorbed materials from theoretical considerations of the behaviour of electrically active substances under the conditions of the thin-layer experiment.

If the compound is adsorbed on the electrode surface, and if the geometry of the cell justifies ignoring the second term in the right-hand side of Eqn. (2), the transient time which characterises the full exhaustion of the depolariser (whether adsorbed or not) can be expressed as

$$\tau=\frac{nFAlc}{i}+\frac{2nFA\Gamma}{i}\ , \qquad (15)$$

where Γ is the amount adsorbed in mole cm^{-2}. The coefficient 2 arises from the fact that adsorption occurs on both electrodes, each of area A. If the adsorbate does not take part in the electrode reaction under conditions leading to reaction by non-adsorbed species, the amount of adsorbate is found from the difference between the experimentally measured quantity of electricity and the quantity of electricity theoretically calculated by Eqn. (5).

The advantages of thin-layer electrochemistry in studies of adsorption phenomena have been demonstrated in a series of papers[22-24] on the adsorption of iodine. It is shown that the adsorption of I_2 and I^- on platinum electrodes can take two forms: an electrochemically active and an inactive state. Initially I_2 is adsorbed in the inactive form (up to $\sim 2\times10^{-9}$ mole cm^{-2}); this is followed by adsorption in the active form (a further 10^{-9} mole cm^{-2}).

Adsorbed, active I^- ($\sim 1.2\times10^{-9}$ mole cm^{-2}) blocks the adsorption of the inactive forms of I_2 and I^-. Adsorbed, inactive I_2 prevents further adsorption of I^-.

The adsorption of active I_2 is unaffected by whether the electrode is covered with I^- ions or by free iodine. The adsorption of inactive I^- can be estimated from the equations for the anodic transient time of the oxidation of I^- to I_2.

The presence of inactive, adsorbed I_2 can be confirmed by oxidative desorption ($n = 5$), followed by estimation of the resulting iodate.

In a study of the behaviour of the I_2/I^- couple it was found that the adsorbed iodide ion is not oxidised at potentials sufficient to oxidise non-adsorbed iodide.

These results suggest that adsorbed I^- and I_2 are not likely to be the species responsible for the electron transfer reactions giving rise to the exchange current at Pt electrodes in I^-/I_2 solutions. Workers who reached the opposite conclusion[25,26] from their kinetic studies must have argued incorrectly.

The conclusions made from the study of the electrochemical behaviour of the I_2/I^- couple on Pt electrodes in thin layers of solution are somewhat inconsistent with conclusions based on other methods[27-33]. However, some aspects of the thin-layer work[22-24] are not entirely convincing, and should be re-examined.

2. Voltammetry

(*a*) Reversible processes

If a depolariser is present in the thin layer of solution, the application of a prescribed potential to the electrode will cause a current to flow through the cell as a result of the electrochemical reaction. The layer of solution immediately adjacent to the electrode surface will be gradually depleted of depolariser; however, a new supply of depolariser is available by diffusion from within the solution. This process produces a thickening of the diffusion layer, which in the thin-layer experiment cannot exceed the value l. On raising the electrode potential the rate of the electrochemical process increases, but at the same time the supply of depolariser is hindered. As a result, the current increases only to a certain value, and then decreases to zero. Anson and Hubbard[34] have derived an equation which describes the current–voltage characteristic of the process, assuming that the electrode potential is varied linearly with time.

For a reversible reaction ($O + ne \rightleftharpoons R$) and a relatively slow rate of change of potential (not more than 20 mV s^{-1}), the following expressions for c_O and c_R can be used:

$$c_O=c_O^0\left\{1/\left[1+\exp\frac{nF}{RT}(E^0-E)\right]\right\}\ , \qquad (16)$$

$$c_R=c_R^0\left\{1/\left[1+\exp\frac{nF}{RT}(E-E^0)\right]\right\}\ . \qquad (17)$$

The current i flowing through the thin-layer cell when the potential is scanned cathodically can be calculated from the expression

$$i=-nFV\frac{dc_O}{dt}\ . \qquad (18)$$

The expression for the cathodic voltammetric curve can be obtained from Eqns. (16) and (18):

$$i=n^2Vrc_O^0\frac{F^2}{RT}\left\{\frac{\exp\frac{nF}{RT}(E^0-E)}{\left[\exp\frac{nF}{RT}(E^0-E)+1\right]^2}\right\}. \qquad (19)$$

The thin-layer voltammetric curve is bell-shaped and symmetrical about the peak potential (see Fig. 7). The current maximum (i_p) is associated with the potential E^0, and is given by the expression

$$i_p = \frac{n^2 c_O^0 r V F^2}{4RT} . \quad (20)$$

The simplicity of the theory of thin-layer voltammetry in comparison with oscillographic polarography is clearly brought out by comparing Eqn. (19) with the Randles–Ševčik equation[35,36].

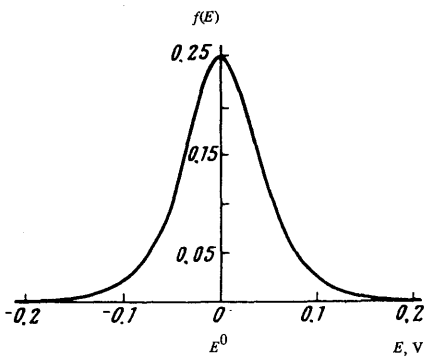

Figure 7. Theoretical i–E voltammetric curve for a reversible process in a thin-layer cell:

$$f(E) = \frac{\exp\left[\frac{F}{RT}(E - E^0)\right]}{\left\{\exp\left[\frac{F}{RT}(E - E^0)\right] + 1\right\}^2} .$$

Comparing the equation for the peak current in normal oscillographic voltammetry,

$$i_p = \frac{0.452 n^{3/2} F^{3/2} c_O^0 D^{1/2} r^{1/2} A}{R^{1/2} T^{3/2}} \quad (21)$$

with Eqn. (20), it can be seen that the current density in thin-layer voltammetry is significantly lower:

$$\frac{i_p}{(i_p)_{tl}} = \left(\frac{RT}{nF}\right)^{1/2} \frac{1.808 D^{1/2}}{r^{1/2} l} = \frac{0.286 D^{1/2}}{n^{1/2} r^{1/2} l} \quad (22)$$

whence $i_p/(i_p)_{tl} = 22$ if $n = 1$, $r = 10^{-3}$ V s^{-1}, $l = 10^{-3}$ cm, and $D = 6 \times 10^{-6}$ cm^2 s^{-1}. However, with small values of r and stationary electrodes these smaller currents can be measured as accurately as the currents encountered in oscillographic polarography, where the large value of r gives rise to substantial capacitive currents.

(*b*) Irreversible processes

Thin-layer voltammetry is very convenient for the study of irreversible reactions[37] ($O + ne \rightarrow R$).

The voltammetric curve for an irreversible system is asymmetric about the peak potential E_p, and the peak potential and its height (peak current) are related to the kinetic parameters k^0 and αn_0 by simple expressions.

We start from the basic equation of electrochemical kinetics, which describes both the forward and the reverse reaction

$$i = nFAk^0 \left\{c_O \exp\left[\frac{-\alpha n_0 F}{RT}(E - E^0)\right] - c_R \exp\left[\frac{(1-\alpha) n_0 F}{RT}(E - E^0)\right]\right\} . \quad (23)$$

If the peak current is at least two orders of magnitude greater than the exchange current the contribution of the reverse reaction to the voltammetric curve is negligible, and we can write

$$i = nFAk^0 c_O \exp\left[(-\alpha n_0 F/RT)(E - E^0)\right] . \quad (24)$$

Combining Eqns. (18) and (24) we obtain

$$\frac{dc_O}{dt} = -\frac{Ak^0 c_O}{V} \exp\left[\frac{-\alpha n_0 F}{RT}(E - E^0)\right] . \quad (25)$$

Integration of Eqn. (25) affords an expression for c_O. Inserting it into Eqn. (24), we arrive at an expression for the cathodic i, E curve in terms of the initial concentration only:

$$i = nFAk^0 c_O^0 \exp\left\{\frac{-\alpha n_0 F}{RT}(E - E^0) - \frac{ARTk^0}{\alpha n_0 FV(-r)} \exp\left[\frac{-\alpha n_0 F}{RT}(E - E^0)\right]\right\} . \quad (26)$$

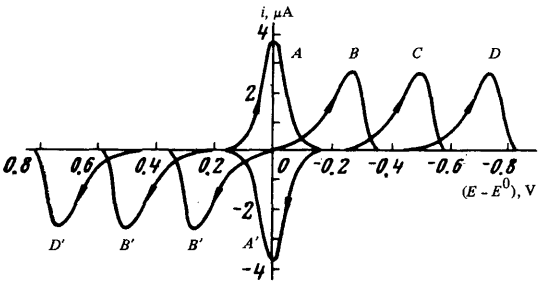

Figure 8. Theoretical voltammetric curves for a reversible reaction and for fully irreversible reactions in a thin layer of solution: *A*) reversible reaction, $k^0 \geq 4 \times 10^{-3}$ cm s^{-1}, *B*)–*D*) fully irreversible reactions, $k^0(B) = 10^{-6}$, $k^0(C) = 10^{-8}$, $k^0(D) = 10^{-10}$ cm s^{-1}. ($\alpha n_0 = 0.5$, $V = 2 \times 10^{-3}$ cm^3, $|r| = 2 \times 10^{-3}$ V s^{-1}, $n = 1$, $A = 0.5$ cm^2, $C^0 = 10^{-6}$ mole cm^{-3}, $T = 298$°K).

Fig. 8 shows plots of Eqn. (26) for several values of k^0 and one value of αn_0. It can be seen that the shape of the curves is independent of k^0, the curves being merely shifted along the potential axis. However, the peaks become broader and flatter if αn_0 decreases (Fig. 9).

The equations for the cathodic peak potential and for the peak current are obtained by equating to zero the differential di/dE from Eqn. (26).

The peak potential depends on αn_0 and on k^0, but is independent of concentration

$${}_cE_p = E^0 - (2.3RT/\alpha n_0 F) \lg\left[\alpha n_0 F(-r)V/ARTk^0\right] \quad (27)$$

whereas the peak current is directly proportional to αn_0 and to concentration

$${}_ci_p = \alpha n_0 n F^2 V(-r) c_O^0/2.718RT . \quad (28)$$

From Eqn. (28) we can calculate αn_0, and hence we can find k^0 from Eqn. (27) if E^0 is known.

Eqns. (27) and (28) can be applied to an anodic reaction by replacing α by $(1-\alpha)$ and c_O^0 by c_R^0.

If a cyclic voltammetric curve is plotted, the same kinetic parameters can be obtained without a knowledge of E^0. In this case we write equations for ${}_cE_p$ and ${}_aE_p$, from which E^0 can be eliminated. The final expression for k^0 is

$$k^0 = \left\{\frac{2.718\,{}_ci_p}{nFAc^0}\left(\frac{-2.718\,{}_ai_p}{nFAc^0}\right)^{{}_ci_p/{}_ai_p}\cdot\exp\left[\frac{-2.718\,{}_ci_p}{nFV|r|c^0}({}_aE_p-{}_cE_p)\right]\right\}^{{}_ai_p/({}_ai_p-{}_ci_p)}. \quad (29)$$

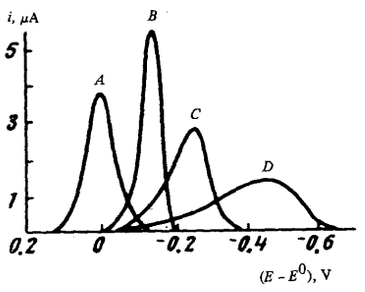

Figure 9. Theoretical voltammetric curves for a reversible reaction and for fully irreversible reactions in a thin layer of solution for different values of αn_0: *A*) reversible reaction, *B*)–*D*) irreversible reactions; $\alpha n_0(B) = 0.75$, $\alpha n_0(C) = 0.50$, $\alpha n_0(D) = 0.25$. ($k^0 = 10^{-6}$ cm s^{-1}, all other parameters as in Fig. 8).

For $\alpha n_0 = 0.5$ and ${}_ci_p = {}_ai_p$, Eqn. (29) simplifies to

$$\lg k^0 \overset{a}{=} -(1260/T)({}_aE_p - {}_cE_p) + \lg(VF|r|/2ART). \quad (30)$$

An equation for α can be obtained by eliminating n_0 from equations for ${}_ci_p$ and ${}_ai_p$ of the type of Eqn. (28). For $c_O^0 = c_R^0$ we have

$$\alpha = {}_ci_p/({}_ci_p - {}_ai_p). \quad (31)$$

Thus, α and n_0 can be evaluated separately in cyclic thin-layer voltammetry, but of course only if n_0 is the same for the cathodic and the anodic process.

Eqn. (26) describes the current–voltage curve of an irreversible reaction with a relative error of 2% if the exchange current does not exceed 2% of the peak current.

Thus, using the equation

$$i_0 = nFAk^0c \quad (32)$$

to calculate the maximum value of the exchange current i_0, and Eqn. (28) to calculate the smallest value of the peak current i_p, we obtain

$$i_0/i_p = 2.718ARTk^0/\alpha n_0FVr > 0.02 \quad (33)$$

or

$$k^0 < (\alpha n_0FV|r|/2.718ART)\cdot 0.02\ . \quad (34)$$

For normal values of the experimental parameters ($\alpha n_0 = 0.5$; $V = 2\times10^{-3}$ cm^3; $|r| = 2$ mV s^{-1}; $T = 298$°K; $A = 0.5$ cm^2) we obtain $k^0 < 1.2\times10^{-6}$ cm s^{-1}.

Hence, Eqn. (26) is applicable to fully irreversible processes, having rate constants of the order of 10^{-6} or less.

Eqn. (19) describes the current–voltage curve for a reversible reaction, with a relative error of 2%, for the condition

$$i_0/i_p = 4ARTk^0/nFV|r| > 50\ . \quad (35)$$

This condition is satisfied if

$$k^0 > (nFVr/4RTA)\cdot 50 \quad (36)$$

With the values of the parameters assumed above, we obtain $k^0 < 4\times10^{-3}$ cm s^{-1}. Hence, a "reversible" reaction is a reaction whose rate constant does not exceed 4×10^{-3} s^{-1}.

(*c*) Effect of double layer structure

All the above equations have been obtained without allowing for the effect of the structure of the electrical double layer. The basic equation of electrochemical kinetics which allows for the effect of the double layer on the surface concentration of the depolariser is

$$i = nFAk^0c_O^0f(\psi_1)\exp[(-\alpha n_0F/RT)(E-E^0)] \quad (37)$$

where $f(\psi_1) = \exp[(\alpha n_0 - z_0)(F/RT)\psi_1]$, and z_0 is the charge on a particle of the substance under study.

The equation for the cathodic i–E curve follows from Eqns. (26) and (37):

$$i = nFAk^0c_O^0f(\psi_1)\exp\left\{\frac{-\alpha n_0F}{RT}(E-E^0) + \frac{Ak^0}{V(-r)}\int_{E_i}^{E} f(\psi_1)\exp\left[-\frac{\alpha n_0F}{RT}(E-E^0)\right]dE\right\} \quad (38)$$

where E_i is the potential at which the scan is started.

Assuming that the electrode potential is divided between two capacitances in series, the fixed (C) and the diffuse (C_d) parts of the double layer, and assuming these capacitances to be independent of potential over the narrow range of potential for which the current is fairly large (about $200/n$ mV), we can write

$$\psi_1 \simeq (C/C_d)(E-\varphi_0) \quad (39)$$

where φ_0 is the zero-charge potential.

Combining Eqns. (38) and (39),

$$i = nFAk^0c_O^0f(\psi_1)\exp\left\{\frac{-\alpha n_0F}{RT}(E-E^0) - \frac{ARTk^0}{FV(-r)}\frac{f(\psi_1)\exp\left[\frac{-\alpha n_0F}{RT}(E-E^0)\right]}{[\alpha n_0 + (z_0-\alpha n_0)C/C_d]}\right\}. \quad (40)$$

The equation for the peak potential is

$${}_cE_p = \frac{\alpha n_0E^0 + (z_0-\alpha n_0)\frac{C}{C_d}\varphi_0 - \frac{RT}{F}\ln\left\{\frac{FV(-r)}{ARTk^0}\left[\alpha n_0 + (z_0-\alpha n_0)\frac{C}{C_d}\right]\right\}}{\alpha n_0 + (z_0-\alpha n_0)C/C_d}. \quad (41)$$

Eqn. (41) reduces to Eqn. (27) when C is much smaller than C_d. (This case is found in the presence of an excess of indifferent electrolyte.) Eqns. (38) and (40) are fully analogous to Eqn. (26) except for the function $f(\psi_1)$ which replaces the factor $\exp[(-\alpha n_0F/RT)\cdot(E-E^0)]$ in Eqn. (40). Taking Eqn. (39) into account, the product $f(\psi_1)\exp[(-\alpha n_0F/RT)\cdot(E-E^0)]$ becomes

$$f(\psi_1)\exp\left[\frac{-\alpha n_0F}{RT}(E-E^0)\right] = \exp\left\{\frac{F}{RT}\left[\frac{C}{C_d}(z_0-\alpha n_0)\cdot\varphi_0 + \alpha n_0E^0\right]\right\}\exp\left[\alpha^*\frac{F}{RT}E\right] \quad (42)$$

where

$$\alpha^* = (z_0-\alpha n_0)C/C_d + \alpha n_0\ . \quad (43)$$

Finally, the peak current with allowance for the effect of double layer structure is given by

$${}_ci_p = \alpha^*nF^2V(-r)c_O^0/2.718RT\ . \quad (44)$$

It follows from Eqns. (43) and (44) that α^* (and therefore also c^i_p) should be smaller for anion reactions than for cation reactions. Thin-layer i–E curves for intermediate and low concentrations of indifferent electrolyte contain information on the ratio C/C_d.

(*d*) Multistage processes

If a compound is reduced in two fully irreversible steps, for example

$$(PtCl_6)^{2-} + 2e \xrightarrow{k_1^0} (PtCl_4)^{2-} + 2Cl^-$$

and

$$(PtCl_4)^{2-} + 2e \xrightarrow{k_2^0} Pt + 4Cl^- \ ,$$

the current–voltage curve (Fig. 10) should have two peaks if the first step is the faster (curve *A*), or one peak if the second step is the faster or if the two steps have comparable rates (curves *B* and *C*).

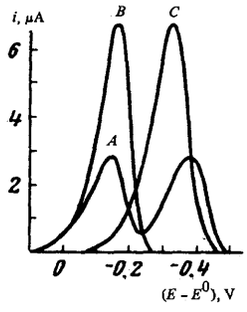

Figure 10. Theoretical thin-layer curves for a two-step fully irreversible reaction: *A*) $k_1^0 = 10^{-5}$, $k_2^0 = 10^{-7}$; *B*) $k_1^0 = k_2^0 = 10^{-5}$; *C*) $k_1^0 = 3 \times 10^{-7}$, $k_2^0 = 10^{-5}$ cm s^{-1} (all other parameters as in Fig. 8).

If $k_1^0 \geq 10^3 k_2^0$ the equations presented in the previous sub-sections can be used to describe both steps.

The basic i–E equation for a fully irreversible, two-step reaction such as

$$O + n_1 e \rightarrow R_1$$
$$R_1 + n_2 e \rightarrow R_2$$

but without allowance for the influence of the double-layer structure is obtained as follows. The contribution to the current from the first step is expressed by Eqn. (26):

$$i_1 = n_1 F A k_1^0 c_1^0 \exp\left\{\frac{-(\alpha n_0)_1 F}{RT}(E - E_1^0)\right\} \frac{-ART k_1^0}{(\alpha n_0)_1 FV(-r)} \cdot \exp\left[\frac{-(\alpha n_0)_1 F}{RT}(E - E_1^0)\right]\Big\} . \quad (45)$$

The current associated with the second step is given by

$$i_2 = -n_2 FV \frac{dc_2}{dt} + i_1 = n_2 F A c_2^0 k_2^0 \exp\left[\frac{-(\alpha n_0)_2 F}{RT}(E - E_0^0)\right] . \quad (46)$$

Eqn. (46) is solved for c_2 and i_2 using the normal methods for linear first-order differential equations

$$c_2 = c_1^0 H^{-1} \int_{E_i}^{E} GH dE \ , \quad (47)$$

$$i_2 = n_2 F A k_2^0 c_1^0 H^{-1} \exp\left[\frac{-(\alpha n_0)_2 F}{RT}(E - E_2^0) \int_{E_i}^{E} GH dE\right] , \quad (48)$$

where

$$G = \frac{n_1 A k_1^0 c_1^0}{n_2 Vr} \exp\left\{\frac{-(\alpha n_0)_1 F}{RT}(E - E_1^0) + \frac{Ak_1^0 RT}{(\alpha n_0)_1 FVr} \exp\left[\frac{-(\alpha n_0)_1 F}{RT}(E - E_1^0)\right]\right\} ,$$

$$H = \exp\{[Ak_2^0 RT/V(-r)(\alpha n_0)_2 F] \exp[(-(\alpha n_0)_2 F/RT)(E - E_2^0)]\} ,$$

c_1^0 is the initial concentration of O and c_2^0 is the initial concentration of R_1. Since the total current is $i = i_1 + i_2$, the expression for the i–E curve becomes

$$i = n_2 FVr c_1^0 G + n_2 F A k_2^0 c_1^0 H^{-1} \exp\left[\frac{-(\alpha n_0)_2 F}{RT}(E - E_2^0) \int_{E_i}^{E} GH dE\right] . \quad (49)$$

The integral term in the right-hand side of Eqn. (49) cannot be solved analytically. Plots obtained by numerical integration for $(\alpha n_0)_1 = (\alpha n_0)_2 = 0.5$ and several pairs of values of k_1^0 and k_2^0 are reproduced in Fig. 10.

(*e*) Partially reversible reactions

The current–voltage curve for fast but not fully reversible reactions, in which the contribution of the reverse reaction cannot be neglected, is described by the equation

$$i = -nFA\left\{k_b c_O^0 - \frac{Ac_O^0}{Vr}(k_f + k_b) X^{-1} \int_{E_i}^{E} X k_b dE\right\} \quad (50)$$

where

$$X = \exp\{[ART/V(-r) n_0 F][k_f/\alpha - k_b/(1-\alpha)]\} ,$$

$$k_f = k^0 \exp[(-\alpha n_0 F/RT)(E - E^0)] ,$$

$$k_b = k^0 \exp\{[(1-\alpha) n_0 F/RT](E - E^0)\} .$$

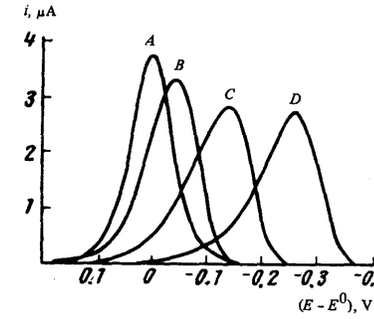

Figure 11. Theoretical voltammetric curves for reactions of intermediate reversibility in a thin layer: $k^0(A) = 4 \times 10^{-3}$, $k^0(B) = 10^{-4}$, $k^0(C) = 10^{-5}$, $k^0(D) = 10^{-6}$ cm s^{-1} (all other parameters as in Fig. 8).

An analogous equation for anodic reactions is obtained from Eqn. (50) by replacing c_O^0 by c_R^0. A plot of Eqn. (50) is shown in Fig. 11. The size of the current peak is intermediate between those given by Eqns. (20) and (28) for reversible ($k^0 > 4 \times 10^{-3}$ cm s^{-1}) and fully irreversible ($k^0 > 1 \times 10^{-6}$ cm s^{-1}) reactions respectively.

(*f*) Competitive reactions

When the starting material can undergo two parallel, fully irreversible reactions, as in

$$O + n_1 e \rightarrow R_1 ,$$
$$O + n_2 e \rightarrow R_2 ,$$

the shape of the current–voltage curve (Fig. 12) differs from that of the corresponding curve for a reaction which takes place by a single path (Fig. 8). In spite of the presence of two reactions, a single peak is obtained. The current–voltage characteristic for an electrode process of this type is derived as follows. The current in this case is given by

$$i = FAc_O(n_1 {}_1k_f + n_2 {}_2k_f) \quad (51)$$

where

$${}_1k_f = {}_1k^0 \exp\{[-(\alpha n_0)_1 F/RT](E - E^0_1)\},$$
$${}_2k_f = {}_2k^0 \exp\{[-(\alpha n_0)_2 F/RT](E - E^0_2)\} .$$

The current must also obey the equation

$$i = -FV\left(\frac{n_{11}k_f + n_2 {}_2k_f}{{}_1k_f + {}_2k_f}\right)\frac{dc_O}{dt} \quad (52)$$

The quantity in brackets in the right-hand side of Eqn. (52) is the instantaneous effective value of n for the mixed reaction. Eqns. (51) and (52) are easily solved:

$$i = FAc^0_O(n_1 {}_1k_f + n_2 {}_2k_f)\exp\left\{\frac{ART}{VFr}\left[\frac{{}_1k_f}{(\alpha n_0)_1} + \frac{{}_2k_f}{(\alpha n_0)_2}\right]\right\} . \quad (53)$$

Plots of Eqn. (53) are given in Fig. 12.

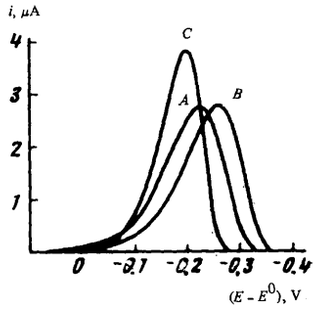

Figure 12. Theoretical voltammetric curves for two parallel reactions: *A*) $E^0_1 = E^0_2 = 0.0$, $(\alpha n_0)_1 = (\alpha n_0)_2 = 0.5$; *B*) $E^0_1 = 0.0$, $E^0_2 = -0.20$, $(\alpha n_0)_1 = (\alpha n_0)_1 = 0.5$; *C*) $E^0_1 = 0.0$, $E^0_2 = 0.20$, $(\alpha n_0)_1 = 0.7$, $(\alpha n_0)_2 = 0.5$. ($n_1 = n_2 = 1$, $k^0 = 10^{-6}$ cm s^{-1}, $c^0_O = 10^{-6}$ mole cm^{-3}, all other parameters as in Fig. 8).

(*g*) Practical applications

The cyclic thin-layer voltammetric method has been used to study the adsorption on platinum of complex ions in the Co^{3+}/Co^{2+}–EDTA‡ and Fe^{3+}/Fe^{2+}–EDTA systems[22]. The Co^{3+}/Co^{2+}–EDTA couple is appreciably irreversible; addition of iodide ions makes the reaction almost reversible (Fig. 13). A probable explanation is that the preferred adsorption of iodide ions causes desorption of the cobalt complexes which inhibit the electrode reaction when they are adsorbed. This property of the iodide ion has been used[22] for the quantitative determination of cobalt complexes, which are readily adsorbed on a smooth platinum surface[38,39]. The full desorption of the cobalt complexes from the platinum surface by the I^- was demonstrated by the following experiment: 0.94 μl of the sample (10^{-3} M CoY^- or CoY^{2-} in 1 M phosphate buffer, pH 7) was introduced into the clean thin-layer cell. The volume of the interelectrode gap was exactly equal to the volume of solution. The distance between the electrodes was first increased to 2–3 mm, and 0.94 μl of 2×10^{-3} M solution of KI was added to the initial solution. The volume of the gap was then decreased to 1.88 μl, and the cobalt complexes were determined. The results are given in Table 3.

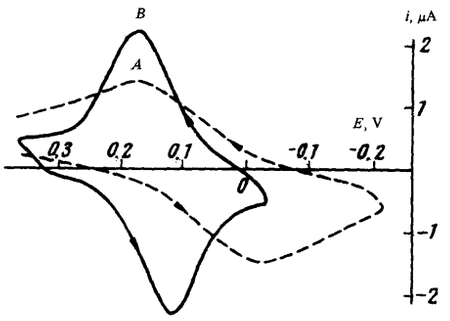

Figure 13. Single-cycle thin-layer voltammetric curve for Co^{3+} and Co^{2+} complexes with EDTA: *A*) without added iodide, 1.77×10^{-3} ml of 1.0 mM Co^{3+}–EDTA in 1 M (pH 7) phosphate buffer; *B*) with added iodide, 1.4×10^{-3} ml of 1.0 mM Co^{3+}–EDTA in 1 M $NaClO_4$ (pH 5) + 1.0×10^{-3} ml 2.0 nM solution of KI. Sweep rate 2 mV s^{-1}.

Table 3. Desorption of CoY^- and CoY^{2-} from a platinum surface by iodide ions.

No. of experiments	total quantity of electricity measured experimentally, Q_{tot} microcoulombs	quantity of electricity in blank experiment, Q_x microcoulombs	$Q_{tot} - Q_x$ microcoulombs	theoretical value of Q microcoulombs
Reduction of CoY^- (Co^{3+}-EDTA)				
6	106±3	14±2	92±5	91
Oxidation of CoY^{2-} (Co^{2+}-EDTA)				
5	115±6	24±2	91±8	91

The scanning range of potential was from 0.25 to −0.05 V (relative to the normal calomel electrode) in the first case, from 0.00 to 0.3 V in the second case. The Q_x values were obtained by repeating the experiment with a solution of phosphate buffer to which no depolariser had been added. The fact that the cobalt complex is completely reduced indicates that the iodide ion itself has no electrochemical activity in this range of potentials.

‡EDTA is ethylenediaminetetra-acetate.

Conversely, the Fe^{3+}/Fe^{2+}–EDTA system is reversible even in the absence of iodide ions. Thus, the displacement of adsorbed ions by more surface-active particles can be used for the quantitative study of the adsorption of ions under thin-layer conditions.

Thin-layer voltammetry has been applied to the study of the stoichiometry of the electrochemical oxidation of $PtCl_4^{2-}$ and $PtBr_4^{2-}$, of the reduction of $PtCl_6^{2-}$ and $PtBr_6^{2-}$, and also of their hydrolysis products[40]. It has been shown that in acid solution the reduction of $PtCl_6^{2-}$ proceeds to the stage of $PtCl_4^{2-}$, and in neutral solutions or solutions free from chloride ions the reduction goes to metallic platinum. The reduction of $PtBr_6^{2-}$ in 1 M bromide solutions goes to $PtBr_4^{2-}$, and in acid solutions or solutions free from bromide ions the reduction goes to Pt. The oxidation of $PtCl_4^{2-}$ in 1 M chloride solutions apparently gives a mixture of $PtCl_6^{2-}$ and $Pt(OH)_2Cl_4^{2-}$, whereas the oxidation of $PtBr_4^{2-}$ in 1 M bromide solutions gives only $PtBr_6^{2-}$. It was also found that the hydrolysis products of $PtCl_6^{2-}$ and $PtBr_6^{2-}$ are reduced with greater ease than their parent complexes.

Thin-layer studies with a very slow voltage scan[34] give valuable information on the mechanism of electrode reactions.

Because of the lower current densities employed, the reversibility of the Cr^{3+}–Cr^{2+} couple under the conditions of thin-layer voltammetry is much better ($E_c = -0.8$, $E_a = -0.6$ V NCE) than under semi-infinite diffusion conditions ($E_c = -0.95$, $E_a = -0.45$ V NCE).[8]

The application of thin-layer voltammetry to the electrolytic oxidation of bivalent platinum complexes of the $Pt(NH_3)_m(NO_2)_{4-m}^{m-2}$ and $Pt(NH_3)_mCl_{4-m}^{m-2}$ type has shown[41,42] that the process is strongly catalysed by free chloride and iodide ions, and that some of the ligands in the reaction product (i.e. the Pt^{IV} complex) are replaced by chloride ions. In the absence of free chloride ions the reactivity of these complexes is strongly reduced.

3. Stead-state Current Method

The existence of a limiting diffusion current depends on the establishment of a steady-state concentration polarisation.

A limiting diffusion current is observed when the thickness of the diffusion layer does not change with time. These conditions are realised at a dropping mercury electrode or at a solid electrode moving relative to the solution. Paired, thin-layer electrolytic cells also enable a constant concentration gradient to be set up; the value of the gradient can be controlled by varying the interelectrode spacing.

Material obtained by reduction at one electrode of a paired cell can diffuse and be oxidised at the other working electrode. Since these processes take place in a closed system, a steady-state current can be obtained.

The formation of the steady-state current i_{ss} is illustrated in Fig. 14.[43] Initially, the potential applied to the working electrodes is made sufficiently negative to ensure that the solution is depleted of the oxidised form O. If the potential of one of the electrodes (the anode) is shifted towards positive values, oxidation of R will begin at some value of the anode potential; the concentration of the oxidised form will increase, and the concentration of the reduced form will decrease. The flow of each form across the thin layer towards the appropriate electrode can be expressed in terms of its surface concentration:

$$\frac{i_{ss}}{nFA} = D_R\frac{(c_R)_{x=0} - (c_R)_{x=l}}{l} = D_O\frac{(c_O)_{x=l}}{l} \quad (54)$$

The total number of moles of O and R contained in the thin layer between the electrodes is constant: $N_O + N_R = N$. Hence

$$\frac{lA\,(c_O)_{x=l}}{2} + \frac{lA\,[(c_R)_{x=0} + (c_R)_{x=l}]}{2} = N. \quad (55)$$

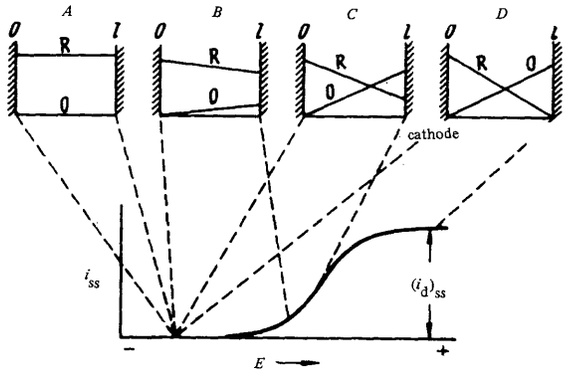

Figure 14. Schematic illustration of the formation of a steady-state current by reference to the concentration profiles of O and R in a thin layer for gradually increasing values of E at one of the electrodes (anode).

Solving Eqns. (54) and (55) simultaneously we obtain

$$(c_O)_{x=l} = \frac{i_{ss}l}{nFAD_O}, \quad (56)$$

$$(c_R)_{x=l} = -\frac{i_{ss}l}{2nFA}\left(\frac{1}{D_R} + \frac{1}{D_O}\right) + \frac{N}{lA}, \quad (57)$$

$$(c_R)_{x=0} = \frac{i_{ss}l}{2nFA}\left(\frac{1}{D_R} - \frac{1}{D_O}\right) + \frac{N}{lA}. \quad (58)$$

When the anode potential becomes sufficiently positive $(c_R)_{x=l}$ vanishes and the current tends to a maximum value $(i_d)_{ss}$. Hence it follows from Eqn. (56) that

$$(i_d)_{ss} = \frac{nFADc}{l}$$
$$\text{where } c = c_O + c_R, \text{ and } D = \frac{2D_OD_R}{D_O + D_R}. \quad (59)$$

Thus, the limiting steady-state current is directly proportional to a function of the diffusion coefficients of the oxidised and the reduced form, the total concentration, and the electrode area, and inversely proportional to the distance between the electrodes.

(*a*) Determination of the kinetic parameters of an electron transfer reaction

Steady-state currents can be used to determine the electron transfer rate constant k_s and the transfer coefficient α. In its most general form, the variation of the current with anode potential is given by

$$i_{ss} = nFAk_s\left\{(c_R)_{x=l}\exp\frac{(1-\alpha)\,nF\,(E-E^0)}{RT} + (c_O)_{x=l}\exp\left[\frac{-\alpha nF\,(E-E^0)}{RT}\right]\right\}. \quad (60)$$

Replacing $\exp[-nF/RT(E-E^0)]$ by θ, and $(cO)_{x=l}$ and $(cR)_{x=l}$ by their values given by Eqns. (56) and (57), we obtain after some simplification

$$\frac{1}{\theta^{\alpha-1}lk_s}+\frac{\theta}{D_O}=\left[\frac{(i_d)_{ss}-i_{ss}}{i_{ss}}\right]\left(\frac{D_O+D_R}{2D_OD_R}\right) \quad (61)$$

This equation describes the variation of the steady-state current with anode potential when the concentration of the oxidised form at the cathode is zero, i.e. $(cO)_{x=0}=0$. Analogous expressions can be obtained for the cathode. If the second term in the left-hand side of Eqn. (61) is much greater than the first (i.e. if k_S is large) this equation reduces to the equation which describes the reversible behaviour of the material:

$$E_{anode}=E^0-\frac{RT}{nF}\ln\left(\frac{1}{2}+\frac{D_O}{2D_R}\right)-\frac{RT}{nF}\ln\left[\frac{(i_d)_{ss}-i_{ss}}{i_{ss}}\right]. \quad (62)$$

If, on the other hand, the first term in the left-hand side of Eqn. (61) is predominant (k_S small), the resulting equation describes the fully irreversible behaviour of the substance under study:

$$E_{anode}=E^0-\frac{RT}{(1-\alpha)nF}\ln\left[\frac{lk_s(D_O+D_R)}{2D_OD_R}\right]-\frac{RT}{(1-\alpha)nF}\ln\left[\frac{(i_d)_{ss}-i_{ss}}{i_{ss}}\right]. \quad (63)$$

The electron transfer rate constant k_S can be evaluated by plotting $\lg\left[\frac{(i_d)_{ss}-i_{ss}}{i_{ss}}\right]$ against E. The plot is a straight line of slope $2.3RT/(1-\alpha)nF$, intersecting the horizontal axis at the potential

$$E^0-[2.3RT/(1-\alpha)nF]\lg\{[lk_s(D_O+D_R)]/2D_OD_R\}.$$

As in other methods, k_S can be found if E^0 is known. To find the rate constant k_S we may use the following approach. If the quantity $\left[\frac{(i_d)_{ss}-i_{ss}}{i_{ss}}\right]$ is plotted against $1/l$ for a series of anodic potentials, we should obtain (according to Eqn. (61)) a family of straight lines of slope $2D_OD_R/[\theta^{\alpha-1}k_S(D_O+D_R)]$, intersecting the vertical axis at the ordinate $2D_R\theta/(D_O+D_R)$. When the intercept is equal to $2D_R/(D_O+D_R)$, and therefore $\theta=1$, the value of k_S can be found from the slope at $E=E^0$. The value of α can then be found from the other curves.

(b) Determination of the diffusion coefficient

Since the steady-state current, according to Eqn. (54), depends on the diffusion coefficients of the oxidised and the reduced form, the equation can be used to evaluate these coefficients. If the concentrations of the oxidised form at $x=0$ and of the reduced form at $x=l$ are zero, Eqn. (54) can be re-written

$$(i_d)_{ss}=nFAD_R\frac{(c_R)_{x=0}}{l}=nFAD_O\frac{(c_O)_{x=l}}{l}. \quad (64)$$

Eqn. (64) can be used to determine the diffusion coefficients from a knowledge of the limiting steady-state current, the concentrations at the electrodes, the electrode area, and the distance between the electrodes. The number of moles of O and R in the thin layer can be measured coulometrically. If one of the electrodes of the thin-layer cell is disconnected (for example, the anode) the current will flow only to the cathode and as long as oxidised material remains in the thin layer. By measuring the quantity of electricity used in the reduction of O, and inserting $Q_c=nFAlc_O$ in Eqn. (64), we obtain

$$D_O=(i_d)_{ss}^2/2Q_c \quad (65)$$

D_R can be expressed in a similar way.

The numerical values of the diffusion coefficients are obtained from the slopes of plots of l against $1/i_{SS}$ and l against Q. The diffusion coefficients for Fe^{2+} and Fe^{3+} in 0.1 M $HClO_4$, measured by this method, are 0.421×10^{-5} and 0.392×10^{-5} cm^2 s^{-1} respectively; those for benzoquinone and hydroquinone in 0.3 M $HClO_4$ are 1.15×10^{-5} and 1.16×10^{-5} cm^2 s^{-1}.

(c) Determination of the rate constants of chemical reactions

The rate constants of chemical reactions can be determined from measurements of steady-state currents.

For slow chemical reactions of the type

$$O+ne\rightleftharpoons R;\ mR+pZ\xrightarrow{k}F$$

we can use the expression

$$i_{ss}=nFAlk(R_{ss})^m(Z)^p \quad (66)$$

where R_{SS} is the steady-state concentration of the reduced form. Under normal conditions ($n=2$, $lA=2\times10^{-3}$, $k(Z)^p=10^{-1}$, $R_{SS}=10^{-6}$) the system will reach steady state in 10 s for a current of 4×10^{-5} A. R_{SS} can be evaluated by anodic scanning and integration of the current associated with the fast oxidation of the substance R. Introducing into Eqn. (66) the quantity of electricity Q_R consumed by the oxidation of R_{SS}, we can write

$$i_{ss}=nFAk\left(\frac{Q_R}{nFA}\right)^m(Z)^p\left(\frac{1}{l^{m-1}}\right). \quad (67)$$

If the reaction is of the first order with respect to R, it follows from Eqn. (67) that the slope of the plot of Q_R against i_{SS} is independent of l. In this case we can determine p from experiments at different concentrations of the component Z, and hence we can arrive at the rate constant.

If the kinetic order of the reaction is 2 or more, the slope of plots of $(Q_R)^m$ against i_{SS} is a function of l, but the dependence is always one order less than in plots of $(R_{SS})^m$ against i_{SS}, as in Eqn. (66). The upper limit of the rate of a pseudo-first order reaction, measured by this method, depends on the rate of diffusion. Assuming that the concentration of R must be constant to within 1% the highest value of k which can be measured by this method is 10^{-1} s^{-1}.

To measure very small reaction rates, we need a high concentration (R_{SS}) and a large interelectrode distance, so as to raise i_{SS} above the level of the background current. For the highest reasonable values ($R_{SS}=10^{-6}$ mole cm^{-3} and $l=2\times10^{-2}$ cm), and assuming that the smallest measurable current is $i_{SS}=10^{-6}$ A, the smallest rate constant which can be determined by this method is 0.5×10^{-3} s^{-1}.

The rates of slow reaction can be studied also by a different method: the method of current decay in the pseudo-stationary state. The electrode potentials of a thin-layer cell are fixed on either side of the equilibrium potential of the redox couple (R–O) in order to establish a limiting steady-state current proportional to the concentration of R.

If the concentration of Z is constant, the current i_{SS} will fall according to the law which describes the rate of

a reaction of the m-th order. Hence, for $m = 1$, the function $i_{SS} = f(t)$ should be of the form

$$\ln \frac{(i_d)_{ss}}{nFAD_R} = -\frac{k(Z)^p t}{(D_R/D_O + 1)} . \quad (68)$$

The upper limit of reaction rate which can be measured by this method is the same as for the previous method. However, there is no lower limit in this case because the steady-state current can be monitored as long as necessary.

Steady-state currents can be used also to measure the rate constants of fast and intermediate bimolecular reactions of the type

$$\begin{aligned} A + ne &\rightarrow B \qquad x = 0 \\ C &\rightarrow D + ne \qquad x = l \\ B + D &\xrightarrow{k} A + C \qquad 0 < x < l . \end{aligned}$$

Measurements of the steady-state current i_{SS} as a function of time offer the possibility of continuous control of chemical reactions leading to changes in the concentration of O and R in the thin layer.

This approach has been used to measure the rate constants of a number of reactions [44,45]. McDuffie and coworkers [44] applied the principle in their work on the rate of the benzidine rearrangement, which occurs by the mechanism

$$O \underset{-ne}{\overset{+ne}{\rightleftharpoons}} R \xrightarrow{k} P .$$

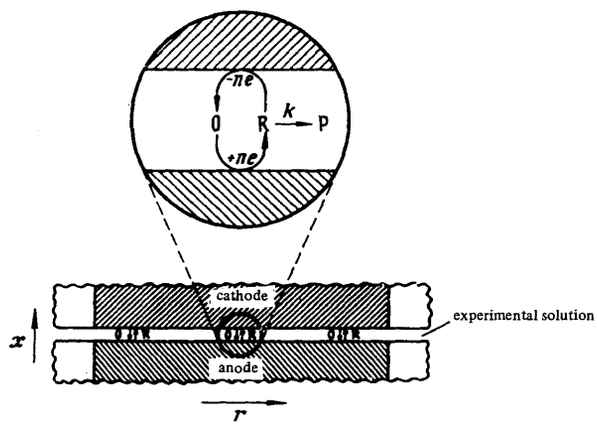

Figure 15. Cross-section of a thin-layer cell with paired electrodes.

A solution of azobenzene of known acidity, ionic strength, and ethanol concentration is added to the thin-layer cell. In order to obtain the limiting steady-state current, the electrode potentials are set so that the concentrations of O and R at the appropriate surface are both zero (Fig. 15). This current falls off exponentially with time, because the species R is consumed in the pseudo-first order irreversible rearrangement. The steady-state current is related to the concentrations of electrically active substances by the expression

$$i_{ss} = \frac{2nFAc}{l}\left(\frac{D_O D_R}{D_O + D_R}\right) \quad (69)$$

where $c = cO + cR$.

The mutual interconversion of O and R takes place at opposite electrodes. It is assumed that mass transfer is much faster than the chemical rearrangement, i.e. $(D/l^2) \gg k$, where $D = DO + DR$.

Under these conditions the distribution of O and R between the electrodes is effectively linear. The rate of a pseudo-first order chemical reaction is

$$\frac{dc_P}{dt} = \frac{dc}{dt} = kc_P . \quad (70)$$

Since the flows to the two electrodes are equal under quasi-steady state conditions, $DOcO = DRcR$. Hence, cR, which is equal to $(c - cO)$, can be expressed as

$$c_R = \frac{c}{1 + D_R/D_O} . \quad (71)$$

Inserting this expression into Eqn. (70), and integrating, we obtain

$$\ln\left(\frac{c}{c^0}\right) = -\frac{kt}{1 + D_R/D_O} \quad (72)$$

where c^0 is the total concentration of O and R at time $t = 0$. Replacing concentrations by currents (see Eqn. (69)) we obtain an expression for the decrease in current:

$$\ln(i_{ss}/i_{ss}^0) = -\frac{kt}{1 + D_R/D_O} . \quad (73)$$

The rate constant for the decay of the steady-state current is

$$k/(1 + D_R/D_O) .$$

If $D_R = D_O$, the rate constant for the current decay is $k/2$, and the plot of $\lg i_{SS}$ against t is a straight line of slope $-k/4.606$ for a pseudo-first order reaction.

Thus, the measurement of rate constants from the decay of the steady-state current i_{SS} is independent of the parameters of the thin-layer cell and of the initial concentration of the material. The experimental values of the rate constant for the acid-catalysed benzidine rearrangement, using the steady-state current decay method, are 0.113 s^{-1} in 0.25 M $HClO_4$, 0.0422 s^{-1} in 0.15 M $HClO_4$, 0.0223 s^{-1} in 0.1 M $HClO_4$, and 9.0×10^{-3} s^{-1} in 0.063 M $HClO_4$. These values are in good agreement with measurements [18] of k for the benzidine rearrangement by the thin-layer potentiostatic method (0.02 s^{-1} in 0.0997 M $HClO_4$ and 0.0086 s^{-1} in 0.063 M $HClO_4$).

The steady-state current decay method can be used also to measure the rate constants of second-order reactions. As an example, McDuffie and Reilley [45] consider the disproportionation of quinquevalent uranium in perchloric acid:

$$\begin{array}{ccc} O & \overset{e}{\rightleftharpoons} & R \\ \uparrow & & \downarrow \\ 2R & \longrightarrow & aO + (2-a)Z \end{array} .$$

Another possible example is dimerisation, when O is not regenerated. These second-order systems are difficult to investigate by the usual electrochemical methods [46–49] because of the need to use non-linear differential equations, for which analytical solutions are not available, in the interpretation of the results.

III. SPECIAL FEATURES AND SCOPE OF THIN-LAYER ELECTROCHEMISTRY

1. Edge Effect

One of the special features of thin-layer electrochemistry is the presence of an edge effect, i.e. the effect of diffusion of electrically active substances from the bulk of the solution into the narrow gap between the working electrodes or between the working electrode and the inert substrate. The edge effect is responsible for an appreciable fraction of the residual current in the thin-layer cell. The error introduced by the edge effect into the observed steady-state current is proportional to the total excess number of moles of O and R (N_{exc}) in the thin layer of solution at time t.

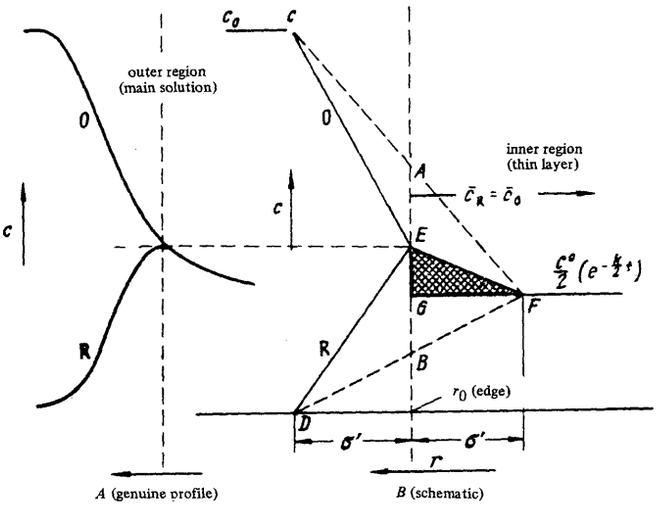

Figure 16. Schematic representation of the concentration profiles of O and R in the thin layer, used in the definition of the edge effect.

The quantity N_{exc} depends on the combined rates of diffusion of both forms of the material from the main bulk of the solution through the cylindrical edge of the thin layer. This rate of diffusion, in turn, depends on the concentration gradients of the electrically active species in the thin-layer region. It is very difficult to allow for all these conditions in a calculation of the contribution of the edge effect to the observed steady-state current. However, an approximate calculation can be made using a simplified model[44]. Immediately after the application of the potential difference ΔE the average concentration of the two forms in the thin layer is $c^0/2$, and there is no nett flow of material into the thin layer. After time t the concentration profile in the region of the edge of a thin-layer element of volume (of radius r_0) can be assumed to be of the type shown in Fig. 16. The concentration distribution is plotted for a point on the x-axis at $l/2$. In the central region of the thin-layer volume ($r/2$) the concentrations of R and O show an exponential decrease which is not distorted by the edge effect. In the schematic diagram the excess of material (N_{exc}) is found mainly in the concentration region within the triangle EGF, which penetrates from the edge into the thin layer to a depth σ^1. The region of excess concentration has the volume $\pi l[r_0^2 - (r_0 - \sigma^1)^2]$ or $\pi l\sigma^1 - (2r_0 - \sigma^1)$. The total excess of O and R, c_{exc}, can be expressed

$$c_{exc} = (c_{edge} - c_{centre})/2 \qquad (74)$$

where c_{edge} and c_{centre} denote the mean combined concentrations (O + R) at $r = r_0$ and $r = 0$ respectively. Point E is taken half-way between points A and B, and from the condition that c_{edge} can be obtained by doubling c_R or c_O at the point E we find

$$c_{edge} = (c^0 + c_{centre})/2 \, . \qquad (75)$$

Using the expression

$$c_{centre} = c^0 e^{-(k/2)t},$$

we obtain

$$c_{exc} = \frac{c^0}{4}[1 - e^{-(k/2)t}] \, . \qquad (76)$$

Multiplying Eqn. (76) by the volume,

$$N_{exc} = \frac{c^0}{4}[1 - e^{-(k/2)t}]\pi l\sigma'(2r_0 - \sigma') \qquad (77)$$

and after dividing by $N^0 = c^0\pi l r_0^2$ we arrive at

$$\frac{N_{exc}}{N^0} = [1 - e^{-(k/2)t}]\left(\frac{\sigma'}{2r_0}\right)\left(1 - \frac{\sigma'}{2r_0}\right). \qquad (78)$$

Since the limiting steady-state current is proportional to the number of moles in the thin layer of solution[43], and since σ' is approximately equal to $2(Dt/\pi)^{1/2}$, we finally obtain the equation for the relative error in the current:

$$\frac{i_{ss\ (error)}}{i^0_{ss}} = \left\{[1 - e^{-(k/2)t}]\left(\frac{Dt}{\pi r_0^2}\right)^{1/2}\left[1 - \left(\frac{Dt}{\pi r_0^2}\right)^{1/2}\right]\right\}. \qquad (79)$$

The edge effect can be minimised by increasing the radius of the working electrode. However, errors due to lack of parallelism between the electrodes become predominant above a certain electrode size. An alternative approach is to fit a plastic ring round the periphery of the thin layer, but in this case it becomes impossible to use an auxiliary and a standard electrode.

2. Influence of Lack of Parallelism and of Surface Roughness of the Working Electrode

A knowledge of the effective thickness l of the layer of solution is essential in all experiments with thin-layer electrolytic cells. The largest steady-state currents are obtained with the smallest layer thicknesses. Furthermore, the electrode separation determines the number of moles of O and R in the thin layer of solution. Both these effects can be perturbed by lack of parallelism and of smoothness in the electrode surfaces. Any roughness protruding into the layer of solution decreases the average thickness of the layer[43], and may decrease i_{ss} by a large amount. The effect of deviations from the ideal plane-parallel geometry of the electrodes can be discussed in terms of the simple model shown in Fig. 17. Using Eqn. (55) we obtain the following equation for the dependence of i_{ss} on $1/l$

$$(i_d)_{ss} = \int_0^a \frac{anFD\,(c_{R_{ss}})_{x=0}}{(l-q) + 2q/ay}\,dy = \frac{a^2nFD\,(c_{R_{ss}})}{2q}\ln\left(\frac{l+q}{l-q}\right). \qquad (80)$$

The equation has been tested, and found to be sufficiently accurate for $l \ll 4q$.

When $l = 4q$ the value of $(id)_{ss}$ calculated by Eqn. (80) is 91% of the ideal value (calculated by Eqn. (64)). These calculations suggest that the effects arising from lack of parallelism can be reduced to an acceptable minimum.

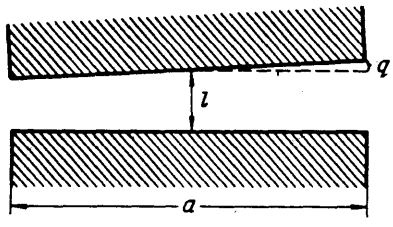

Figure 17. Lack of parallelism between the electrodes of a thin-layer electrolytic cell.

3. Scope and Advantages of the Methods of Thin-layer Electrochemistry

The main advantages of the methods of thin-layer electrochemistry were mentioned in the theoretical discussion given in the previous Sections. The most obvious attractions of thin-layer electrochemistry are the shorter analysis times and the very small volumes of solution needed.

The thin-layer electrochemical cell with a pair of working electrodes can also be used successfully when one of the reactions is hindered by the insoluble product of the other reaction. For example, if I^- and Cl^- ions are present in solution, one of the working electrodes can be used to accommodate a film of Hg_2I_2 (using mercury or an amalgam electrode), and the chloride ion is subsequently deposited on the other electrode.

Like the rotating-disk method with guard ring, the thin-layer methods are particularly useful for studies of chemical reactions preceding or following the electrode reaction, for monitoring short-lived intermediate states of the products of the electrode reaction, and for studying adsorption on the electrode surface.

Thin-layer methods show special promise in the study of adsorption processes, because they offer the possibility of working with such small volumes and concentrations that the total number of moles contained in the interelectrode gap need not be greater than the amount of material adsorbed on the electrode surface.

Thin-layer electrochemistry offers a convenient method of measuring the number n of electrons which take part in the electrode reaction, because the diffusion coefficient need not be known if n is measured by thin-layer chronopotentiometry.

Another potential advantage of thin-layer electrochemistry is the absence of hydrodynamic motion in the solution: as a result, the intermediate products of the reaction are not removed from the sphere of action by convection. The rate of supply of material by diffusion can be varied by varying the distance between the electrodes, and can be made very large. By using optically flat surfaces, the thickness of the diffusion layer can be made as small as 0.1 μm. [50] This is an order of magnitude less than the thickness of the diffusion layer for the rotating electrode (for $D = 10^{-5}$ cm^2 s^{-1}, and with a speed of rotation of 6000 r.p.m., the thickness of the diffusion layer can be reduced only to 5μm).

The use of thin-layer methods in studies of bimolecular reactions also deserves a mention.

When a pair of electrodes of different metals is used, each of the electrodes can be used in the most favourable conditions. Some other advantages of the thin-layer method are mentioned by Andersen and coworkers [51].

IV. PRACTICAL APPLICATIONS OF THIN-LAYER ELECTROCHEMISTRY

In addition to their applications (already mentioned) in the measurement of the rate of chemical reactions [1,16,20,42-45], the study of adsorption processes [3,22-24], the study of irreversibility in electrode reactions [8,24,34,43], the determination of the number of electrons involved in reactions in aqueous and non-aqueous media [2,4,40] and of diffusion coefficients [13,43,44], thin-layer methods can be used to enhance the sensitivity of analytical methods by dissolving weighed amounts of solute in very small volumes of solvent [7,9,52].

Using the equation for the limiting steady-state current $(id)_{ss}$

$$\frac{N}{lA} = \frac{(i_d)_{ss} l}{2nFA}\left(\frac{1}{D_R} + \frac{1}{D_O}\right) \qquad (81)$$

where N is the total number of moles of the oxidised and the reduced form, we can readily calculate the lower concentration limit for a one-electron reaction.

It can be seen from Eqn. (81) that $(id)_{ss}$ is proportional to the total number of moles in the thin layer and inversely proportional to the distance between the electrodes. If the steady-state current is set at 1 μA, and $l = 10^{-3}$ cm, we find that $N/lA = 10^{-9}$ mole cm^{-3} for $D_R = D_O$ (usually $\sim 10^{-5}$ cm^2 s^{-1}).

Thin-layer cells can be used also in combined electrochemical and spectral studies, which offer a powerful means of investigating the nature of electrolysis products [10,11,53].

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