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Paramagnetic Reagents for the Investigation of the Structures of Organic Ligands

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This review illustrates the effectiveness of the methods for the investigation of the structures of organic ligands based on the characteristics of the NMR spectra of paramagnetic complexes.
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I. INTRODUCTION

Despite the fact that the first study on nuclear magnetic resonance (NMR) in paramagnetic systems was published in 1949,[1] the most fruitful investigations in this field were made in the last ten years concurrently with general progress in the technique of NMR spectroscopy. Studies carried out outside the Soviet Union by McConnell, Eaton, and others and in the Soviet Union by Molin and coworkers significantly extended our ideas concerning the mechanism of the electronic-nuclear (hyperfine) interaction in paramagnetic systems. Moreover, studies published in 1968 to 1972 showed that the specific features of the NMR of paramagnetic complexes can be used successfully to investigate the structures of organic ligands.

II. NUCLEAR MAGNETIC RESONANCE IN PARAMAGNETIC SYSTEMS

The use of NMR for the investigation of the electronic and geometrical structures of organic ligands is based on the characteristics of the NMR spectra of paramagnetic compounds[2,3]. If the resonating nucleus (for example a proton) forms part of a paramagnetic molecule, i.e. a molecule having a non-compensated electronic spin moment, it is subjected to an additional magnetic influence by the electron spin. The leads to a broadening and also to paramagnetic shifts (contact and pseudocontact) of the resonance lines in relation to the widths and positions of the lines in the NMR spectra of diamagnetic compounds. A contact shift is observed in those cases where the probability that the unpaired electron is located at the site of the resonating nucleus is non-zero. This shift is proportional to the proton–electron interaction constant and (when the spin–orbital interaction is slight) is defined by the expression[2]

$$\omega_k = -A \cdot \frac{\gamma_e}{\gamma_p} \cdot \frac{g\beta S(S+1)}{3kT}, \qquad (1)$$

where γ_e and γ_p are the gyromagnetic ratios for the electron and proton, g is the g-factor of the paramagnetic compound, S the spin of the complex, β the Bohr magneton, T the absolute temperature, and k the Boltzmann constant.

A, which can be both positive and negative, is determined by the magnetic moment of the unpaired electrons of the paramagnetic species and the orientation of the unpaired electron at the given proton. According to the Fermi formula,

$$A = \frac{4}{3}\pi g\beta g_n\beta_n\rho(N),$$

where g_n is the nuclear g-factor, β_n the nuclear magneton, $\rho(N)$ the unpaired electron spin density at the given nucleus defined by the expression

$$\rho(N) = \int \psi^* \sum_k 2S_{zk}\,\delta(N)\,\psi\,d\tau,$$

and ψ the wave function of the electrons in the molecule; the remaining symbols in the last expression have the usual significance[2,3].

The pseudocontact shift† is due to the fact, that when the g-factor of the paramagnetic compound is anisotropic, the dipole–dipole interaction between the magnetic moments of the unpaired electron and the nucleus does not average out to zero[2]. This shift is defined by the following expression in an implicit form:

$$\omega_p = \frac{\text{const}}{T} \cdot f(g)\, f(\varphi, r).$$

Here the multipliers $f(g)$ and $f(\varphi, r)$ are determined by the anisotropy of the g-factor and the geometry of the complex respectively. The explicit form of these functional relations and hence the magnitude and sign of ω_p depend on the type of symmetry of the paramagnetic complex. For a paramagnetic ion moving at random in solution, the electric field around which has a tetragonal symmetry, the pseudocontact shift is given by the expression[2]

$$\omega_p = \frac{\beta^2 S(S+1)(3\cos^2\varphi - 1)(g_\parallel - g_\perp)(g_\parallel + 2g_\perp)}{27kTr^3}, \qquad (2)$$

where φ is the angle between the symmetry axis and the radius-vector directed from the centre of the coordinating ion to the proton, r the radius-vector, and $g_\parallel$ and $g_\perp$ are the electronic g-factors in directions parallel and perpendicular to the symmetry axis.

For molecules containing different protons (i, j, ...), the pseudocontact shifts for different nuclei i and j are

† Studies on contact interaction in paramagnetic complexes with organic ligands based on NMR spectra have been described[2,4-30].

linked by the relation

$$\omega_i : \omega_j = \frac{3\cos^2\varphi_i - 1}{r_i^3} : \frac{3\cos^2\varphi_j - 1}{r_j^3} , \qquad (3)$$

which makes it possible to obviate the difficulties associated with the measurement of the g-tensor components.

The pseudocontact interaction described by Eqn.(2) was introduced by McConnell and Robertson for an anisotropic g-factor, i.e. for a paramagnetic ion with degenerate levels in the absence of an external magnetic field when the Zeeman interaction depends on the relative orientation of the external field and the symmetry axis of the paramagnetic complex[31]. Bleaney[32] showed that the pseudocontact shifts in the NMR spectra due to paramagnetic complexes of lanthanides, which are characterised by an isotropic g-factor, are a consequence of the anisotropy of the susceptibility. In this case ω_p for an axially symmetrical complex is defined by the expression[32,33]

$$\omega_p = \frac{\beta^2}{60\,(kT)^2} \times \left(\frac{3\cos^2\varphi - 1}{r^3}\right) \times 2A_0^2 \langle \bar{a}^2 \rangle \times \\ \times g^2 J\,(J+1)\,(2J-1)\,(2J+3) \langle J \| \alpha \| J \rangle \qquad (2\text{–A})$$

where A_0^2 is the crystal field coefficient, $\langle \bar{a}^2 \rangle$ the mean square of the radius of $4f$ electrons, and $\langle J \| \alpha \| J \rangle$ a numerical coefficient; the remaining symbols are analogous to those in Eqns.(1) and (2). The first multiplier in Eqn.(2–A), depends on T^{-2} and not on T^{-1} [cf. Eqn.(2)]. However, the dependence on φ and r of the second multiplier is the same as for the anisotropic g-factor of axially asymmetric complexes. The third and fourth multipliers characterise the state of the paramagnetic ion. When Eqn.(2–A) is employed in structural studies, the influence of the third multiplier may be taken into account by means of an appropriate procedure, while the fourth multipler has been tabulated for tervalent lanthanides[33]. Since Eqn.(2–A) was obtained taking into account the ground state only, the europium complex should not induce shifts because $J = 0$ for Eu^{3+}. However, Eu^{3+} has an excited level with $J = 1$, which is close to the ground level (the energy of the first excited state is about 300 cm^{-1}). Allowance for this factor leads to a non-zero value of the fourth term in Eqn.(2–A), which accounts for the appearance of shifts in the spectra of europium complexes[32]‡.

The longitudinal (T_1M) and transverse (T_2M) relaxation times of the protons in the coordination sphere are given by the formulae[2]

$$\frac{1}{NT_{1M}} = \left(\frac{2}{15}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\left(3\tau_c + \frac{7\tau_c}{1+\omega_s^2\tau_c^2}\right) + \\ + \left(\frac{2}{3}\right) S(S+1)\,\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\cdot\left(\frac{\tau_e}{1+\omega_s^2\tau_e^2}\right) , \qquad (4)$$

$$\frac{1}{NT_{2M}} = \left(\frac{1}{15}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\left(7\tau_c + \frac{13\tau_c}{1+\omega_s^2\tau_c^2}\right) + \\ + \left(\frac{1}{3}\right) S(S+1)\,\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\left(\tau_e + \frac{\tau_e}{1+\omega_s^2\tau_e^2}\right) , \qquad (5)$$

where n_h is the number of nuclei in the sphere of the paramagnetic complex, N_p the molar concentration of the resonating nuclei, N the molar concentration of paramagnetic ions, ω_s the Larmor precession frequency of the electron, and τ_e and τ_c are the correlation times of the contact and pseudocontact interactions respectively, which are defined by the expressions

$$\frac{1}{\tau_e} = \frac{1}{\tau_s} + \frac{1}{\tau_h} ; \quad \frac{1}{\tau_c} = \frac{1}{\tau_s} + \frac{1}{\tau_r} + \frac{1}{\tau_h} . \qquad (6)$$

Here τ_s is the electron spin relaxation time, τ_h the residence time of the resonating nucleus in the coordination sphere, and τ_r the time required for the reorientation of the paramagnetic species. τ_h and τ_s must satisfy the condition $\tau_h^{-1} \gg A$; $\tau_s^{-1} \gg A$.

Since τ_e and τ_c are characteristics of random processes, each specific situation must be considered separately. However, in the general case τ_e and τ_c are determined by the fastest molecular processes. Moreover, τ_e^{-1} and τ_c^{-1} may differ appreciably from ω_s, which results in different contributions by dipole and contact interactions to T_1M and T_2M. This follows from Eqns.(4) and (5) containing the products $\omega_s\tau_e$ and $\omega_s\tau_c$, which satisfy different inequalities in the case of a significant different between τ_e and τ_c. For example, at a proton resonance frequency of 30 MHz, it is found that for Mn^{2+}

$$\omega_s\,\tau_e \gg 1; \qquad \omega_s\,\tau_c \ll 1 . \qquad (7)$$

When inequalities (7) hold, Eqns.(4) and (5) are replaced by other expressions:

$$\frac{1}{NT_{1M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c , \qquad (8)$$

$$\frac{1}{NT_{2M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c + \left(\frac{1}{3}\right) S(S+1)\cdot\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\tau_e . \qquad (9)$$

Consequently contact interaction (the second term in the last equation) will contribute to line width. This contribution may be reduced if

$$\omega_s\,\tau_c \ll 1 \quad \text{и} \quad \omega_s\,\tau_e \ll 1 . \qquad (10)$$

In this case

$$\frac{1}{NT_{1M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c + \left(\frac{2}{3}\right) S(S+1)\,\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\tau_e , \qquad (11)$$

$$\frac{1}{NT_{2M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c + \left(\frac{2}{3}\right) S(S+1)\,\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\tau_e , \qquad (12)$$

or

$$\frac{1}{T_{1M}} = \frac{1}{T_{2M}} .$$

Like the preceding expression, the last equation for $1/T_2$M contains a second term, but its contribution is significantly smaller. Inequalities (10) hold where the characteristic relaxation times τ_e and τ_c are equal or differ insignificantly, which can happen, in particular, when the electron spin relaxation is fast[34] ($\tau_s \ll \tau_h, \tau_r$). At a proton resonance frequency of 100 MHz, $\omega_s\tau_e \ll 1$, provided that τ_e is of the order of magnitude of 10^{-12} s. A significant enhancement of the inequality $\omega_s\tau_e \ll 1$ (i.e. a narrowing of the resonance lines) occurs also with increase of the temperature of the test specimen.

It follows from a comparison of Eqns.(1) and (12) that

$$\frac{1}{NT_{2M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c + \frac{24k^2T^2}{\hbar^2 g^2 S(S+1)}\cdot\left(\frac{n_h}{N_p}\right)^2 \tau_e^2\omega_k^2$$

or

$$1/T_{2M} = B\ r^{-6} + C\,(\delta_k')^2 , \qquad (13)$$

where δ'_k is the observed contact shift of the resonance line and B and C are constants for the test specimen at the given temperature. For complexes in which there is no

‡ The nature of the shifts induced by paramagnetic europium complexes has also been discussed by Weissman[109].

contact interaction, the relaxation time of the nucleus is determined by the distance from the coordinating ion:

$$1/T_{2M} = C\ r^{-6}\ . \qquad (14)$$

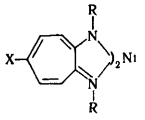
The study of the NMR phenomenon in paramagnetic systems yields important information about the structure of many-electron systems. This becomes evident if one remembers that Eqns.(1), (2), (2—A), and (3), which define the parameters of the NMR spectra of paramagnetic systems, are related to the electronic and geometric structures of molecules. Paramagnetic shifts are much greater than chemical shifts in the spectra of diamagnetic compounds and moreover they exhibit a characteristic temperature variation. A wide variety of relaxation effects are possible for paramagnetic substances and hence a broadening of the spectral lines, which significantly extends the scope of NMR as a research technique. This is because a decrease of the electron spin relaxation time leads to a broadening of the resonance lines in the ESR spectra, while NMR signals become narrower (the conditions governing the recording of the NMR spectra are improved)[4]. This interrelation between the relaxation times of electron and nuclear spins enables one to influence the form of the NMR and ESR spectra of paramagnetic systems (provided that electronic-nuclear interactions occur in them). For example, on dissolution in chloroform (0.001 M), bishexafluoroacetylacetonatocopper and bistrifluoroacetylacetonatocopper give rise to satisfactorily resolved ESR spectra in which a hyperfine structure is observed. When the stable di-t-butyl nitroxide (DBNO) radical is added to the solution to give a concentration as low as 0.01 M, the ESR spectra are broadened, so that their hyperfine structure is not resolved and the ^{19}F NMR spectra of these complexes in chloroform cannot be observed. However, when they are dissolved in DBNO [solution?], the ^{19}F NMR spectra can be recorded. This is because the spin exchange between the free radicals and the copper complexes reduces the electronic relaxation time and permits the detection of the NMR signal[35].

III. ANALYSIS OF NUCLEAR MAGNETIC RESONANCE SPECTRA USING THE NMR PHENOMENON IN PARAMAGNETIC COMPLEXES

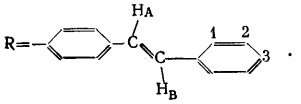
Nowadays NMR is a powerful tool for the investigation of many-electron systems, since the parameters of the NMR spectra carry valuable information about the electronic and geometric structures of the molecules[36]. However, the assignment of the resonance lines in NMR spectra on the basis of the simple rules for the analysis of the spectra (in the first-order perturbation theory) is impossible. On the other hand, it follows from Eqns.(2) and (2—A) that in the coordination of the molecules to a paramagnetic ion the resonance lines may shift unequally relative to their positions in the spectrum of the free ligand. This should make the difference between the proton chemical shifts greater than the spin—spin coupling constant between them and the analysis of the spectrum is significantly simplified.

1. Complexes of Elements in the First Transition Group

The factor noted above was apparently used for the first time to determine the spin—spin interaction constants J for substituted aminotroponeiminatonickel coordination complexes I. Eaton et al. examined this problem in detail[37]. They assumed that the spin—spin interaction in aromatic and unsaturated compounds is transmitted, predominantly by σ-electrons, over distances not greater than that corresponding to three bonds[38]. On the other hand, in paramagnetic nickel complexes (I) the contact shifts are due to the perturbation of the π-electron system of the ligand molecule[7]. Therefore one may expect that J found from the ^1H NMR spectrum of the paramagnetic complex will be close to the value of J for a diamagnetic molecule. The complex has the structure



where X = H or Br and R are different aliphatic and aromatic groups. Fig. 1B illustrates part of the spectrum of the paramagnetic complex due to the protons of the ligand molecule:



For comparison, the ^1H NMR spectrum of *trans*-stilbene taken from the catalogue of the Varian Company is also included[39]. The olefinic protons in *trans*-stilbene are chemically equivalent so that the spin—spin interaction between them is not observed and their signal in the spectrum consists of a singlet (δ = 7.10 p.p.m.). The aromatic protons form an unresolved multiplet. In a paramagnetic complex the resonating nuclei of the same molecule become significantly non-equivalent (Fig. 1*B*). The nickel complex (I) in solution is characterised by a rapid intramolecular equilibrium of the type

$$\underset{\text{(square)}}{\text{diamagnetic form}} \rightleftharpoons \underset{\text{(tetrahedron)}}{\text{paramagnetic form.}}$$

This leads to a narrowing of the resonance lines in the ^1H NMR spectra of the complexes to such an extent that it is possible to observe the spin—spin interaction characterised by J = 2—3 Hz.[7]

The high-resolution spectrum of a paramagnetic complex cannot usually be recorded owing to the considerable width of the resonance lines. However, this difficulty can be obviated by recording the spectra of specimens in which the metal/ligand ratio is much less then unity. As a result of the rapid exchange of molecules between the coordination sphere of the complex and the free ligand, an average spectrum is observed. Its form depends particularly on the nature of the electron—nuclear interaction in the paramagnetic complex. The use of this method becomes evident from an examination of the influence of exchange effects on the form of the NMR spectrum[36]. Evidently, when the proton H is involved in rapid exchange of the type HA + B $\rightleftharpoons$ HB + A, the observed shift of its signal is defined by the expression

$$\delta_H = P_A\ \delta_A + P_B\ \delta_B\ ,$$

where P_A and P_B are the mole fractions of H_A and H_B, and δ_A and δ_B are the chemical shifts of the proton signal in the environments of A and B. In our case A and B are the free molecule (P_C, δ_C) and the molecule coordinated (P_M, δ_M) to the paramagnetic ion, whence

$$\delta_H = P_C\,\delta_C + P_M\,\delta_M = \delta_C + (\delta_M - \delta_C)P_M = \delta_C + \omega\ P_M\ , \qquad (15)$$
$$\delta_M - \delta_C = \omega;\quad P_C + P_M = 1\ .$$

In order to assign the resonance lines in the spectra of specimens containing paramagnetic complexes, it is necessary that the solution should contain only one complex when the metal/ligand ratio is varied; if there are several complexes, their proportions must remain fixed. It is readily seen that the linear relation between δ_H and P_M is a criterion of the characteristics of complex formation in the test specimen. Moreover, Eqn.(15) can be used to determine ω when $P_M = 1$ and δ_C when $P_M = 0$ by the graphical extrapolation of the $\delta_H = f(P_M)$ relation. This method was used to assign the signals in the ^{1}H NMR spectra of pyridine, quinoline, and isoquinoline N-oxides[5,8].

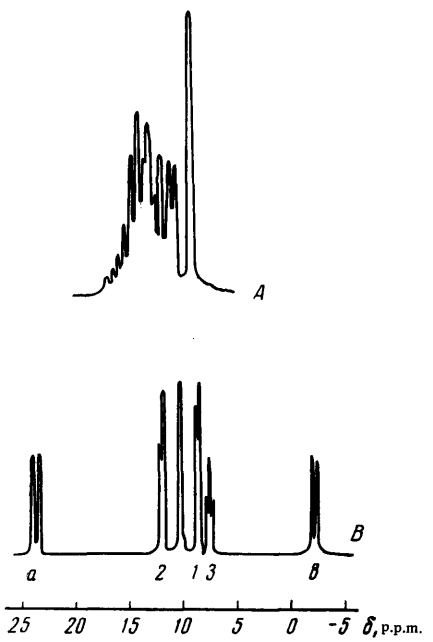


Figure 1. *A*) The ^{1}H NMR spectrum of *trans*-stilbene; *B*) part of the ^{1}H NMR spectrum of a paramagnetic complex due to the protons of *trans*-stilbene.

A method has been proposed[40] for the determination of the functional groups in organic compounds capable of forming paramagnetic complexes, which is also based on the employment of the characteristics of the NMR spectra of paramagnetic compounds. Its application is illustrated by the interpretation of the ^{1}H NMR spectra of certain methyl derivatives of pyrazole. The same method has been used also to assign the resonance lines in the spectra of N-vinylimidazole(II) and N-ethylimidazole(III).[41] The assignment was based on an estimate of the broadening (Δ) and shifts (δ) of the resonance lines due to the influence of the non-compensated electron spin of the paramagnetic complex. The estimation of Δ and δ' for labile complexes reduces to the solution of the Bloch equations modified by McConnell. For a two-component system, analysis of the Bloch–McConnell equations leads to the following expressions defining the observed Δ and δ' relative to the widths and positions of the lines in the spectrum of a diamagnetic compound[42]:

$$\Delta = \frac{P_M[(1/T_{2M})^2 + 1/T_{2M}\cdot\tau_M + \omega^2]}{\tau_M[(1/T_{2M} + 1/\tau_M)^2 + \omega^2]}, \quad (16)$$

$$\delta' = \delta'_c + \delta'_p = -\frac{P_M\cdot\omega}{\tau_M^2[(1/T_{2M} + 1/\tau_M)^2 + \omega^2]}, \quad (17)$$

where τ_M is the lifetime of the ligand molecule in the first coordination sphere of the complex, P_M the mole fraction of the complex in the specimen, $\omega = \omega_C + \omega_p$ the shift of the resonance line of the nucleus entering into the composition of the paramagnetic complex§, and T_{2M} the transverse relaxation time of the resonating nucleus in the complex.

Evidently, depending on the relative values of τ_M, T_{2M}, and ω, Eqns.(16) and (17) may be simplified[42].

1) Slow exchange:

$$\Delta = \frac{P_M}{\tau_M}, \quad (18)$$

$$\delta' = -P_M\ \omega\ \frac{T_{2M}^2}{\tau_M^2}, \quad \text{or} \quad \delta' = -\frac{P_M}{\tau_M^2\cdot\omega}. \quad (19)$$

2) Fast exchange:

$$\Delta = P_M\cdot\tau_M\cdot\omega^2 \quad (20)$$

or

$$\Delta = \frac{P_M}{T_{2M}}, \quad (21)$$

$$\delta' = -\omega\cdot P_M. \quad (22)$$

3) Intermediate case:

$$\Delta = \frac{P_M}{T_{2M}} + P_M\cdot\tau_M\cdot\omega^2, \quad (23)$$

$$\delta' = -\omega\cdot P_M. \quad (24)$$

The simplification of Eqns.(16) and (17) involves the derivation of the relations

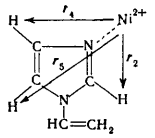
$$\Delta = f(T), \quad (25)$$

$$\delta' = f(T), \quad (26)$$

where T is the absolute temperature of the test specimen. Here it is necessary to note the importance of the fact that Δ and δ' are functions of the same variables. Therefore, depending on the nature of the complex and the experimental conditions, it is possible to obtain both Eqns.(25) and (26) or one of them. The above considerations were used to assign the ring proton signals in the ^{1}H NMR spectra of compounds (II) and (III). The experiments were performed in the presence of an excess of the ligand in the specimen. Fig. 2 presents the temperature variation of the broadening of the ring proton signals in the spectrum of compound (II) with the added paramagnetic complex $NiCl_2.4L$ [L = (II)]. The plots show that up to 313°K the broadening Δ is determined by Eqn.(18). In order to find approximate expressions for Eqns.(16) and (17) in the range 313–370°K, account was taken of the temperature variation of δ'. Moreover, the ratios $(r_5/r_2)^6$, $(r_5/r_4)^6$, and $(r_4/r_2)^6$ were estimated from data for the geometry of imidazole[43] and

§ One should note here that in a number of studies[6,10,12] the pseudocontact shifts were found to be insignificant in those cases where the nickel atom was the coordinating species.

also the ionic radius of Ni^{2+} and the van der Waals radius of nitrogen



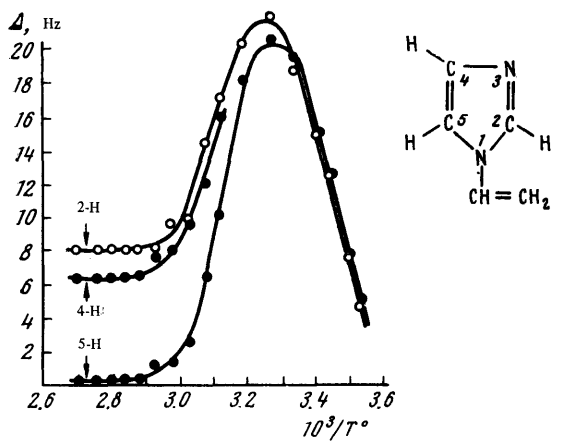


Figure 2. Temperature variation of the broadening of the signals of the imidazole ring protons.

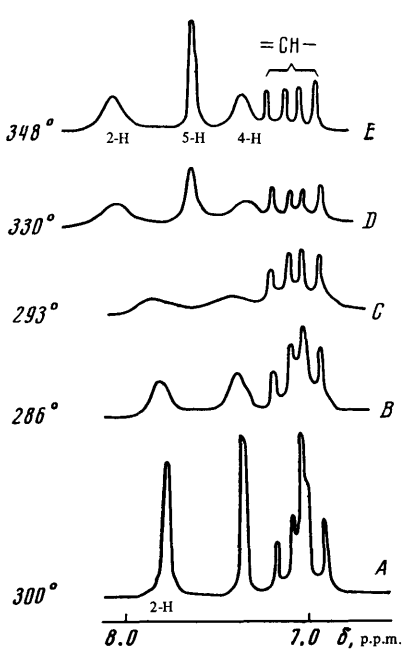


Figure 3. The positions of the ring and CH proton signals in the spectrum of *N*-vinylimidazole without the addition (*A*) and with addition (*B* – *E*) of the paramagnetic complex at different temperatures.

By comparing Δ and δ′ and taking into account the fact that the 2-H proton of imidazole resonates in a lower field than the 4-H and 5-H protons, it was found that the signals of the imidazole ring protons in the spectrum of compound (II) are in the sequence $\delta_2 > \delta_5 > \delta_4$. When the temperature of the test specimen with the added complex $NiCl_2.4L$ is altered, the signals of the vinyl protons hardly shift in relation to their positions in the spectrum of the specimen without the paramagnetic additive. Since these protons are quite far (compared with 2-H and 4-H) from the coordinating ion, their resonance lines are hardly broadened, i.e. over the entire range of variation of temperature Δ is determined by the first term of Eqn.(16). The positions of the signals of the 2-H, 4-H, 5-H, and CH protons in the spectrum of compound (II) with and without the addition of the paramagnetic complex at different temperatures are illustrated in Fig. 3. The ^1H NMR spectrum of compound (III) was analysed similarly. The following two examples illustrate the results of Zaev and coworkers' study[40]. Fig. 4 presents the spectrum of 1,3,5-trimethylpyrazole (IV) without the addition (*A*) and with addition (*B*) of the salt $NiBr_2.3H_2O$, which forms a paramagnetic complex with compound (IV). Fig. 4*A* shows that the assignment of the $3\text{-}CH_3$ and $5\text{-}CH_3$ signals is not unambiguous, since their protons resonate at high field and are responsible for the appearance of two singlets with an insignificant difference between the chemical shifts (0.03 p.p.m.).

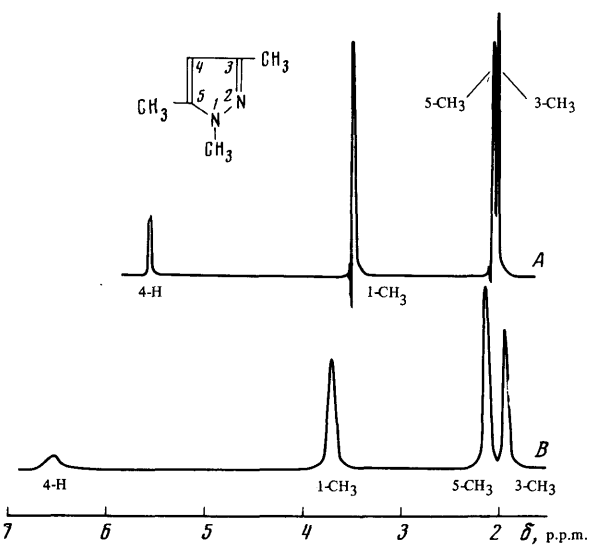


Figure 4. ^1H NMR spectrum of 1,3,5-trimethylpyrazole without the addition (*A*) and with addition (*B*) of $NiBr_2.3H_2O$.

The formation of complexes leads to a shift of the singlets in opposite directions and to different degrees of broadening. Comparison of the values of Δ and δ′ with the distances from the coordinating ion to the resonating nuclei showed that in the spectrum of compound (IV) without $NiBr_2.3H_2O$ the singlet in the high field is due to the protons of the $3\text{-}CH_3$ group. Fig. 5 presents the spectra of one of the isomers of dimethylpyrazole without the addition (*A*) and with addition (*B*) of the same nickel salt. Since Δ for the signal of the 4-H proton, the position of

which in the spectrum is known, is significantly smaller than Δ for the signal of the other proton of the pyrazole ring, the above isomer is 1,5-dimethylpyrazole in which $r^6_{3\text{-H}} \ll r^6_{5\text{-H}}$. In the above investigations[40,41] the mole fraction of the paramagnetic complex did not exceed $10^{-2}-10^{-3}$, which ensures constancy of the composition of the complex and a linear relation between δ′ and P_M. Carbon tetrachloride, chloroform, and nitromethane were used as solvents. Any substance can be used for this purpose, provided that it does not displace the ligand molecules from the paramagnetic complex.

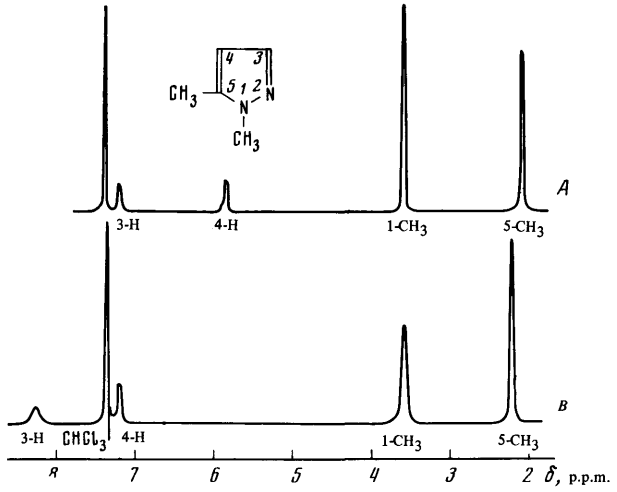


Figure 5. ^{1}H NMR spectrum of 1,5-dimethylpyrazole without the addition (*A*) and with addition (*B*) of $NiBr_2.3H_2O$.

Other investigators[13,44-46] also used the addition of salts of metals of the first transition group in order to analyse the ^{1}H NMR spectra. In particular, the relative positions of the NH_2 and NHR groups and the aromatic ring were established[13] in aniline derivatives coordinated to $Ni(AA)_2$¶ and $Co(AA)_2$. The conformation of the tropane ring was refined[44]. Account was taken of the effect of the orientation of the nitrogen atom lone pair and the paramagnetic shifts in the spectra of piperidines induced by $Ni(AA)_2$.[47] A study was made of the effect of $Co(AA)_2$, $Ni(AA)_2$, and $Cu(AA)_2$ on the ^{1}H NMR spectra of various alcohols and amines at room temperature[45].

To conclude this section, we may mention that, for different ligands and coordinating ions, which can form complexes differing in the values of ω and T_{2M}, Eqns. (16) and (17) can be represented approximately by Eqns. (18) to (24) at different temperatures of the test specimens. Since the complexes formed by elements of the first transition group are characterised by different values of τ_S (τ_S^{Mn} and $\tau_S^{Cu} \gg \tau_S^{Ni}$, τ_S^{Co}, τ_S^{Fe}),[34] it follows that comparison of the values of Δ and δ′ for the purpose of the assignment of the resonance lines is also possible at different temperatures of the test specimens. This fact is illustrated in Fig. 6.[48] A similar behaviour may be shown for the same coordinating ion with different ligands.

¶ AA = acetylacetonato-group.

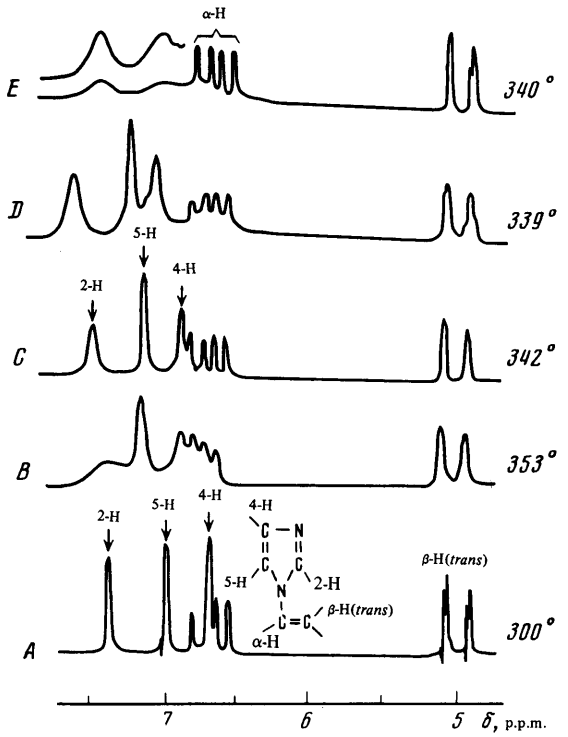


Figure 6. ^{1}H NMR spectrum of *N*-vinylimidazole without the addition (*A*) and with addition of a paramagnetic complex at different temperatures: *B*) $NiCl_2.4L$; *C*) $FeCl_3.4L$; *D*) $CoCl_2.4L$; *E*) $CuCl_2.4L$.

2. LANTHANIDE COMPLEXES

The vast majority of studies in which the ^{1}H NMR spectra were simplified using the spectra of paramagnetic systems were made after the publication of Hinckley's paper[49], which reported a comparison of the ^{1}H NMR spectrum of a cholesterol solution with and without the addition of the paramagnetic complex $Eu(DPM)_3.2Py$ (DPM = dipivaloylmethane or 2,2,6,6-tetramethylheptane-3,5-dione[50] and Py = pyridine). The author justifies the use of the europium complex by the very short electronic relaxation time (τ_S) of lanthanide ions. Therefore (see Section II) the formation of a complex with tris(dipivaloylmethane)europium lead to only a slight broadening of the resonance lines, while their paramagnetic shifts are significant. Fig. 7 illustrates the spectrum of cholesterol (V) in carbon tetrachloride solution without addition (Fig. 7*A*) and with addition of $Eu(DPM)_3.2Py$.[49] In the free ligand the protons of the methyl and also methylene and methine groups, which are not bound to an oxygen atom, resonate in a high field, forming an unresolved multiplet in the spectrum. The remaining protons resonate in the weaker field. The coordination of cholesterol to the europium ion leads to an appreciable shift of the signals in the spectrum. The greatest paramagnetic shifts are observed for the signals of the vinyl proton *f* and the proton *e*, which indicates coordination via the hydroxy-group. The signals of the methyl groups *a*, *b*, and *c* are also displaced. Moreover, new resonance lines *g*, *h*, and *i* appear in a weak field. The assignment of the resonance

line was based on a comparison of the spectra at different $Eu(DPM)_3.2Py$ concentrations in the test specimen with allowance for the integrated signal intensities. Moreover, account was taken of the fact that, when the coordinating centre is the lanthanide ion, the paramagnetic shift is due to a pseudocontact interaction[4]. The paramagnetic shifts were therefore compared with the corresponding values of r. For this purpose, the possible structure of the complex was examined using a model of cholesterol. It was found that the metal ion is in the *trans*-position relative to the proton *e*, i.e. that the configuration of the complex depends significantly on the steric factor, determined by the mutual orientations of the proton and the hydroxy-group. The dependence of the observed paramagnetic shifts on r^{-3} shows that the paramagnetic shifts are mainly determined by the distance from the coordinating ion to the resonating nuclei. This analysis of the ^1H NMR spectra of cholesterol led to the conclusion that $Eu(DPM)_3.2Py$ can be used for the conformational analysis of steroids and similar compounds. The capacity of $Eu(DPM)_3.2Py$ to induce relatively large paramagnetic shifts, which depend on the concentration of the complex in the test specimen, without a significant broadening of the resonance line shows that this complex can be used as a shift reagent[49].

In his next paper[51] Hinckley reported the use of a paramagnetic europium complex for the assignment of the signals of the methyl protons in the ^1H NMR spectrum of (+)-camphor, since there had been no unanimous view in the literature concerning this problem. Hinckley preceded the spectrum analysis by the following justification of the use of paramagnetic additives.

When a complex $M(DPM)_3.2Py$ (M is a lanthanide element) is dissolved in carbon tetrachloride, its molecule dissociates in accordance with the equations

$$M(DPM)_3.2Py \rightleftharpoons M(DPM)_3.Py + Py,$$
$$M(DPM)_3.Py \rightleftharpoons M(DPM)_3 + Py.$$

If an organic compound B with a coordinating group is added to the solution, association of the following type will take place:

$$M(DPM)_3.Py + B \rightleftharpoons M(DPM)_3.Py.B.$$

The paramagnetic shifts in the spectrum of B are then a consequence of such association.

According to Hinckley[51], the use of lanthanide complexes must involve the following procedures: 1) the recording of the ^1H NMR spectrum of compound B dissolved in carbon tetrachloride without an additive and then with one or several additions of $Eu(DPM)_3.2Py$; the determination of the concentration variation of the observed shifts is necessary in those cases where it is difficult to analyse the spectrum at one concentration; 2) the construction of a model of compound B and the measurement of the distances r from the coordinating metal ion to the resonating protons (the ionic radius of Eu^{3+} is 0.950 Å). The spectrum of B is interpreted accordingly.

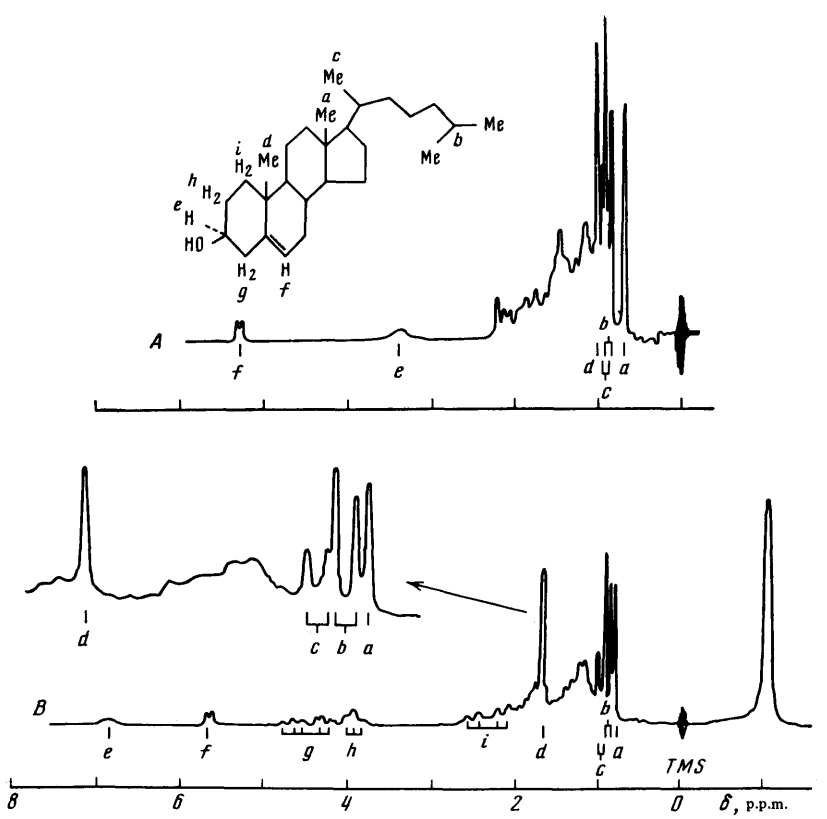
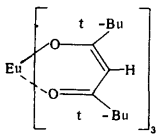


Figure 7. *A*) ^1H NMR spectrum of cholesterol in carbon tetrachloride; *B*) the spectrum of cholesterol after the addition of the complex $Eu(DPM)_3.2Py$. The high-field signal is due to the methyl protons of DPM.

Although Hinckley's paper[49] was published in the middle of 1969, more than 200 reports of the use of shift reagents for the analysis of NMR spectra have already been published. These studies, illustrating the scope of the method of analysing NMR spectra with the aid of lanthanide complexes, are described below.



After Hinckley[49], Sanders and Williams reported that Eu(DPM)$_3$ is an excellent shift reagent[52]. This europium compound induces considerable paramagnetic shifts by coordinating the lone electron pair of the functional group. For example, the aromatic protons in the ^{1}H NMR spectra of benzyl alcohol give rise to a broad spectrum. When Eu(DPM)$_3$ is added to the solution (0.39 M), the spectrum becomes susceptible to a first-order analysis (Fig. 8).

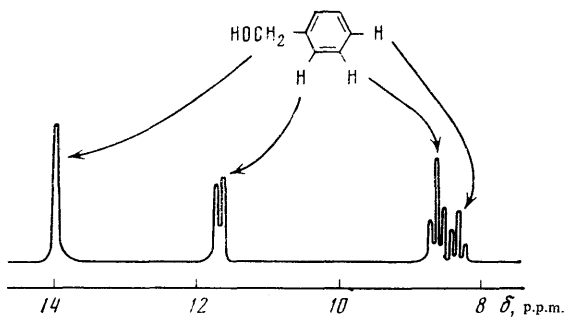


Figure 8. The ^{1}H NMR spectrum of benzyl alcohol in the presence of Eu(DPM)$_3$.

The induced shifts decay rapidly with increase of the number of bonds separating the hydroxy-groups and the corresponding protons. When Eu(DPM)$_3$ is added to a solution of 1-hexanol, the analysis of its spectrum in accordance with the first-order rules is also possible. The signal of the OH group is then broadened to such an extent that it cannot be recorded. However, the broadening of the resonance lines of the other protons is much smaller. It was found that Eu(DPM)$_3$ induces paramagnetic shifts also in the ^{1}H NMR spectra of ketones, ethers, esters, and amines. Ketones form complexes (to an extent of about 35–40%) less effectively than alcohols, and ethers and esters are less effective still. However, amines behave similarly to alcohols. Sanders and Williams believe that Eu(DPM)$_3$ can be extremely effective in the determination of the structures of natural products and supported this view by an analysis of the changes in the ^{1}H NMR spectrum of lupeol recorded after the addition of Eu(DPM)$_3$. They discussed[52] the conditions governing the employment of Eu(DPM)$_3$. In particular, they noted its high solubility in carbon tetrachloride. One of the first studies was that of Wahl and Peterson[53], who employed Eu(DPM)$_3$ for the analysis of the ^{1}H NMR spectra of adamantan-1-ol and adamantan-2-ol.

The effectiveness of Eu(DPM)$_3$ was illustrated by Demarko et al.[54] in the analysis of the spectra of *trans*- and *cis*-4-butylhexanol, isoborneol, and borneol[54]. The signals in the spectra of these compounds were assigned on the basis of a comparison of the paramagnetic shifts with the corresponding distances r' from the resonating nuclei to the oxygen of the hydroxy-group and not to the coordinating ion†. This approach was justified by postulating that the values of $3\cos^2\varphi_i - 1$ for the protons of the test compounds would be significantly different. It is impossible to calculate them owing to the lack of information about the geometry of the paramagnetic complex in solution. It was established that a relation between the shift‡ and the distances from the protons to the oxygen atom can be expressed by a straight line on a logarithmic scale with a slope of -2.3. This is evidence of a correspondence between the induced shifts and r': $\lg(r')^{-3} = (-3)\lg r'$. The replacement of r by r' must be regarded as justified, since it implies a shift of the origin of the readings of the power base r in the functional relation $y = r^3$, the shape of the plot of which is determined by the cube of the distance. Evidently for small values the use of r' in comparing the paramagnetic shifts will yield less satisfactory results. Therefore the replacement of r by r' should be most successful for protons remote from the europium atom. Fig. 9 illustrates the results of Demarko et al.[54]. Only two signals may be assigned in the spectrum of a solution of *cis*-butylhexanol (Fig. 9*A*) without Eu(DPM)$_3$. However, for a molar ratio alcohol/Eu(DPM)$_3$ = 0.7, the recorded spectrum meets the requirements for a first-order interpretation (Fig. 9*E*). The signals were assigned on the basis of the spin–spin interaction constants taking into account double resonance experiments. Demarko et al. also illustrated the efficiency of the shift reagent method in the study of the structures of steroids and triterpenes by a detailed analysis of the ^{1}H NMR spectra of 5α-androstan-2β-ol and friedelan-3-β-ol.[56] The possibility of employing the shift reagent method for the determination of the numbers and positions of the methyl groups in molecules of natural products was demonstrated by comparing the shifts induced by Eu(DPM)$_3$ in the ^{1}H NMR spectra of 22 triterpenes[57]. In order to obtain spectra with non-overlapping signals, account was taken in the above study of both the concentration and temperature variation of the observed shifts. The compared values of the latter were normalised in relation to the low-field signal of the protons in the 4-CH_3 group, the chemical shift of which was assumed to be 10 p.p.m.

Briggs et al.[58] were the first to report that Pr(DPM)$_3$ induces, like Eu(DPM)$_3$, paramagnetic shifts in ^{1}H NMR spectra. It is striking that these shifts are approximately three times greater than the shifts due to Eu(DPM)$_3$ and are of opposite sign. Briggs et al.[58] quote the paramagnetic shifts induced by complexes of the type M(ClO$_4$)$_3$·{OP[N(CH$_3$)$_2$]$_3$}$_4$ in the ^{1}H NMR spectrum of a solution of acetonitrile (the shifts are quoted relative to the acetonitrile complex in which M is lanthanum; the minus sign

† The r' were calculated by determining the distances between non-linked atoms[55].

‡ The paramagnetic shifts compared with the r' were calculated subject to the condition that the molar ratio alcohol/Eu(DPM)$_3$ = 1.

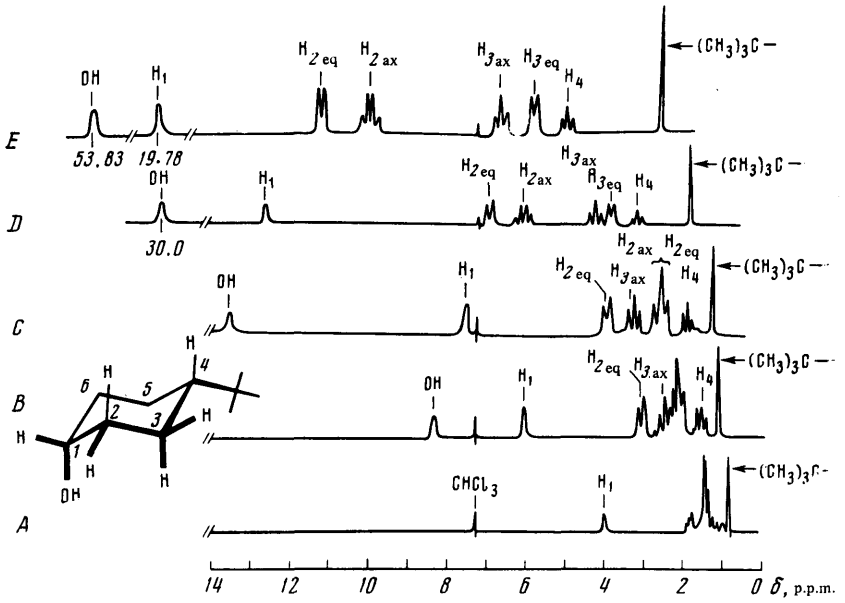


Figure 9. The ^{1}H NMR spectrum of *cis*-4-t-butylcyclohexanol (20 mg) in $CDCl_3$ (0.4 ml) with different contents of $Eu(DPM)_3$ (mg): *A*) 0.0; *B*) 10.3; *C*) 16.0; *D*) 33.1; *E*) 60.2. (The signal of the methyl protons was recorded with a lower amplification than the other signals.)

corresponds to a shift to high field:

Metal	Paramagnetic shift, p.p.m.
Ce	−1.5
Pr	−3.0
Nd	−1.75
Sm	−0.27
Eu	+1.33
Gd	not observed
Tb	−19.2
Dy	not observed
Ho	−17.0
Er	+4.4
Tm	+6.9
Yb	+6.66
Lu	0

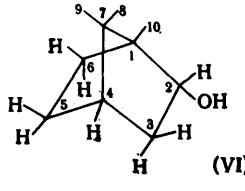
The above example shows that complexes of other lanthanides, together with $M(DPM)_3$, can be used as shift reagents. At the same time there are important limitations to the use of these complexes, which are determined in particular by the following causes[58].

1. The $M(DPM)_3$ form complexes with a coordination number of 6, which is suitable for the coordination of organic molecules.

2. The shift reagent method is based on the use of nonpolar solvents.

3. One must bear in mind that (a) the test substance may not be coordinated to the lanthanide compound due to steric hindrance and (b) that the signals of the resonating nuclei may not be affected significantly by complex formation. For example, it has been found that $Pr(NO_3)_3(OPPh_3)_3$, $Pr(ClO_4)_3\{OP[N(CH_3)_2]_3\}_4$, $Eu(NO_3)_3(OAsPh_3)_4$, $Ce(NCS)_3 \cdot (OPPh_3)_4$, and lanthanide perchlorates induce insignificant paramagnetic shifts in the spectra of alcohols and ketones (the signal of α-protons is displaced only by approximately 0.5 p.p.m.).

Briggs et al. were the first to compare the observed and calculated paramagnetic shifts induced by $Pr(DPM)_3$.[59] They used borneol (VI), which has a fixed conformation, as the ligand

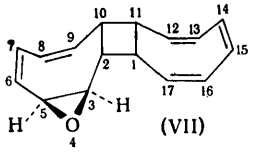


(VI)

An unambiguous assignment of the observed paramagnetic shifts was achieved by a preliminary analysis of the ^{1}H NMR spectrum of borneol recorded at three frequencies (60, 100, and 220 MHz) using the double resonance and deuteriation techniques. It was assumed (1) that the paramagnetic shifts are due to a pseudocontact interaction and (2) that the complex is axially symmetric in solution.

This implied that the induced shift must be proportional $(3\cos^2\varphi - 1)r^{-3}$. The orientation of the resonating nuclei was specified by the Pr—O distance, the Pr—O—(2-C) angle, and the Pr—O—(2-C)—(H-2)-dihedral angle. The values of these parameters in the initial model (2.6 Å, 109°, and 33°) were then varied until agreement was reached between the calculated and experimental shifts to within a constant factor. This agreement was found for the following values: 3 Å, 126°, and 25°. The authors concluded that the problem of the orientation of the hydroxy-groups in various lanthanide complexes should probably be solved separately in each specific case. The importance of the $3\cos^2\varphi - 1$ contribution to the paramagnetic shifts was also demonstrated (particularly for resonating nuclei close to the coordinating ion). This conclusion is confirmed by the ^{1}H NMR spectrum of a

tetracyclic epoxide (VII) recorded in the presence of $Eu(DPM)_3$.[60]



(VII)

It was found that, in contrast to the signals of other protons, those of 15-H and 16-H are displaced to high field. The explanation is that $\varphi_{15\text{-H}} = 58°$ and $\varphi_{16\text{-H}} = 55$, i.e. is greater than 54.7° (if $\varphi < 54.7°$, then $3\cos^2\varphi - 1 < 0$). Therefore complex formation leads to additional screening of the 15-H and 16-H protons and displaces their signals to high field. The shifts to high field induced by $Eu(DPM)_3$ were also reported in other investigations[61-63]. It is noteworthy that Tjan and Visser[62] believe that the hypothesis of a contact and pseudocontact mechanism for the interaction of unpaired electrons and resonating nuclei constitutes the most acceptable explanation of the paramagnetic shifts to high field which they observed. These two mechanisms lead to the appearance of paramagnetic shifts with opposite signs, which is in fact reflected in the ^1H NMR spectra.

Bélanger[64] examined the shifts induced by $Pr(DPM)_3$ in the spectra of certain ketones and found that the shifts are greater by a factor of 1.4 than the shifts induced by $Eu(DPM)_3$.

Wolkowski and coworkers[65,66] used addition of the ytterbium compound $Yb(DPM)_3$ for the analysis of ^1H NMR spectra. In the first study they investigated primary, secondary, and tertiary amines and established that the induced paramagnetic shifts depend on the steric factor and on the charge of the nitrogen atom. They compared the paramagnetic shifts and r for pyridine and quinuclidine, which have a characteristic orientation of a lone electron pair orbital available for coordination. The N...Yb distance was varied from 1 to 5 Å. It was found that, for a N...Yb distance of 3 ± 0.3 Å, the graphical relation between the shifts and r (on a logarithmic scale) is linear.

Wolkowski[66] illustrated the effectiveness of $Yb(DPM)_3$ for the assignment of the signals in the ^1H NMR spectra of ketones and aldehydes. A significant influence of steric factors and of the charge of coordinating atoms on the shifts induced by lanthanides was observed also by Ernst and Mannschreck[67] who found, in particular, a linear correlation between the basicity of the substitutent and the paramagnetic shifts of the signals of the *ortho*- and *meta*-protons in the ^1H NMR spectra of substituted anilines. The application of the shift reagent method to compounds having more than one coordinating centre was examined in a number of studies. It was found, for example, that *trans*- and *cis*-1-hexyl-2-phenylazetidin-3-ol is coordinated to $Eu(DPM)_3$ via the oxygen of the hydroxy-group and not via the nitrogen atom of the four-membered ring[68]. Details of the analysis of the paramagnetic shifts in the spectra of compounds with several coordination centres can be found in studies by Hinckley[69] and Sanders and coworkers[70].

The dependence of the pseudocontact interaction not only on r_i but also on φ_i complicates the assignment of the signals on the basis of a comparison of the observed paramagnetic shifts. At the same time, in the case of rapid exchange the difference between the broadening of the resonance lines at the given specimen temperature depends only on r^{-6}. Therefore, when the broadening can be determined as the signals are displaced, the values of Δ can be used for the same purpose as δ'.

This was taken into account by Morallee et al.[71] who reported that not only the shift but also the broadening of the resonance lines, due to the lanthanide ions, permits their use as excellent NMR probes for the investigation of biological systems. This was specifically illustrated in a study of the ^1H NMR spectrum of lysozyme in the presence of europium(III), holmium(III), and gadolinium(III) ions. Comparison of the broadening of the signals due to gadolinium enabled the distances from the coordinating ion to the protons of the acetamide and glycosidic methyl groups to be determined. The effectiveness of the joint analysis of δ' and Δ in the ^1H NMR spectra of pyridine and quinoline was demonstrated by Reuben and Leigh[72].

It is noteworthy that, in assigning the resonance lines in the spectra, some investigators compared the induced paramagnetic shifts with $(r')^{-2}$, motivating this approach by the uncertainty of the relative positions of the resonating nuclei and the centra ion. Rafalski et al.[73] compared the following two correlations: (1) between δ' and r^{-n} or $(r')^{-n}$ ($n = 2, 3$) and (2) between $\lg\delta'$ and $\lg r^{-n}$ or $\lg(r')^{-n}$. The values of n calculated from the experimental data of different workers served as a criterion for the comparison. The following remarks are appropriate to the study of Rafalski et al.[73].

1. The replacement of δ' and r (or r') by their logarithms implies only a change in the scale of the quantities compared. Therefore the above correlations must not be contrasted with one another.

2. The above investigations showed that the magnitude of the induced paramagnetic shifts is determined by the relative positions of the resonating nuclei and the central atom and also by the nature of the electron-nuclear interaction in the complex. Therefore the problem of choice of n is not fundamental, particularly since the pseudocontact shifts depend on $n = -3$.

Examination of NMR in paramagnetic systems showed that the observed values of Δ and δ' are determined, in particular, by the nature of the coordinating ion. Therefore Crump et al.[74] made a comparative study of complexes of the type $M(DPM)_3$, where M = Pr, Sm, Eu, Tb, Ho, or Yb§. The criteria of this comparison were (a) the position of the signal due to the protons of the t-butyl groups of DPM, (b) the slopes of the linear plot of $\delta' = \delta'(X_M)$, where X_M is the molar ratio $M(DPM)_3$/ test substance, (c) the relative shifts in the spectra of complexes of the type $M\{OP[N(CH_3)_2]_3\}_4(ClO_3)$ taken from the study of Briggs et al.[58], and (d) the ratio of the broadening (Hz) to the shift (Hz) of the signal due to the protons of the methyl groups of t-butyl alcohol in the presence of the complexes $M(DPM)_3$. The comparison showed that, in order to obtain first-order ^1H NMR spectra with retention of multiple structure, it is best to employ $Eu(DPM)_3$. The signal of the t-butyl groups of this salt appears in high field relative to tetramethylsilane and is therefore not superimposed on the signals of the test substances. Moreover, the paramagnetic shifts to low field induced by $Eu(DPM)_3$ are more suitable from the experimental standpoint. $Pr(DPM)_3$ should be used in addition to $Eu(DPM)_3$, particularly for the assignment of the signals of the t-butyl groups in the spectra of steroids. One must note that the signal of the t-butyl groups of $Pr(DPM)_3$, which

§ See also Refs. 75–77.

appears in the region of 3–5 p.p.m. (δ), may be superimposed on the signals of the test compounds. Conditions governing the use of $M(DPM)_3$ (solubility¶, effect of H_2O, etc.) have been described [74,78]. The stoichiometry in the solute (test substance)–shift reagent system has been analysed in a number of publications. It has been established [80] that, when the ligand concentration is much higher than that of the shift reagent, the paramagnetic complexes have the 1 : 2 composition and not 1 : 1, as believed by Armitage et al. [81] Shapiro and Johnston [80] also examined in detail the use of the relation between the observed paramagnetic shifts and the ratio of the ligand and lanthanide concentrations. Careful analyses of the application of the $M(DPM)_3$ complexes as displacing agents and also of the scope of the method have been made [75,82].

The investigations showed that the paramagnetic shifts induced by lanthanides depend significantly on the structure of the diketone [82–84]. It was established that the tris-[3-t-butylhydroxymethylene-(+)-camphorato]europium can be used to determine the degree of enantiometric purity [85]. However, its applicability proved to be limited [86,87] Tris-[3-heptafluoropropylhydroxymethylene-(+)-camphorato]europium proved to be a more effective optically active displacing agent [86]. At the same time the use of $Eu(DPM)_3$ for similar purposes can also be successful [87]. A comparison of $Eu(DPM)_3$, $Eu(FOD)_3$ [FOD = tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato)europium], and $Eu(FND)_3$ [FND = tris-(1, 1, 1, 2, 2, 6, 6, 7, 7, 7-decafluorheptane-3,6-dionato]europium has been made [76].

It was noted in Section II that in the general case the paramagnetic shifts δ′ and the broadening Δ of the resonance lines observed in the NMR spectra are defined by Eqns. (16) and (17). On the other hand, the practical employment of δ′ and Δ is based on Eqns. (18)–(24) the validity of which is determined by the nature of the paramagnetic complex and the temperature of the test specimens. For lanthanide complexes, this problem has been hardly discussed in the literature. Only the effect of varying temperature has been reported [57,71,77,88–92]. In this connection the effect of the specimen temperature on the paramagnetic shifts induced by $Eu(FOD)_3$ in the ^1H NMR spectra of limonoids is of interest [88]. It was found that, with increase of temperature, the δ′ for the signals of certain protons increase. This finding was regarded [88] as unexpected on the grounds that the paramagnetic shifts are inversely proportional to the temperature of the test specimen (Section II). However, in the case of a slow exchange an increase of temperature leads to a decrease of τ_M and therefore δ′ in the NMR spectra should increase. In particular, when the spectrum of the ligand molecule contains signals with significantly different values of ω, cases are possible for which Eqns. (16) and (17) can be represented approximately by different expressions from the set of Eqns. (18)–(24). Therefore the determination of the $\delta' = \delta'(T)$ relation may be not only desirable but also essential.

NMR studies on other nuclei (other than the proton) with addition of lanthanide complexes have already been published. The effect of $Eu(DPM)_3$ and $Yb(DPM)_3$ on the ^{14}N NMR spectra of pyrrolidinone, n-propylamine, pyridine, *N*-methylimidazole, acetonitrile, and dimethylformamide has been examined [93]. Briggs et al. demonstrated the effectiveness of the interpretation of ^{13}C NMR spectra with the aid of tris(dipivaloylmethane)lanthanides [94]. Duggan and Urry [95] used the paramagnetic shifts induced by $Eu(DPM)_3$ in the ^{13}C NMR spectra for structural investigations. A method of assignment of the ^{13}C NMR signals based on the joint use of $M(DPM)_3$ and $^{13}C-\{^1H\}$ heteronuclear double resonance has also been proposed [96]. Mention should be made of the work by Sanders and Williams [97] concerning the nature of the shift induced by lanthanides in the ^{31}P NMR spectra. In particular they established that $Eu(NO_3)_2{\cdot}6H_2O$ is an effective shift reagent in polar solvents for compounds with a $X-O^-$ (X = R–CO, $R_3\overset{+}{P}$, or $R_3\overset{+}{A}s$) functional group. Interesting results were obtained in studies [98,99] in which the isotope effect of deuterium on the paramagnetic shifts induced in NMR spectra by lanthanide complexes was considered. Mention should also be made of the work by Willcott and coworkers [100,101] who considered a statistical method for the analysis of paramagnetic shifts induced by lanthanide complexes. Finally a fairly complete list of publications in 1969–71 and also some of the publications in 1972 can be found in studies [102,103] on the use of shift reagents.

The following remarks must be made in conclusion. Firstly, the change in the relative contents of the ligand and the lanthanide within wide limits can influence significantly the constancy of the composition of the complex in solution. Secondly, X-ray diffraction analysis of the complexes† $Ho(DPM)_3{\cdot}(VIII)_2$ [104] and $Eu(DPM)_3{\cdot}(IX)$ [105] showed that the paramagnetic lanthanide complexes used as shift reagents can have a symmetry other than axial‡. For example, Uebel and Wing [105] found agreement between the experimental and calculated (for axial symmetry) paramagnetic shifts only for a signal assignment known to be incorrect. Thirdly, the nature of the electron-nuclear interaction in lanthanide complexes with organic ligands has been comparatively little investigated, in contrast to the complexes of the first transition series. The majority of investigators do not think it obligatory to resort to a contact mechanism in order to account for the nature of the paramagnetic shifts induced by lanthanide complexes. However, according to one view, the contribution of the contact interaction to the paramagnetic shifts induced by lanthanide complexes may be significant [20,21,72]. Therefore, caution must be exercised in using the paramagnetic shifts induced in the NMR spectra by lanthanide complexes for structural investigations. If the paramagnetic complex is used only to increase the ratio of the difference between the chemical shifts and the spin–spin interaction constants, it is sufficient to record the NMR spectrum of the test substance with one or several additions of the shift reagent. However, one must bear in mind that coordination to the lanthanide may influence the spin–spin interaction constants for the nuclei in the ligand molecule [107]. The suggestion that germanium–porphyrin systems be employed as shift reagents is interesting [108]. Maskasky and Kenney [108], who described a method for the formation of such systems, note, in particular, that they are diamagnetic, and, in contrast to the paramagnetic displacing agents, do not broaden the resonance lines in the NMR spectra.

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The paramagnetic complexes of lanthanides can be used to facilitate significantly the interpretation of NMR spectra,

¶ For the use of carbon disulphide as a solvent, see Walters [79].

† (VIII) = 4-picoline; (IX) = 1,2-epoxy-3,3-dimethylethane.

‡ See also Honeybourne [106].

which extends the scope of the NMR method in the study of the structures of organic ligands. Further progress in the use of shift reagents requires a more profound study of the nature of the electron-nuclear interaction in the paramagnetic lanthanide complexes. The name of the method (the shift reagent method), which has become common in the literature outside the Soviet Union, reflects exactly the consequences of the use of lanthanides. However, bearing in mind the nature of the shifts and the broadening of the resonance lines, the method based on the characteristics of the NMR spectra of paramagnetic systems should be logically termed the method of paramagnetic additives.

The NMR spectrum analysed frequently satisfies the requirements for first-order spectra but its interpretation is ambiguous owing to the uncertainty of the molecular geometry. In such cases the use of complexes of elements in the first transition series for the structural determination of organic ligands may also prove to be effective.

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