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Nuclear Magnetic Resonance and Its Applications in Chemical Research

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The fundamentals of nuclear magnetic resonance spectroscopy are briefly described. The applications of the method in chemistry are demonstrated and the possible developments of the application of nuclear magnetic resonance in studies on molecular and crystal structures are indicated.
The bibliography includes 75 references.

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I. INTRODUCTION

Nuclear magnetic resonance (NMR) is one of the outstanding discoveries of the twentieth century, which has now taken an honourable place among the principal methods for research in structural chemistry. The method needs no special recommendation. The literature devoted to NMR is enormous. The bibliography in Leche's monograph published in 1963 includes about three thousand references and in the last two years more than two hundred papers, dealing either with the method itself or demonstrating its possibilities in various branches of solid state physics, molecular physics, in structural studies, and in the solution of the principal problems of theoretical chemistry, have been published. This journal has already included a review on the chemical applications of NMR. The aim of the present review is to give a simple systematic account of the principles of NMR and its main applications, and this has largely determined its form. However, the embodiment of this aim in print may fall short of these words—of the kind that might have been used in a lecture or in a leisurely conversation. Therefore it must be emphasised that the description of the principal problems of NMR spectroscopy within the framework of a journal article is exceptionally difficult and the present review is merely a compromise between the intention and the feasibility of its realisation.

The treatment of the subject should include a detailed description of problems such as magnetic anisotropy of bonds, multiplicity of the spectra, and the role of the strength of the permanent magnetic field and of interactions with nuclei having a spin $I > 1/2$; certain facts are included for the first time in a review of this type. Its bibliography in no way claims to give an exhaustive coverage of the literature. The interested reader should consult the required references in monographs [1-10].

II. MAGNETIC PROPERTIES OF ATOMIC NUCLEI

Many stable nuclei have spins $I > 0$ (Table 1). The presence of the spin leads to a magnetic moment: if the spin I is compared with the circulation of the nuclear charge, then its rotation is equivalent, in accordance with the usual classical concepts of magnetic phenomena, to a circular current which gives rise to a magnetic moment $\mu = e\hbar/2m_pc$. For a proton,

$$\mu_p \simeq \frac{4.8\times10^{-10}\times1\times10^{-27}}{23\times10^{10}\times1836\times9\times10^{-28}} \simeq \frac{1}{2}\times10^{-23}.$$

As a rule, heavier nuclei have magnetic moments smaller than μ_p. The existence of the nuclear magnetisation of matter was confirmed experimentally in 1937 by Lazarev and Shubnikov [11], who measured the static magnetic susceptibility of solid hydrogen in the temperature range between 1.76° and 4.22°K. The magnetic properties of atomic nuclei have played a notable role in many branches or optical spectroscopy, in electron spin resonance (ESR) spectroscopy, in nuclear quadrupole resonance (NQR), etc. The vast majority of NMR studies have been made on nuclei having a spin $I = 1/2$. Their sequence in terms of decreasing numbers of relevant papers is as follows: ^{1}H, ^{19}F, ^{31}P, ^{13}C, ^{29}Si, etc.

III. RESONANCE CONDITIONS

A nucleus with a spin $I = 1/2$ has two allowed orientations in an external magnetic field: roughly speaking, the magnetic moment of such a nucleus may be oriented either parallel or antiparallel to the vector H_0. Evidently the parallel orientation is energetically favourable and the antiparallel orientation is not. When a specimen containing such nuclei is placed in a magnetic field H_0, its energy

structure becomes enriched by two magnetic energy levels, the distance between which is

$$\Delta E = g\mu_0 H_0 \quad (1)$$

where $g = \mu/I\mu_0$ is the splitting factor (i.e. gI is the number of nuclear magnetons μ_0 in the experimental value of the nuclear magnetic moment). Therefore transitions between the levels involve the following energy quanta:

$$h\nu_0 = g\mu_0 H_0 \quad (2)$$

or, in other words, at a frequency

$$\nu_0 = \frac{g\mu_0}{h} \cdot H_0 = \gamma_0 H_0 \quad (3)$$

there is an effective interaction between the electromagnetic radiation incident on the specimen and the series of energy levels of the magnetic moments of the nuclei.

Table 1. Properties of the nuclei.

Isotope	γ_0, Hz g^{-1}	Natural content, %	Spin I	Isotope	γ_0, Hz g^{-1}	Natural content, %	Spin I
1	2	3	4	1	2	3	4
^{1}H	4257.7	99.984	1/2	^{95}Mo	277.4	15.78	5/2
^{2}H	653.6	$1.56\cdot10^{-2}$	1/2	^{97}Mo	283.3	29.60	5/2
^{6}Li	626.5	7.43	1	^{103}Rh	134.0	100	1/2
^{7}Li	1654.7	92.57	3/2	^{105}Pd	174	2.23	5/2
^{9}Be	598.3	100	3/2	^{107}Ag	172.2	51.35	1/2
^{10}B	457.5	18.83	3	^{109}Ag	198.1	48.65	1/2
^{11}B	1366.0	81.17	3/2	^{111}Cd	902.8	12.86	1/2
^{13}C	1070.5	1.108	1/2	^{113}Cd	944.4	12.34	1/2
^{14}N	307.6	99.635	1	^{113}In	931.0	4.16	9/2
^{15}N	431.5	0.365	1/2	^{115}Sn	1322.0	0.35	1/2
^{17}O	577.2	$3.7\cdot10^{-2}$	5/2	^{117}Sn	1577.0	7.67	1/2
^{19}F	4005.5	100	1/2	^{119}Sn	1587.0	8.68	1/2
^{23}Na	1126.2	100	3/2	^{121}Sb	1019.0	57.25	5/2
^{25}Mg	260.6	10.05	5/2	^{123}Sb	551.8	42.75	7/2
^{27}Al	1109.4	100	5/2	^{123}Te	1159	0.89	1/2
^{29}Si	846.0	4.7	1/2	^{125}Te	1345	7.03	1/2
^{31}P	1723.5	100	1/2	^{127}I	851.9	100	5/2
^{33}S	326.6	0.74	3/2	^{129}Xe	1178	26.24	1/2
^{35}Cl	417.2	75.4	3/2	^{131}Xe	349.0	21.24	3/2
^{37}Cl	347.2	24.6	3/2	^{133}Cs	558.5	100	7/2
^{39}K	198.7	93.08	3/2	^{135}Ba	425	6.59	3/2
^{41}K	109.2	6.91	3/2	^{137}Ba	476	11.32	3/2
^{43}Ca	286.5	0.13	7/2	^{139}La	601.4	99.91	7/2
^{45}Sc	1034.3	100	7/2	^{141}Pr	1130	100	5/2
^{47}Ti	240.0	7.75	5/2	^{143}Nd	220	12.2	7/2
^{49}Ti	240.1	5.51	7/2	^{145}Nd	140	8.3	7/2
^{50}V	424.5	0.24	6	^{147}Sm	147	15.07	7/2
^{51}V	1119.3	99.7	7/2	^{149}Sm	119	13.84	7/2
^{53}Cr	240.6	9.54	3/2	^{151}Eu	1000	47.8	5/2
^{55}Mn	1055.3	100	5/2	^{153}Eu	460	52.2	5/2
^{59}Co	1010.3	100	7/2	^{171}Yb	690	14.3	1/2
^{63}Cu	1128.5	69.09	3/2	^{173}Yb	198	16.1	5/2
^{65}Cu	1209.0	30.91	3/2	^{175}Lu	570	97.4	7/2
^{67}Zn	263.5	4.12	5/2	^{181}Ta	460	100	7/2
^{69}Ga	1021.8	60.2	3/2	^{185}Re	958.6	37.1	5/2
^{71}Ga	1298.4	39.8	3/2	^{187}Re	968.4	62.9	5/2
^{73}Ge	148.5	7.61	9/2	^{189}Os	330.7	16.1	3/2
^{75}As	729.2	100	3/2	^{191}Ir	81	38.5	3/2
^{77}Se	813.1	7.5	1/2	^{193}Ir	86	61.5	3/2
^{79}Br	1066.7	50.57	3/2	^{195}Pt	915.3	33.7	1/2
^{81}Br	1149.8	49.43	3/2	^{197}Au	69.1	100	3/2
^{83}Kr	164	11.55	9/2	^{199}Hg	761.2	16.80	1/2
^{85}Rb	411.1	72.8	5/2	^{201}Hg	308	13.2	3/2
^{87}Rb	1393.2	27.2	3/2	^{203}Tl	2433	29.5	1/2
^{87}Sr	184.5	7.02	9/2	^{205}Tl	2457	70.5	1/2
^{89}Y	208.6	100	1/2	^{207}Pb	889.9	21.1	1/2
^{91}Zr	400	11.23	5/2	^{209}Bi	684.2	100	9/2
^{93}Nb	1040.7	100	9/2				

Eqn. (3) defines the condition for nuclear magnetic resonance. The values of γ_0 (in units of Hz G^{-1}) are listed in Table 1. Thus, when the field strength H_0 of the laboratory magnet is known, the NMR frequency for the given nucleus can be calculated simply by multiplying together γ_0 and H_0. For protons at field strengths of 9400, 14 092, and 23 450 G, the resonance frequencies are 40, 60, and 100 MHz respectively, for ^{31}P nuclei in a 14 092 G field $\mu_0 = 24.4$ MHz, etc. Condition (3) was obtained on the basis of quantum concepts. It is interesting that the classical treatment leads to exactly the same resonance condition. Let us consider a magnetic dipole moment μ in a field H_0. According to Larmor's theorem [12], the dipole μ will precess around the direction of H_0 at a frequency

$$\nu_0 = \frac{\gamma}{2\pi} H_0,$$

where γ is the gyromagnetic ratio of the dipole. When an additional small magnetic field H_1 is applied at right angles to H_0 in the plane of the vectors $\vec{\mu}$ and H_0, the dipole is subjected to a force which tends to alter the angle θ between $\vec{\mu}$ and H_0. When the field H_1 remains in the plane of the vectors $\vec{\mu}$ and H_0 for an unlimited time (synchronisation of the Larmor precession of the vector $\vec{\mu}$ and the rotation of the additional field H_1), the angle θ will change significantly, i.e., in other words, the application of an external field H_0 leads to a marked change in the nuclear magnetisation of the specimen. On the other hand, if the rates of rotation of μ and H_1 do not coincide, and field H_1 will not affect appreciably the overall magnetic moment of the specimen. Next it was found that $\gamma/2\pi = \gamma_0$, i.e. on the basis of Larmor's theorem, we obtain the same resonance condition as from quantum considerations.

The above discussion based on vectors enriched our ideas about NMR: in order to induce resonance, electromagnetic radiation must be circularly polarised and the magnetic vector H_1 must rotate in a plane perpendicular to the vector H_0. In practice a rotating magnetic field is created as a component of a linearly oscillating field: an electric field at a frequency ν_0 is applied to the coil of the circuit tuned to the same frequency; the axis of the coil is positioned at right angles to a permanent magnetic field H_0. It is well known that a field $2H_1\sin 2\pi\nu_0 t$ varying sinusoidally with time may be regarded as a superposition of two fields $H_1\sin 2\pi\nu_0 t$ rotating in opposite directions. One of these components gives rise to NMR and the other hardly interacts with the specimen.

IV. NUCLEAR MAGNETIC RELAXATION

The above resonance conditions indicate merely the possibility of the phenomenon but do not guarantee that it will occur. Both groups of discoverers of NMR [13,14] were extremely worried about the difficulties associated with the relaxation processes in the system of nuclear spins. In fact, having carried out an experiment in which the specimen is exposed to quanta of the required magnitude, we stimulate transitions between the magnetic energy levels. Then the probability of transitions from a lower to an upper level (absorption of energy) w^+ and transitions from an upper to a lower level w^- are equal: $w^+ = w^-$. If the populations of the lower and upper levels are identical, the same number of nuclei would pass from the lower to the upper level and conversely per unit time and NMR would not be observed at all.

It was found that within the spin system energy exchange processes take place very effectively and it may be assumed that the system is in thermal equilibrium at a certain temperature (spin temperature), which, generally speaking, is not equal to the temperature of the specimen T. This implies that the attainment of thermal equilibrium within the spin system takes place many powers of ten faster than processes involving energy exchange between the spin system and its surroundings.

In this case the populations of the upper (n_2) and lower (n_1) nuclear magnetic energy levels will not be equal; according to the Boltzmann distribution law, their ratio is

$$\frac{n_2}{n_1} = \exp\left(-\frac{2\mu H_0}{kT_s}\right). \quad (4)$$

If it is assumed that $T_S \simeq T$, then in a field $\geqslant 10^4$ G, we have for protons

$$\frac{n_2}{n_1} \simeq 1 - \frac{2\mu H_0}{kT}. \quad (5)$$

This small difference between the populations is in fact responsible for the occurrence of NMR: w^+n_1 and w^-n_2 nuclei undergo transitions per unit time from below upwards and from above downwards respectively; it is clear from the foregoing that $w^+n_1 > w^-n_2$, i.e. power is absorbed from the radiofrequency field H_1 by the system of nuclear spins. In the absence of some external process which acts in the opposite sense, the field H_1 equalises the populations of the nuclear magnetic levels after a finite time interval and absorption ceases. Such a situation is called saturation.

Regardless of the state of aggregation of the specimen (liquid, gas, or solid), the substance containing nuclear magnetic moments is called a "lattice".

Since nuclear magnetic resonance is observed in practice (and has actually become one of the principal physical research methods in chemistry!), we must conclude that there exists an effective process which returns the spin system to thermal equilibrium with the lattice. Such a process is called spin–lattice relaxation.

On complete saturation, $n_2 = n_1$. Eqn. (5) shows that formally this implies an exceptionally large increase in the temperature of the spin system: $T_S \to \infty$. According to the Second Law of Thermodynamics, the energy exchange process between the heated spin system and the lattice, which is, for example, at room temperature, then takes place in only one direction, from the hot to the cold object, i.e. there must be spin–lattice relaxation.

Indeed simple considerations show that the temperature equalisation process between the spin system and the lattice takes place exponentially:

$$\Delta n_0 - \Delta n_t = (\Delta n_0 - \Delta n_a)\, e^{-t/T_1},$$

where Δn_0 is the difference between the populations of the nuclear magnetic energy levels at $T_S = T$, Δn_1 the difference between the populations observed at time t, Δn_a the initial difference between the populations, and T_1 the time constant or simply the spin–lattice relaxation time.

The physical cause of the spin–lattice relaxation in diamagnetic specimens is the thermal fluctuation of the local magnetic field of the specimen. Bloembergen[15] showed that one can isolate from the thermal vibration spectrum a component with a frequency ν_0 which corresponds to a randomly varying magnetic field in the specimen; this gives rise to transitions between nuclear magnetic energy levels, and is in fact responsible for the lowering of the spin temperature T_S.

These fluctuating local magnetic fields are also one of the causes of spin–spin relaxation, which is responsible for the rapid attainment of the spin temperature T_S. Spin–spin coupling can take place without energy exchange with the external medium. This is the so called "flip-flop" process, in which two interacting nuclei change orientations simultaneously in an external field. Since they do not require an expenditure of energy, such processes can occur very rapidly. They restrict significantly the lifetime of the nucleus in a fixed state and make an appreciable contribution to the line width observed for solids.

In liquid and solid specimens magnetic nuclei are separated by distances of the order of 1 Å and therefore any nucleus is in a local field $\mu r^{-3} \simeq 10$ G, which upsets the resonance condition (3) obtained for an isolated nucleus. This infringement is not very serious if resonance is observed in strong fields; its effect is that NMR is not observed at a single rigorously defined frequency ν_0 but over a range of frequencies $\Delta\nu_0$. The width of this range depends on the effectiveness of the averaging of the local field under the action of thermal motion. In crystals, where the nuclei do not change places,

$$\Delta\nu_0 \simeq \frac{H_{\text{loc}}}{\gamma_0} \simeq 10\,\text{kHz}.$$

This implies that, when the precession phases of two nuclear magnetic moments coincide at any instant but their resonance frequencies differ by 10 kHz, then after only 10^{-4} s their phases will diverge. The time required for the loss of "phase memory" is called the spin–spin relaxation time; in contrast to the spin–lattice relaxation time, it is denoted by T_2. It follows from the foregoing considerations that the time T_2 is closely related to the NMR line width. One of these relations has already been used implicitly. If $\Delta\nu_0$ is the line width, then $T_2 = (\Delta\nu_0)^{-1}$. On the other hand, when the NMR line has the form described by the function $g(v)$ and its area is constant, the amplitude $g(v)_0$ should fall as a consequence of line broadening. For this reason, there should be a direct proportionality between the NMR line amplitude and the spin–spin relaxation time:

$$T_2 = k\,|g(\nu_0)|.$$

Below it will be shown that $k = 0.5$.

For crystals, the NMR lines are broad and $T_2 \leqslant 10^{-4}$ sec. At the same time the spin–lattice relaxation in diamagnetic crystals is very ineffective; T_1 may reach 10^4 s and more. Thus T_2 is smaller by a factor of tens of millions than T_1. This marked inequality ensures, firstly, the validity of the concept of the spin temperature, and, secondly, the possibility of experiments with *negative* values of T_S.

After the specimen has been placed in a magnetic field H_0, equilibrium nuclear magnetisation will be attained after a time interval which is several times longer than the spin–lattice relaxation time T_1. If, observing certain precautions[16], the direction of the field H_0 is then rapidly reversed, the populations of the nuclear magnetic energy levels are also reversed: the upper unfavourable level will contain more nuclei than the lower favourable level. In accordance with Eqn. (5), this means that the absolute spin temperature $T_S < 0$. It is quite clear that a spin system with a negative absolute temperature is essentially much "hotter" than a spin system in a state of saturation, for which the temperature was considered to be infinitely high. Experiments with negative spin temperatures have served as a starting point for purposeful research, which culminated in the creation of masers and lasers.

However, the simple concepts in nuclear magnetic relaxation employed by Bloch, who gave the first quantitative description of the phenomenon of nuclear magnetic resonance, are more important for the purposes of the present review.

V. BLOCH EQUATIONS

Let us consider the formulation of an NMR experiment in a specific form. In order to describe the phenomenon, rectangular coordinates are introduced with the z axis

directed along the lines of force of the magnetic field, the y axis is vertical (the coil giving rise to the radiofrequency field H_1 is also as a rule directed along the vertical axis), and the x axis is perpendicular to the yz plane.

Bloch's approach consists in a detailed examination of the components M_X, M_Y, and M_Z of the nuclear magnetisation of the specimen. It is simplest to elucidate the behaviour of the longitudinal component M_Z. If there were no spin–lattice relaxation ($T_1 \to \infty$), then M_Z would be constant, since the Larmor precession of the nuclear magnetic moments around the direction of the magnetic field does not affect their z-projections, i.e. it does not alter their sum either: $dM_Z/dt = 0$.

The question now arises of the changes occurring in the presence of relaxation. We already know that spin–lattice relaxation equalises the temperatures of the spin system and the lattice. If at a temperature T we have a corresponding equilibrium nuclear magnetisation and at some instant the magnetisation M_Z deviates from M_0 for any reason, spin–lattice relaxation should ensure an exponential return of M_Z to M_0, the time constant of this process being T_1. The mathematical form of the situation outlined above is evident:

$$\frac{dM_z}{dt} = -\frac{M_z - M_0}{T_1}. \qquad (6)$$

The fate of the other two components of magnetisation, M_X and M_Y, is somewhat more complex. In fact, even in the absence of spin–lattice relaxation one cannot assume that these components are constant, since we have the Larmor precession. By exact analogy with the equations for the motion of a top, we must write

$$\frac{dM_x}{dt} = \omega_0 M_y \text{ and } \frac{dM_y}{dt} = -\omega_0 M_x.$$

We have already spoken of the short period of phase memory, which is characteristic of a nuclear spin system. Mention was also made of the energy transitions between the nuclear magnetic moments, which do not affect the overall energy of the system. From the standpoint of the classical vector model, such processes involve changes in M_X and M_Y without changing M_Z. Thus, for a given overall nuclear magnetisation M_Z, deviations of M_X and M_Y are possible; clearly, such a distinction need be introduced only when the characteristic time T_2 for this transverse (spin–spin) relaxation is not equal to T_1. When $T_2 \neq T_1$, the equations for the transverse components must be written in the form

$$\begin{aligned} \frac{dM_x}{dt} &= \omega_0 M_y - \frac{M_x}{T_2}, \\ \frac{dM_y}{dt} &= -\omega_0 M_x - \frac{M_x}{T_2}. \end{aligned} \qquad (7)$$

Eqns. (6) and (7) are known as the Bloch equations.

VI. NMR LINE FORM FOR LIQUIDS AND GASES

In order to make any useful deductions from the Bloch equations, it is necessary to consider the factors responsible for the deviations of the components M_X, M_Y, and M_Z from their equilibrium values. We are principally interested in the electromagnetic wave having quanta $h\nu_0$, with the aid of which the NMR phenomenon is in fact observed. The transitions stimulated by these quanta actually give rise to the difference between the populations of the energy levels at the given temperature, which in practical terms implies changes in M_X, M_Y, and M_Z. In the analysis of Eqns. (6) and (7) one should speak not of the quanta $h\nu_0$ but of the magnetic field of the coil, with a current generated by a radiofrequency oscillator at a frequency ν, which is close to ν_0. This weak magnetic field $H_1 \sin 2\pi\nu t$ is added geometrically to the external magnetic field H_0.

When account is taken of the field H_1, Bloch's equations become markedly complicated. A natural method of simplifying the equations is to introduce new variables in which the radiofrequency field H_1 is at rest. In other words we introduced an observer "sitting" at the end of the vector H_1 and undergoing tens of millions of revolutions per second in this imaginary centrifuge. For such an observer, Bloch devised new components ($\omega = 2\pi\nu$) instead of the mutually perpendicular nuclear magnetisation components M_X and M_Y:

$$\begin{aligned} u &= M_x \cos\omega t - M_y \sin\omega t, \\ v &= -M_x \sin\omega t - M_y \cos\omega t. \end{aligned} \qquad (8)$$

In Eqns. (8) u is the component of the magnetisation of the specimen varying in phase with H_1 and v is the component displaced by 90° relative to H_1. When the u and v components are employed, Bloch's equations become

$$\begin{aligned} \frac{du}{dt} + \frac{u}{T_2} + (\omega_0 - \omega)v &= 0, \\ \frac{dv}{dt} + \frac{v}{T_2} - (\omega_0 - \omega)u + \gamma H_1 M_z &= 0, \\ \frac{dM_z}{dt} + \frac{M_z - M_0}{T_1} - \gamma H_1 v &= 0. \end{aligned} \qquad (9)$$

Eqns. (9) have a wide variety of consequences, but, from our point of view, the most important are their steady-state solutions corresponding to the case where M_Z = const., u = const., and v = const., i.e. to rotation of u and v synchronised with the vector H_1 and to a constant z-component of the nuclear magnetisation. All three derivatives of Eqn. (9) are then zero and we obtain three equations in three unknowns: u, v, and M_Z. By solving these equations, it is easy to derive the following formulae:

$$\begin{aligned} u &= \frac{\gamma H_1 T_1 T_2 (\omega_0 - \omega) M_0}{1 + T_2^2(\omega_0 - \omega)^2 + \gamma^2 H_1^2 T_1 T_2}, \\ v &= -M_0 \cdot \frac{\gamma H_1 T_2}{1 + T_2^2(\omega_0 - \omega)^2 + \gamma^2 H_1^2 T_1 T_2}, \\ M_z &= M_0 \cdot \frac{1 + T_2^2(\omega_0 - \omega)^2}{1 + T_2^2(\omega_0 - \omega)^2 + \gamma^2 H_1^2 T_1 T_2}. \end{aligned} \qquad (10)$$

To elucidate the significance of these results, we shall consider the case where the oscillator producing H_1 is tuned exactly to the NMR frequency: $\omega = \omega_0$. From Eqn. (10), we obtain for exact resonance ($u = 0$)

$$v = -\frac{M_0 \gamma H_1 T_2}{1 + \gamma^2 H_1^2 T_1 T_2} \quad \text{and} \quad M_z = \frac{M_0}{1 + \gamma^2 H_1^2 T_1 T_2}.$$

We now compare these results with the quantum characteristics of NMR which are also already known. Clearly the v component describes the absorption of the energy of the electromagnetic wave incident on the spin system. The lower longitudinal magnetisation M_Z compared with the equilibrium value M_0 (before the spin system is exposed to the quanta $h\nu_0$), due to the presence in the denominator of the term $\gamma^2 H_1^2 T_1 T_2$, can be reasonably related to saturation.

Consequently the expression for v in Eqn. (10) describes the NMR absorption line shape. In physics this is known as a Lorentzian line. A second important result is a quantitative estimate of the saturation effect. In fact, when $\gamma^2 H_1^2 T_1 T_2 \ll 1$, saturation does not affect the NMR line form. Evidently, in the absence of saturation the amplitude of the NMR signal is directly proportional to the

radiofrequency field strength H_1. It is frequently important to achieve the maximum amplitude of the NMR signal. However, it is clear from Eqn. (10) that the maximum amplitude is achieved at the expense of an appreciable broadening of the magnetic resonance line. On further increase of the radiofrequency field strength, saturation is fully shown: the signal shows a simultaneous decrease of its amplitude and broadening.

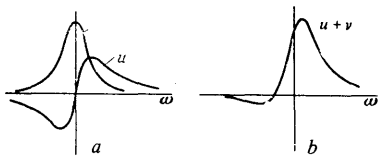


Figure 1. *a*) Absorption (v) and dispersion (u) signals; *b*) sum of absorption and dispersion signals.

The practical conclusion is that, in order to attain maximum resolution, it is necessary to employ minimum values of H_1 compatible with adequate sensitivity. The somewhat indefinite nature of this recommendation reflects the necessity to seek a compromise, the adequacy of which in each particular case depends on the skill of the operator.

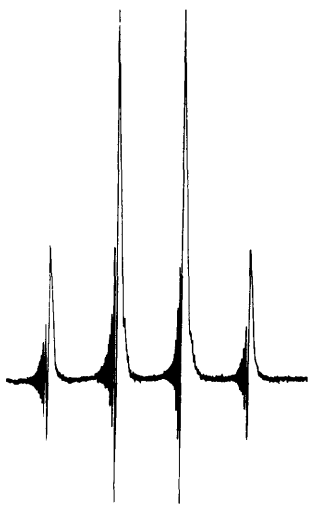


Figure 2. Quartet of the CHO proton in acetaldehyde. With a resolution of about 3×10^{-9}, slow pass conditions are not fulfilled even at a sweep rate of 0.05 Hz s^{-1}; RYa-2305 spectrometer.

It follows from Eqn. (10) that, apart from the absorption signal (the v component), there exists also another component of the NMR signal (the u component) in phase with the radiofrequency field H_1. The form of this signal is shown in Fig. 1*a*. When the NMR spectrometer is not accurately tuned, the signal recorded may contain a fraction of the u component or the so called dispersion signal. An example of such incorrect tuning is presented in Fig. 1*b*. Evidence of this type of error by the operator is revealed by the passage of the signal through the zero line.

It is important to note that the Lorentzian line should be symmetrical about the resonance frequency ω_0. The maintenance of this symmetry in high-resolution NMR spectra is difficult, since it can be achieved only by fairly slow sweep through the NMR line.

In the most frequently encountered design of the NMR spectrometer the spectrum is recorded by a slow linear variation (sweeping) of the magnetic field H. Usually this is done with the aid of special sweep coils. It would appear that there are no obstacles to varying the current in the sweep coil within any desired limits. However, we then encounter the problem of the stability of the high-resolution spectrometer. Therefore in practice there exists for each spectrometer an optimum sweep rate for which a reasonable compromise is achieved between the requirements of optimum resolution and adequate stability of the resonance conditions. For the vast majority of NMR spectrometers at present in use, this compromise is achieved for the narrowest NMR signals at the expense of a more or less serious infringement of the slow sweep conditions. Appropriate analysis of the complete Bloch equations [8] shows that the absorption signal symmetry is then distorted; the passage through the NMR line is accompanied by distinct transient processes (Fig. 2). In the American literature these oscillations have been called "wiggles". The existence of wiggles sometimes leads to misunderstanding in the estimation of the resolution achieved and interpretation of the spectra. Sometimes instead of "wiggles" the term "ringing" is used. This is a very graphic term. The system of nuclear spins is similar to an unusually sensitive resonator. A slow pass resembles the stroking of a bell, but when the bell is struck, it rings! For solids, Eqn. (10) does not hold (see Section XIV).

VII. HIGH AND LOW RESOLUTION

We have now acquired sufficient information to explain quantitatively the origin of the terms "high" and "low" resolution which are popular in NMR spectroscopy. The resolving power of spectroscopic apparatus is limited by the width $\Delta\nu$ of the line recorded at a frequency ν (Fig. 2). The width is measured in different ways; one of the usual definitions is that of the distance between the points at a height equal to half of the line amplitude. It is clear from Eqn. (10) that $|\nu_{max}| \simeq M_0\gamma H_1 T_2$ when saturation effects are not observed. On substituting in Eqn. (10) the particular value $v_1 = \frac{1}{2}M_0\gamma H_1 T_2 = v_{max}/2$ and neglecting saturation as before, we find that the NMR line width is $\Delta\nu = 1/\pi T_2$. Experiments showed that pure diamagnetic liquids give rise to a line with a width of 0.1–0.2 Hz. Consequently, for such lines $T_2 \simeq 1$ s. At operating frequencies of 60 and 100 MHz lines as narrow as this ensure a resolution $\Delta\nu/\nu \simeq 10^{-9}$. This is the maximum resolution achieved at the present time in nuclear magnetic resonance; for a long time nuclear magnetic resonance was a "world champion" among spectroscopic research methods. In the Mössbauer effect [nuclear gamma resonance (NGR)] discovered ten years ago resolutions up to 10^{-16} are achieved but the actual quanta which have to be employed in the Mössbauer effect are 10^{10} to 10^{11} times larger than in nuclear magnetic resonance. Therefore the NMR method remains unsurpassed as regards the details which can be

distinguished with its aid in the energy structure of matter. The boundary separating high and low resolution is of course arbitrary. In proton magnetic resonance (PMR) of organic liquids a resolution ranging from $(1-2)\times 10^{-8}$ to $(2-5)\times 10^{-9}$ is usually achieved. One begins to regard the resolution as unquestionably low when $\Delta\nu/\nu > 10^{-6}$. Estimates of the quality of resolution in the range $10^{-6}-10^{-8}$ depend on which end of the range is approached: the resolution is regarded as high in experiments with solids, viscous liquids, and liquid crystals, and low in those with non-viscous liquids.

The role of the viscosity η was established in a classical study by Bloemberger et al.[17], who showed that the spin–lattice relaxation time T_1 depends on η. T_1 varies within wide limits when the ratio $\eta/T(^\circ K)$ is altered; this variation has a minimum in the vicinity of $\eta/T(^\circ K) = 1$ P deg^{-1}. The minimum value of T_1 is in the range $10^{-2}-10^{-4}$ s. For such rapid spin–lattice relaxation, the lifetime of each nucleus in the upper energy level is correspondingly very short. The indeterminacy principle predicts that the restriction of the lifetime Δt will widen the nuclear magnetic energy levels, i.e. will increase the width $\Delta\nu$ of the NMR line, since the indeterminacy product $\Delta\nu\Delta t \simeq 1$. Therefore for the minimum values of T_1, $\Delta\nu \simeq 10$ kHz, i.e. we enter the region of low-resolution NMR. In non-viscous liquids and gases $T_1 \simeq T_2$. Thus, if we follow the fate of the NMR line due to a particular specimen on cooling from the gaseous state to the liquid and crystal states, the very narrow peaks become increasingly broader as the temperature is reduced and the viscosity increases; after crystallisation of the specimen, when $\Delta\nu \geq 10$ kHz, the time T_2 remains unchanged on further increase of $\eta/T(^\circ K)$, while the spin–lattice relaxation time increases, which results in the previously described situation, typical for solids, where $T_1 \gg T_2$.

VIII. THE CHEMICAL SHIFT

Almost all the quantities which we introduced in the discussion of the nature of nuclear magnetic resonance were independent of the chemical properties of the specimen. Chemical properties reflect a wide variety of structural features of the electron cloud of the molecule. We have to show how the electronic structure affects the resonance conditions of the magnetic nuclei in the atoms constituting the molecule investigated.

The simplest case is the nuclear magnetic resonance of atomic hydrogen. According to Eqn. (3) and the data in Table 1, the resonance conditions for a proton correspond to $\nu_0 = 4257.7\,H_0$ (Hz). The question arises how the resonance frequency ν_0 varies under the influence of the spherical 1s electron shell surrounding each proton. The answer to this problem comes from the theory of diamagnetism[18]. When a magnetic field H_0 is applied to our hypothetical specimen, a circulating electric field is induced in the electron shell of the atom, and according to Faraday's law this is proportional to the rate of variation of the magnetic field dH/dt. Under the influence of this field, the momentum associated with the electron shell alters and the rate of its variation is proportional to dH/dt. As a result, the total change in momentum is independent of the rate of increase of the magnetic field and is simply proportional to the square of the radius of the orbit in which electron circulation takes place and to the steady magnetic field strength. The increased momentum of the s electron generates a proportionate magnetic moment which, according to the Lenz law, gives rise to a magnetic field opposed to H_0. Thus the nuclei of hydrogen atoms in a magnetic field H_0 are in fact exposed to the field

$$H_{\text{eff}} = H_0(1-\sigma), \tag{11}$$

where σ is the diamagnetic screening constant.

For the purpose of subsequent exposition, it is important to emphasise that the greater is the absolute value of σ the smaller is H_{eff}. This is an obvious consequence of the negative diamagnetic susceptibility of our specimen: $\chi < 0$. Suppose that the specimen investigated contains two types of protons with screening constants σ_1 and σ_2. Then the corresponding effective fields are $H_1 = H_0\,(1-\sigma_1)$ and $H_2 = H_0\,(1-\sigma_2)$. If the spectrometer operates at a fixed frequency ν_0, then, in order to observe the NMR of the first nucleus, it is necessary to apply to the specimen the "resonance" field

$$H_{\text{res}_1} = \frac{\nu_0}{\gamma_0(1-\sigma_1)} \simeq \frac{\nu_0}{\gamma_0}(1+\sigma_1),$$

and the resonance of the second nucleus will be "seen" in the field

$$H_{\text{res}_2} = \frac{\nu_0}{\gamma_0}(1+\sigma_2) = H_0(1+\sigma_2).$$

Consequently the greater is the diamagnetic screening the stronger must be the resonance field; in other words, an increase in screening displaces the NMR signal towards stronger fields. The difference, on the magnetic field scale, between the relevant signals is

$$\Delta H = H_{\text{res}_2} - H_{\text{res}_1} = H_0(\sigma_2 - \sigma_1).$$

Evidently the chemical shift ΔH is proportional to the strength of the magnetic field employed in the apparatus. This is an important factor to which we shall frequently return later.

In order to compare the spectra recorded in different magnetic fields, one usually employs a dimensionless relative chemical shift:

$$\frac{\Delta H}{H_0} = \sigma_2 - \sigma_1. \tag{12}$$

Thus, the intervals between the signals of chemically non-equivalent nuclei observed in the NMR spectra are determined directly by the diamagnetic screening constants. The calculations and estimates of these constants are important for high-resolution NMR spectroscopy. The structural interpretation of chemical shifts is very valuable in modern chemistry.

In successful cases the chemical shifts observed in the NMR spectra indicate directly the number of non-equivalent groups of atoms and the relative signal intensities yield an unambiguous estimate of the numbers of atoms in the corresponding groups. In many cases such information is sufficient to determine the structure of the molecule. However, the diamagnetic screening constants σ are susceptible also to a more profound treatment.

1. Interpretation of Chemical Shifts

The value of σ for the hydrogen atom was calculated for the first time by Lamb[19]. This quantity can be simply estimated. The diamagnetic moment induced in the atom is

$$\mu_d = -\frac{ne^2}{6mc^2}H_0\langle r^2\rangle, \tag{13}$$

where e is the electronic charge, m the electronic mass,

$\langle r^2 \rangle$ the mean square of the radius of the electronic orbit, and $n = 1$ for the hydrogen atom. The magnetic field set up by the moment μ_d at the centre of the electronic orbit is

$$H_d \simeq \frac{\mu_d}{r^3} \simeq \frac{ne^2}{6mc^2} \langle r^{-1} \rangle H_0.$$

The ratio of H_d and H_0 gives an estimate of the screening constant:

$$\sigma = \frac{ne^2}{6mc^2} \cdot \frac{1}{\langle r \rangle}. \qquad (14)$$

By substituting the values of e, m, and c and assuming that $\langle r \rangle = 0.5 \times 10^{-8}$ cm, we obtain $\sigma_H \simeq 10^{-5}$. By a rigorous calculation, Lamb found $\sigma_H = 2 \times 10^{-5}$. Thus the magnetic field at the nucleus of the hydrogen atom is smaller by 20 p.p.m. than the external field H_0. If small changes in n are postulated (equivalent in our estimate to changes in electron density at the atom considered), the screening is directly proportional to such changes. If Eqn. (14) gave an exhaustive description of the magnetic screening of nuclei, proton NMR would be an ideal method for the measurement of the distribution of electron density in organic molecules. However, this is not so.

The calculation of σ for the hydrogen molecule (H_2) proved to be much more difficult. This is quite reasonable: here the problem loses spherical symmetry, which significantly complicates the physical nature of the magnetic screening. In the molecule it is necessary to consider the screening of a given nucleus as the sum of the following contributions: (a) the diamagnetic contribution due to the spherical component of the electron cloud centred at this nucleus and (b) the magnetic fields set up at this point by the magnetic circulation of other electrons. The first contribution is described by an equation of type (14) and always reduces the external field H_0. The magnetic fields set up by other electrons can be of either sign; if they add to the external fields, such a contribution is called "paramagnetic". We shall consider this problem in somewhat greater detail. If the molecule under consideration has an electron cloud with a non-zero overall orbital momentum L and a spin moment S, the energy of the molecule in the ith state will be [3]

$$\varepsilon_i = \varepsilon_i^{(0)} - \frac{ehL_z}{4\pi mc} H_0 - \frac{ehH_0}{2\pi mc} S_z + \frac{e^2 H_0^2}{6mc^2} \Sigma \langle r_i^2 \rangle,$$

where L_Z and S_Z are the projections of the corresponding moments on the direction of the magnetic field H_0 and $E_i^{(0)}$ is the energy of the molecule in the absence of a magnetic field. We shall not consider a molecule with true paramagnetism and throughout subsequent exposition it will be assumed without additional stipulation that the electron shells are filled—all possible states with both positive and negative projections of the moments on the z axis are occupied: $L = 0$ and $S = 0$, i.e. there is no paramagnetism in our specimens in the true sense of the word. The last term in the expression for the energy E_i is responsible only for diamagnetism and the "paramagnetic" contributions to the magnetic field, acting on the given atomic nucleus, arise only because the electron cloud of the molecule is not spherical. The magnetic screening in ^{31}P, ^{19}F, and similar heavy atoms is complicated by the fact that the orbital moment L does not become identically zero; as a result, a large paramagnetic component appears in the screening constant. This will be treated in greater detail below.

If two hydrogen atoms are placed at a small distance from one another and are "forbidden" to form a chemical bond, the screening constant of one atomic nucleus will be independent of the diamagnetic circulation in the electron shell of the neighbouring spherical atom: the orbital moment of the 1s shell is zero ($l = 0$) and the spin moment in this model treatment is neglected in view of the above decision to disregard paramagnetic molecules. The question then arises of the origin of the "paramagnetic" contribution to the screening of the protons in the H_2 molecule. The answer is given below.

2. Magnetic Anisotropy

The covalent H—H bond has axial symmetry—its electron cloud may be approximately represented by an ellipsoid of rotation. Evidently, in contrast to the case where a spherical atom is placed in a magnetic field, the intensity of induced diamagnetic currents will vary for different orientations of the half-axis a of this ellipsoid, which is directed along the bond relative to the constant magnetic field H_0. Moreover the deviations of the electron cloud from the cylindrical form lead to the appearance of Van Fleck paramagnetism [3], i.e. the susceptibilities become

$$\chi_i = \chi_{di} - \chi_{pi} = \alpha_i \chi_{di}; \; i = x, y, z.$$

Therefore the magnetic susceptibility χ_l for $a \parallel H_0$ is not equal to the susceptibility χ_t for $a \perp H_0$. Consequently the deviations from spherical symmetry should make the magnetic susceptibility anisotropic: the longitudinal susceptibility χ_l is not equal to the transverse susceptibility χ_t.

When the molecule participates in thermal motion, it assumes all possible orientations relative to H_0 and the time-average magnetic moment of the bond considered (or group of atoms) is not zero. The following quantity is a measure of the anisotropy of the magnetic susceptibility of an n-electron shell [13]:

$$\Delta\chi = \chi_l - \chi_t = \frac{ne^2}{4mc^2} (\alpha_l \langle r^2 \rangle_l - \alpha_t \langle r^2 \rangle_t); \; 0 \leqslant |\alpha| \leqslant 1. \qquad (15)$$

According to the definition (15), $\Delta\chi$ is a magnetic dipole. It is easy to establish a relation between the anisotropy of the magnetic susceptibility of the given bond $\Delta\chi$ and the change in the screening of the given nucleus $\Delta\sigma$ which arises under the influence of $\Delta\chi$. McConnell [20] showed that

$$\Delta\sigma = \frac{\Delta\chi}{3R^3} (3\cos^2\theta - 1), \qquad (16)$$

where R is the distance from the centre of the dipole $\Delta\chi$ to the given nucleus and θ is the angle between the axis of the anisotropic bond and R. It is important to emphasise that in many cases (C=O, C=C, and other bonds) $\langle r_t^2 \rangle$ has two values: $\langle r^2 \rangle_x$ and $\langle r^2 \rangle_y$, and therefore, strictly speaking, for such bonds it is necessary to introduce two values of the magnetic anisotropy: $\Delta\chi_x$ and $\Delta\chi_y$.

Thus a classification of the model forms of electron shells and the corresponding magnetic susceptibilities may be proposed (Table 2; $ne^2/4mc^2 = k$).

Table 2 shows that in the general case it is virtually impossible to calculate $\Delta\chi$ (the values of α_i are determined by the wave functions of excited molecular states).

Quantum-mechanical calculation [21] yields a screening constant $\sigma(H_2) = 23 \times 10^{-6}$ for the H_2 molecule; the local screening of each proton by "its" electron gives $\sigma_{loc} = 28 \times 10^{-6}$ and the "paramagnetic" contribution is $\sigma_n = -5 \times 10^{-6}$. The accuracy of this calculation is not very great, but on its basis and in combination with Lamb's data one

may assert, firstly, that the 1s electron, distributed around a given proton, is responsible for a screening effect of about 25 p.p.m. in the molecule and, secondly, that the deviations from spherical symmetry of the electron shell can give rise to a 20% change in the local screening. Thus in proton NMR the dominant contribution to screening comes from the proton's "own" electron and the changes of σ under the influence of the anisotropy of the magnetic susceptibility of the neighbouring bonds are smaller by a factor of ten. The effect of the magnetic anisotropy can be of either sign. This is caused, firstly, by the fact that, as the angle θ varies, the factor $3\cos^2\theta - 1$ changes sign in the vicinity of $\theta_0 = 54°44'$. Therefore, when $\Delta\chi > 0$, the correction $\Delta\sigma$ calculated by Eqn. (16) is positive (shift to a stronger field) for $\theta = 0$ and negative (shift to a weaker field) for $\theta = 90°$. Secondly, $\Delta\chi$ can be of different signs. It is then extremely important to agree exactly on the significance of the terms "positive $\Delta\chi$" and "negative $\Delta\chi$".

Table 2.

Form of electron shell	$-\chi_z$	$-\chi_x$	$-\chi_y$	$\Delta\chi$
Ellipsoid	$\alpha_z k\langle r^2\rangle_z$	$\alpha_x k\langle r^2\rangle_x$	$\alpha_y k\langle r^2\rangle_y$	$k(\alpha_z\langle r^2\rangle_z - \alpha_x\langle r^2\rangle_x)$ $k(\alpha_z\langle r^2\rangle_z - \alpha_z\langle r^2\rangle_y)$
Circular cylinder	$k\langle r^2\rangle_z$	$\alpha_x k\langle r^2\rangle_x$	$\alpha_x k\langle r^2\rangle_y$	$k(\langle r^2\rangle_z - \alpha_t\langle r^2\rangle_t)$
Ring (one-dimensional)	kR^2	0	0	kR^2
Sphere	$\frac{3}{2}k\langle r^2\rangle$	$\frac{3}{2}k\langle r^2\rangle$	$\frac{3}{2}k\langle r^2\rangle$	0

Experiment shows that misunderstandings frequently arise in this problem, associated with the differences between the traditional concepts in magnetochemistry and those which have arisen in NMR spectroscopy. Let us consider some examples. In the hypothetical measurement of the magnetic susceptibility of an acetylene single crystal we found that the anisotropy of the diamagnetic susceptibility is positive, i.e. the diamagnetic susceptibility χ_l measured along the triple bond is higher than the diamagnetic susceptibility χ_t measured in a perpendicular direction. But the diamagnetic susceptibility is *negative*. Therefore, strictly speaking, we are dealing with positive anisotropy of negative magnetic susceptibility, i.e. $\Delta\chi < 0$. However, the NMR method is used almost exclusively to investigate diamagnetic properties and for acetylene one usually assumes that $\Delta\chi > 0$. Accordingly, Eqn. (16) predicts a shift to stronger fields for the acetylene proton located on the triple bond axis ($\theta = 0$), which is in fact observed. Because the distance R is short, this shift is very considerable and sets the upper limit to the effect of magnetic anisotropy: $\Delta\sigma(C{\equiv}C) \simeq 4 \times 10^{-6}$. For single and double bonds, the anisotropy of diamagnetic susceptibility is negative, i.e. $\Delta\chi < 0$; accordingly, the NMR signals of nuclei on the bond axis and within a cone with an angle of 54°44′ at the apex are shifted towards weaker fields. A striking case of positive diamagnetic anisotropy is provided by benzene and similar aromatic molecules. The 6π electrons of benzene circulate in a ring of conjugated bonds, the average radius of which is close to 1.4 Å. Using Table 2 (annular current), we obtain $\chi_l \simeq 100 \times 10^{-30}$. Consequently for benzene $\Delta\chi = 100 \times 10^{-30}$ (per molecule) or $\simeq 60 \times 10^{-6}$ (per mole). It is interesting that this rough estimate agrees satisfactorily with the results of the measurements of the static magnetic susceptibility of benzene. Calculation by Eqn. (16) shows that such anisotropy displaces the signal of its "own" protons (i.e. protons in the plane of carbon atoms at a distance $R = 2.48$ Å from the centre of the molecule) by about 2×10^{-6} towards weaker fields. This is the so called "aromatic shift". It is frequently also called the shift due to annular currents. In full agreement with the foregoing, the annular current in benzene can displace the signals of "alien" protons towards stronger fields, when these protons are located in a conical region the axis of which is normal to the plane of the molecule. Thus in pure liquid benzene the proton magnetic resonance (PMR) signal is displaced approximately by 0.6×10^{-6} towards stronger fields relative to a 1% solution of benzene in carbon tetrachloride.

In ferrocene—a sandwich compound of iron with two C_5H_5 rings—the NMR signals of the cyclopentadienyl protons are displaced towards stronger fields by 3.3 p.p.m. relative to benzene[6]. This shift permits an unambiguous choice in favour of the calculation by Shustorovich and Dyatkina[22], according to which, and in contrast to Dahl and Ballhausen[23], there is a negative charge on the C_5H_5 ring of ferrocene (since the molecule is neutral as a whole, a double positive charge is localised at the Fe atom). The conclusion of Dehn and Mulay[24] that 4.8 electrons circulate in each C_5H_5 ring, i.e. that iron has a negative charge appears to contradict the finding of Shustorovich and Dyatkina[22]. The magnetic susceptibilities of ferrocene are $\chi_Z = -162 \times 10^{-6}$, $\chi_X = -104 \times 10^{-6}$, $\chi_Y = -108 \times 10^{-6}$, and $\Delta\chi = 56 \times 10^{-6} \simeq \Delta\chi_{benz}$. The conclusion that iron has a negative charge arose as a result of the application to ferrocene of the annular current model (Table 2). In fact, if one assumes that $\Delta\chi = kR^2$ and remembers that $R_{C_5H_5} < R_{C_6H_6}$ and also that two C_5H_5 rings are responsible for $\Delta\chi$, it is found that the number of electrons in the rings is reduced compared with the initial value $n = 5$. However, it is evident from the comparison of the values of χ_Z and $\chi_\perp$ for ferrocene with Table 2 that the estimate of kR^2 gives a value of χ_Z which leads to $n \simeq 20$, i.e. all the π electrons of the molecule contribute to the longitudinal susceptibility. The charge on the rings cannot be estimated by assuming that $\Delta\chi = kR^2$.

Hence it follows that the dipole $\Delta\chi$ of the real magnetic anisotropy of ferrocene is localised at the centre of the Fe atom and has very little effect on the screening of the C_5H_5 protons, i.e. here $\theta \simeq 60°$ and the angular factor in Eqn. (16) is close to zero. Thus, despite the conjugation of the C_5H_5 rings, the annular current effect in ferrocene is appreciably weaker, i.e. the corresponding PMR signal should be displaced towards stronger fields. The estimates quoted above show that this gives rise to approximately half the shift which needs to be explained. The other half of the observed shift is due to the *negative* charge of the rings, which confirms the view of Shustorovich and Dyatkina: the metal behaves not as an acceptor but as an electron donor in relation to the C_5H_5 rings.

Here it is appropriate to recall yet again that the positive anisotropy of the diamagnetic susceptibility of benzene, ferrocene, and acetylene molecules corresponds exactly to the negative anisotropy of the magnetic susceptibility of the same molecules. In many literature sources the second magnetochemical sign convention is employed; the McConnell formula is then written in the form

$$\Delta\sigma = \frac{\Delta\chi}{3R^3}(1 - 3\cos^2\theta).$$

In the interpretation of the PMR spectra the considerations described above make it possible in most cases to achieve a satisfactory understanding of the experimental data.

3. Paramagnetic Screening in Heavy Atoms

For heavier atoms, the calculation or qualitative treatment of σ involves considerable difficulties. One may regard it as a general rule that σ increases in parallel with the atomic number, i.e. there is an increase in the frequency interval ν_0 in which the NMR signal of nuclei of a given kind may be observed in a given field H_0.

It must be emphasised that, for ^{19}F, ^{31}P, and similar atoms, one can no longer regard diamagnetic screening as the main contribution to the observed chemical shift. In the discussion of the screening in the hydrogen atom and in the H_2 molecule the absence of an orbital momentum in the *s* electron shell plays an important role. For *p*, *d*, and other electrons, the orbital momentum is not zero, i.e. these electrons give rise to a strong magnetic field at the atomic nucleus. The strength of this field is directly proportional to the magnetic moment of the electron (10^{-20} erg Gauss^{-1}) and is inversely proportional to the cube of the average distance between the corresponding electron and the nucleus. For fluorine, the average distance of the $2p$ electron from the nucleus is 0.25 Å, i.e. the magnetic field which it sets up amounts to hundreds of thousands of oersteds. This is tens of times more than the typical values of H_0 in NMR spectrometers and therefore it would appear that ^{19}F NMR should be observed at frequencies many times higher than $\gamma_F H_0$. In reality, when F atoms are bound in molecules, the intramolecular electric fields force the *p* electrons to precess and the so called "freezing" of the orbital motion of the $2p$ electron takes place[3,25]; the magnetic field of the $2p$ electrons at the ^{19}F nucleus is close to zero. In a magnetic field H_0 the orbital momentum is partly "unfrozen" and the *p* or *d* electrons have a very powerful influence on the screening of the nucleus and are responsible for the paramagnetic contribution to σ. For ^{19}F, the diamagnetic term $\sigma_d \simeq 10^{-5}$ and $\sigma_p \simeq -20 \times 10^{-4}$. Thus the chemical shifts of ^{19}F and ^{31}P are largely determined by the paramagnetic contribution to the screening due to the spherically asymmetric electron orbits.

4. Chemical Shift Scales

In the measurement of the PMR chemical shifts standard chemical shift scales are employed. Tetramethylsilane (TMS), which has a very high value of σ, is most used as an internal standard; for the vast majority of substances, the NMR signals of protons occur in weaker fields than the TMS signal. In the so called δ scale the position of the TMS signal is assumed to be zero and the shifts to weaker fields are treated as positive; the shift is measured in parts per million (p.p.m.). The higher is the numerical value of δ, the weaker the screening of the corresponding proton. This is a disadvantage of the δ scale.

The parallel variation of the screening constant and the numerical value of the chemical shift is maintained in the τ scale, where the reference point is also the TMS signal but its position has been arbitrarily and quite unjustifiably assumed to be 10 p.p.m. Consequently the zero of the τ scale corresponds to $\delta = 10$ p.p.m.; evidently

$$\delta = 10 - \tau$$

or

$$\tau = 10 - \delta.$$

A disadvantage of the τ scale is the change in the sign of τ for shifts with $\delta > 10$ p.p.m., characteristic of acids and protons involved in strong hydrogen bonds. The negative signs of τ is physically quite meaningless. On the other hand, the negative sign of δ indicates either a powerful effect of the magnetic anisotropy of the molecule or an unusually effective concentrations of electron density at the corresponding chemical bond. Possibly, the most convenient would be a scale (we shall call it the τ^* scale) in which the TMS signal would be at 25 p.p.m.: on this scale the value of τ^* could be roughly identified with the electron density at the corresponding hydrogen atom.

In order to elucidate the significance of the symbols introduced and to learn how to employ them correctly, we shall consider an example. The PMR signal of the methyl group in ethyl is usually displaced by 1.25 p.p.m. towards weaker fields relative to the TMS signal. Consequently on the δ scale this shift is $\delta(CH_3) = 1.25 \times 10^{-6} = 1.25$ p.p.m. and on the τ scale it is $\tau(CH_3) = 8.75 \times 10^{-6}$. Such notation is sometimes inconvenient in the context of a given paper and a different procedure is resorted to: the scale designation is written as a multiplier of the shift, i.e. the shift of the methyl group on the δ scale is written

$$\sigma(TMC) - \sigma(CH_3) = \delta(CH_3) = 1.25 \times 10^{-6} = 1.25\,\delta.$$

Here the symbol δ on the right-hand side has the significance

$$\delta = \frac{\sigma(TMC) - \sigma(X)}{10^6\,|\,\delta(X)\,|} \equiv 1 \times 10^{-6},$$

i.e. $\delta = 1$ p.p.m. reckoned from the tetramethylsilane signal. Thus the phrases "the methyl group has a shift $\delta(CH_3) = 1.25 \times 10^{-6}$", "the methyl group has a shift $\tau(CH_3) = 8.75 \times 10^{-6}$", "the PMR of the methyl group was observed at 1.25 δ", and "the position of the peak due to methyl protons is at 8.75 τ" have in practice the same significance. Sometimes for brevity the multiplier 1×10^{-6} = p.p.m. is omitted and the chemical shift is written in the form $\delta(CH_3) = 1.25$.

IX. PRINCIPAL EMPIRICAL RELATIONS IN CHEMICAL SHIFT SERIES

The chemical shift is an important parameter of a high-resolution NMR spectrum. Impressive experimental data on the chemical shifts in the NMR of ^1H, ^{19}F, ^{31}P, and certain other nuclei have now accumulated. The chemical shifts in high-resolution PMR have assumed particularly great importance in the structural analysis of organic compounds, organic derivatives of the elements, and inorganic compounds. A typical PMR chemical shift diagram is presented in Fig. 3. Extensive compilations of the chemical shifts of protons and other nuclei can be found in monographs[5,6,9,10]. One of the first such compilations was published in this journal[26].

Handbooks dealing with compounds investigated by the NMR method and compilations of chemical shifts[27,28] are of great assistance in day to day work. Since the number of investigations with active employment of NMR reaches several thousand per year, a complete grasp of this stream of results can be achieved only with the aid of the card indexes published by several firms[29,30].

The following comments may be made on the PMR chemical shift diagrams. The PMR signals of transition metal hydrides occur in the strongest fields (the negative part of the δ scale). The nature of these extremely high shifts has been frequently discussed but its causes are still not clearly understood. The simplest qualitative explanation is based on the high electron-donating activity of

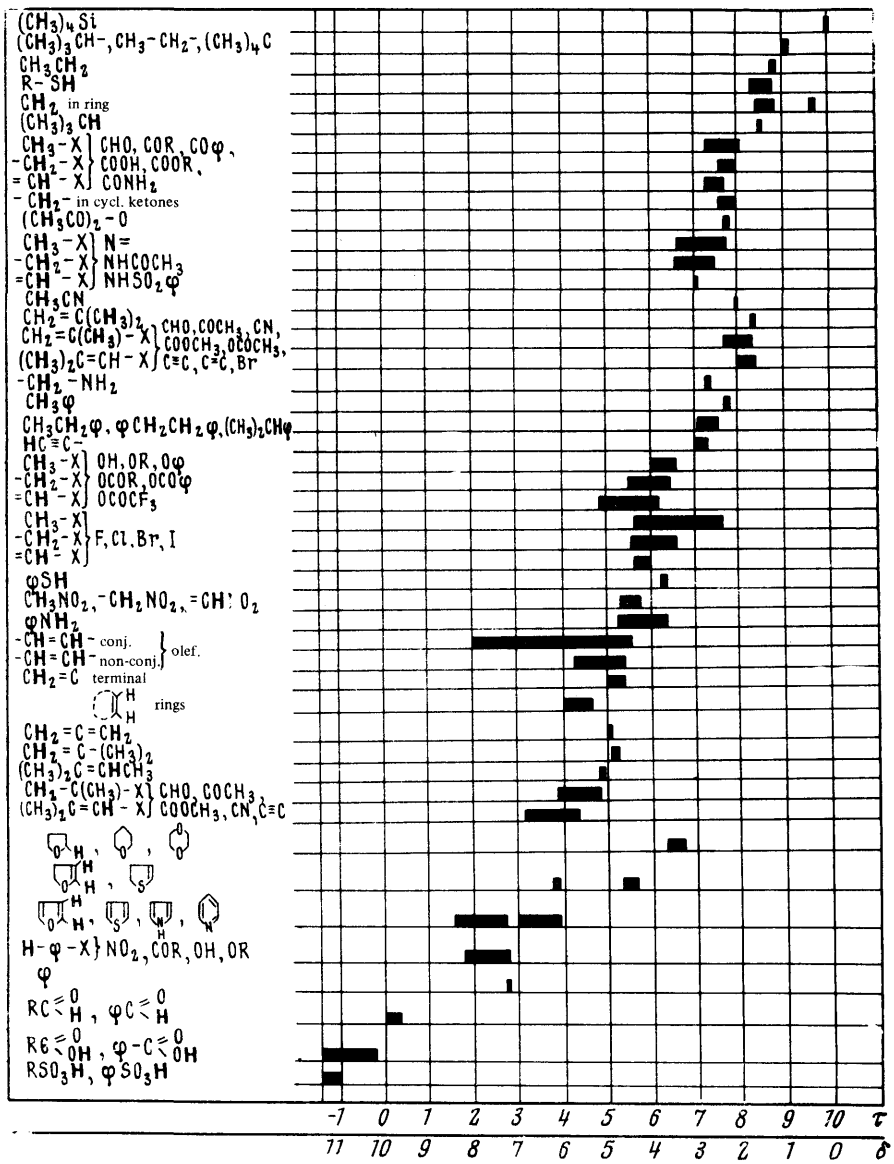


Figure 3. Diagram of NMR chemical shifts of protons.

transition metals and the tendency towards the formation of a helium type electron shell in the hydride hydrogen atom.

In the vicinity of the zero of the δ scale are the signals of the methyl groups attached to germanium and silicon atoms. The signals of cyclopropane and the terminal groups of fairly long ($n > 5$) alkane molecules are located between zero and unity on the δ scale. Methyl groups in ethyl and similar radicals give rise to a signal in the vicinity of 1.25. Methylene groups in the same radicals can give rise to PMR signals in the range $1 \leq \delta \leq 4$, depending on the properties of the atoms to which the radicals are attached; in certain organometallic compounds the CH_2 and CH_3 signals change places: the signal of the CH_2 protons occurs in stronger fields. Olefinic protons give rise to resonance peaks in the region $4 \leq \delta \leq 6.5$. Signals of hydroxyls and similar groups can be very markedly displaced under the influence of solvents which modify the intermolecular hydrogen bonds. In the absence of a hydrogen bond, the PMR of OH protons is in the vicinity of 2δ, very strong intermolecular bonds displace the signal to 10δ, and finally chelate protons give signals in the vicinity of 18δ, which is characteristic of extremely strong acids. However, this cannot be interpreted directly as implying the "stripping" of the chelate proton. Neutral aromatic molecules give signals in the region $6.5 \leq \delta \leq 8.0$. The signal of the aldehyde group is usually observed in the range $8 \leq \delta \leq 10$. It is possible to observe a satisfactory correlation between the donor-acceptor properties of substituents and the chemical shifts. As stated in the preceding

paragraph, electron-donating and electron-accepting substituents displace the signal towards stronger and weaker fields respectively.

As already mentioned, the range of ^{31}P and ^{19}F chemical shifts is much wider than the brief interval corresponding to changes in the screening of protons. The NMR chemical shifts of ^{19}F and ^{31}P are less characteristic than the PMR shifts. As a rule structural conclusions are arrived at on the basis of a detailed spectrum, taking into account the spin–spin interaction. One discusses largely, not the absolute values of the shifts, but the changes under the influence of a suitable selected series of substituents[6,9].

X. SPIN–SPIN COUPLING

Five years after the discovery of NMR, Proctor, Gutowsky, and coworkers[31] observed a characteristic splitting in the NMR signals from many chemical compounds. This discovery was made immediately after this group of investigators succeeded in constructing a magnet with a field homogeneity of the order of 10^{-7} (exceeding by a power of ten the homogeneity of the magnetic fields in the best spectrometers previously available). It was then found that the NMR signals previously incorrectly attributed to chemically different atoms show further splitting into two and more components when the resolving power of the apparatus is increased. The principal feature of these multiplets proved to be that their splitting was independent of the magnetic field H_0. This finding demonstrated unambiguously a fundamental difference between the nature of the splitting and the chemical shift [see Eqn. (12)]. Simple relations observed in the study of the symmetry and the number of components in these new details of NMR spectra showed that the reason for the complication is indirect interaction of the nuclear magnetic moments via bonding electrons located between the atoms to which these nuclei belong.

To illustrate the mechanism of this interaction, we shall turn to the HD molecule. The reason why we are not discussing the spin–spin coupling in the H_2 molecule will be made clear below. The nucleus with a spin of 1/2 then interacts magnetically only with the electron shell of its "own" atom. The direct dipole–dipole effect of the magnetic moment of the electron μ_e on the magnetic moment of the nucleus μ_n in a liquid specimen will be largely averaged out by the thermal motion of the molecule and contact interaction[3] which is proportional to the density of the s electrons of the nucleus, plays the main role. Spin–spin coupling is therefore transmitted only via bonds which have non-zero s character.

Suppose that the HD molecule is in the ground state: two electrons are in the bonding orbital. The coupling of the nuclear and electronic magnetic spin moments in the H atom makes the antiparallel orientation of these moments more favourable than the parallel orientation. The antiparallel orientation of the electron spins in the HD molecule does not require further justification: this is a consequence of the existence of a covalent bond. Consequently the electron in the D atom, for which the mechanism of the coupling between the electronic and nuclear spins is the same as in the H atom, endeavours to orient the nuclear spin of the deuteron antiparallel to its own and hence antiparallel to the spin of the proton, i.e. the sign of the coupling between the nuclei is positive. Theory and experiment[33] have shown that the reversal of the sign of the spin–spin coupling is also possible: situations occur where the mechanism discussed leads to parallel orientation of the magnetic moments of the interacting nuclei.

As a result of the presence of the spin–spin coupling in the HD molecule, the NMR signal of deuterium ceases to be a singlet line. In simple words, the factor which orients the magnetic moment of the nucleus is the magnetic field. As has been frequently mentioned, protons have a spin of 1/2, i.e. are capable of being oriented in the field in two ways: along the field and in opposition to it. We also know that the populations of these states differ at room temperature by several tens of p.p.m. This difference is quite sufficient to detect the NMR signal with the aid of modern electronics. However, its intensity can be measured in the most favourable case only with an accuracy of several thousand p.p.m. Therefore in practice in half of the molecules of the specimen the deuterium nuclei will be subjected to the field

$$H'_{\text{eff}} = H_0(1-\sigma) + H_{ss},$$

while in the other half the magnetic field at the deuterons will be

$$H''_{\text{eff}} = H_0(1-\sigma) - H_{ss}.$$

Consequently the signal of the relevant nucleus will be converted into a doublet with equal component intensities. The distance between the doublet components is $2H_{SS}$ gauss. Since at present precise measurements of magnetic fields are made by determining accurately the NMR frequency[6], it was reasonable to characterise the spin–spin coupling by a constant measured on the frequency scale (not in gauss but in hertz). The value of $2H_{SS}$ measured in hertz units is called the spin–spin coupling constant and is denoted by J. For the HD molecule, J = 43 Hz.

The signal due to the second nucleus of the molecule is of course also a doublet with the same distance between the components. Table 1 shows that it is very difficult to observe the doublets simultaneously: owing to the considerable difference between the magnetic moments of the H and D nuclei, the resonance in a given field H_0 occurs at frequencies which differ by a factor of almost seven in the two cases. Therefore in the HD molecule the total NMR spectrum consists of two doublets the distance between the centres of which exceed by six powers of ten the doublet splitting. In the nomenclature adopted this spectrum is of the type AX: the designation of nuclei by letters from different ends of the alphabet is a symbolic representation of the fact that $\nu_A - \nu_X = \Delta\nu \gg J_{AX}$, i.e. the difference between the resonance frequencies of these nuclei is many times greater than the degree of spin–spin coupling between them.

XI. THE NUMBER OF LINES IN THE SPECTRUM

We established that the NMR spectrum of an AX system with two nuclei having spins of 1/2 consists of four lines—a doublet of doublets. It is not difficult to extend the considerations dealt with in the previous section to an AM...P...Z system of n non-equivalent nuclei with spins of 1/2. If each of the $n - 1$ neighbouring nuclei is linked to the nucleus under consideration by spin–spin coupling, then, by numbering the neighbours in order of decreasing coupling we find that the nearest neighbour splits the signal of the given nucleus into a doublet and each component of this doublet becomes a doublet itself as a result of the interaction with the second neighbour, etc. Thus the signal of the given proton becomes a multiplet consisting of 2^{n-1} components. There will be as many multiplets as there

are nuclei in the system, i.e. altogether in the spectrum of a system of n interacting nuclei there will be

$$m = n \times 2^{n-1} \qquad (17)$$

peaks.

Eqn. (17) gives the multiplicity of the PMR spectrum when the distances between the multiplets exceed greatly the splitting within them, i.e. the chemical shifts $\nu_0\delta_{ik}$ exceed approximately by a power of ten the corresponding spin–spin coupling constants:

$$\nu_0\delta_{ik} \geqslant 10J_{ik}. \qquad (18)$$

If condition (18) holds for each pair of nuclei, then the corresponding spectrum is called a first-order spectrum. Eqn. (17) gives the maximum multiplicity for such spectra.

A decrease in the number of lines in a first-order spectrum may be caused by some kind of equivalence of the nuclei. We shall consider only two principal types: chemically and magnetically equivalent nuclei. Chemically equivalent nuclei are those with identical screening (identical chemical shifts). According to the laws of quantum mechanics, spin–spin coupling within a group of chemically equivalent nuclei cannot be detected. This in fact is the reason for our choice of the HD molecule as a model for the discussion for the mechanism of spin–spin interaction: the chemical equivalence of the protons in the H_2 molecule precludes the observation of a powerful (J = 280 Hz) spin–spin coupling. Therefore, when p nuclei have the same chemical shift, then, instead of $p \times 2^{n-1}$ lines, this group gives only one line, which is split into $2^{(n-p)-1}$ components when there is different spin–spin coupling between the remaining nuclei of the system and each nucleus within the group of the chemically equivalent nuclei. Thus the multiplicity of the spectrum is then significantly reduced.

Further simplification or, the so called degeneracy of the spectra, can occur due to fortuitous equality of certain spin–spin coupling constants or when there are multiple relations between them. Then two or more peaks coincide.

Apart from chemical equivalence, there is also a possibility of magnetic equivalence of the nuclei. A group of chemically equivalent nuclei is said to be magnetically equivalent when each of them undergoes the same spin–spin interaction with any nucleus of another group of nuclei. Naturally, under these conditions the second group also consists of magnetically equivalent nuclei.

The methyl and methylene protons of the ethyl group may be regarded as constituting the most widely known case of magnetic equivalence. For any hindered conformation of the ethyl group, methyl protons, for example, would have the same chemical shifts but would undergo different interactions with the protons of the methylene group, i.e., while maintaining their chemical equivalence, they would be magnetically non-equivalent.

The rapid rotation of the methyl group around a single C–C bond leads to the averaging of the spin–spin interaction constant, and in the presence of sufficiently strong magnetic fields the ethyl group gives rise to a PMR spectrum of the type A_2X_3. It is easy to establish the form of the spectrum. Owing to the equality of the constants, the signal of the methyl group instead of being a doublet of doublets becomes a triplet with intensity ratios of 1 : 2 : 1, since the central peaks coincide. The spectrum of the methylene protons instead of comprising eight (2^3) equal peaks will consist of a quadruplet with a binomial intensity distribution 1 : 3 : 3 : 1. It is easily seen that the sum of the relative intensities is equal to the corresponding spin multiplier 2^{n-1} in Eqn. (17). This is an additional illustration of the fact that binomial multiplets are only a very special case of spin–spin splitting in high-resolution PMR spectra.

When the chemical shifts diminish, there is as a rule an appreciable increase in the number of lines in the spectrum compared with the multiplicity predicted by Eqn. (17). The reason is the occurrence of the so called combination lines. In the examination of the scheme which led to formula (17) it was suggested that only pure transitions take place between the energy levels formed. Thus the A transition is one in which the state of only the A nucleus is altered. However, in many-spin systems there is a possibility also of transitions in which there is a simultaneous change in the state of several nuclei. Thus in three-spin systems there is a possibility of a transition from the situation ↑↓↓ to ↓↑↑. Usually the intensities of these lines are low, but for $\nu_0\delta \leqslant J$ the combination transitions lead to a sharp increase in the number of lines. To illustrate this, the table taken from Braier et al. is quoted[33].

n	2	3	4	5	6	7
m_{min}	4	12	32	80	192	448
m_{comb}	0	3	24	130	690	2555
m_{max}	4	15	56	210	792	3003

Such a large number of lines causes significant difficulties in the interpretation of the spectra: the individual multiplets may overlap and the assignment ceases to be unambiguous. Frequently in the spectra of many-spin systems the lines are so close to one another that instead of individual peaks a common outline is observed. Under these conditions, differing sets of parameters can lead to virtually identical spectra. The calculation of the spectrum should give a set of parameters (chemical shift δ_i and spin–spin interaction constant J_{ik}) corresponding unambiguously to the observed spectrum. Such a calculation is a typical quantum-mechanical problem. For a system of n nuclei with spins of 1/2, the number of energy levels is 2^n, i.e. the secular equation for a two-spin system is of the fourth degree and the equation for a three-spin system is of the eighth degree. In fact the symmetry properties of the spin systems make it possible to reduce significantly the degree of the secular equation. Thus for a two-spin system, the secular equation becomes

$$\begin{vmatrix} H_{11}-E & 0 & 0 & 0 \\ 0 & H_{22}-E & H_{23} & 0 \\ 0 & H_{32} & H_{33}-E & 0 \\ 0 & 0 & 0 & H_{44}-E \end{vmatrix} = 0, \qquad (19)$$

i.e. the problem reduces to the solution of two linear equations and one quadratic equation. Fig. 4 presents the spectrum of an AB system, i.e. a two-spin system with a chemical shift $\nu_0\delta_{AB}$ close in magnitude to the spin–spin coupling constant J_{AB}. The solution of Eqn. (19) leads to the result

$$\nu_0\delta_{AB} = \sqrt{\Delta_{14}\Delta_{23}}; \qquad A_1 : A_2 = \Delta_{23} : \Delta_{14}. \qquad (20)$$

It is important to note that, in contrast to a system AX, in the analysis of a system AB the spectrum yields directly only the value of J_{AB} and the chemical shift is obtained only as a result of the calculation. For more complex systems, none of the NMR spectral parameters can be obtained by direct measurement of any interval between the peaks.

The complex spectra of many-spin systems are analysed on electronic computers[34] and also with the aid of binary and multiple resonance methods[9]. Eqn. (20) shows that the distance between the two inner components of the spectrum of the AB system is appreciably smaller than the chemical shift $\nu_0\delta_{AB}$. As a result of this phenomenon, in the case of small shifts the multiple set of lines in the spectrum frequently merges into one peak, which reduces the reliability of the interpretation. All these difficulties are largely obviated when the operating frequency of the spectrometer is increased: the increase of the chemical shifts is then accompanied by a narrowing of the spin multiplets due to the disappearance of the combination lines; both factors tend to simplify the spectrum up to the limiting case of a set of doublets of equal intensity.

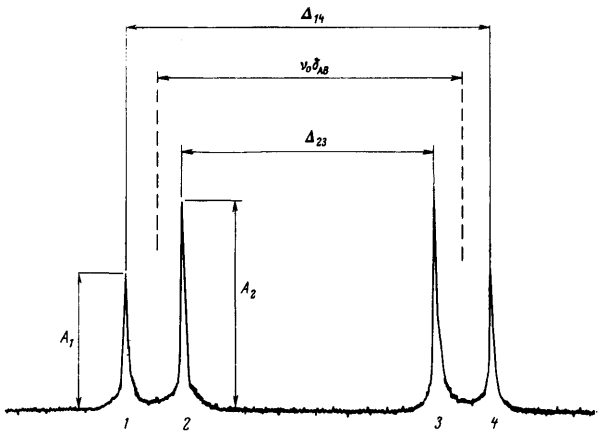


Figure 4. Spectrum of an AB system.

It is not difficult to calculate the frequency at which a given spectrum will become such a simple set of doublets. Suppose that δ_{min} is the minimum chemical shift and J_{max} the maximum spin–spin coupling constant. Then the width of the spin multiplet will be approximately $2J_{max}$ and for the spectrum to be simple the following condition must be fulfilled:

$$\nu_0\delta_{min} \geqslant 2J_{max}$$

If simple spectra are considered necessary for $\delta_{min} \simeq 10^{-8}$ and $J_{max} \simeq 10$ Hz (typical values for monoalkylbenzenes), then the required frequency is $\nu_0 = 2 \times 10^{10}$ Hz. This exceeds by a factor of one hundred the maximum value of ν achieved by 1968.[35] The above estimate clearly illustrates the principal trend in the design of NMR apparatus: a steady increase in the strength of the magnetic fields employed and in the corresponding values of ν_0 (proportional to them).

It is important to note that, apart from simplifying the spectra, an increase in ν_0 greatly improves the sensitivity. This is because an increase in ν_0 entails an increase in the spacing between the nuclear magnetic levels. At the same time there is also an increase in the size of the quantum absorbed by the specimen and in the difference between the populations of the upper and lower levels. In practice the sensitivity increases in proportion to ν_0^n, where the power exponent is in the range $1 \leqslant n \leqslant 2$.

XII. PRINCIPAL EMPIRICAL RELATIONS IN SPIN–SPIN COUPLING CONSTANT SERIES

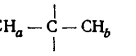
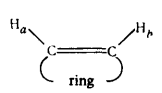
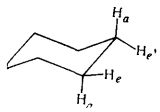
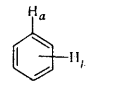
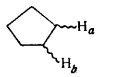
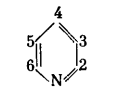
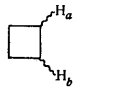
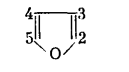
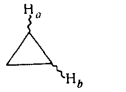
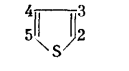
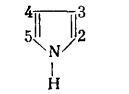
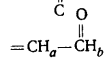
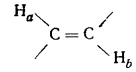
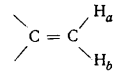
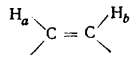
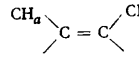
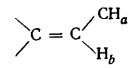
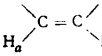
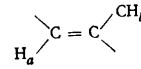
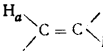
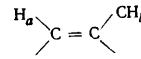
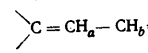
The experimental values of the constants J are very useful in studies on the structures of complex organic compounds. In contrast to the chemical shifts, these values depend little on the nature of the solvent, the concentration of the test substance, etc. The conclusions arrived at with the aid of the spin–spin coupling constants are distinguished by high reliability.

Table 3 lists the values of J for saturated organic compounds. Only individual items in this table need to be commented upon. The change in the sign of the *gem* constant (row 1) with the valence angle was predicted theoretically by Karplus[32] and soon confirmed experimentally by the double resonance method[36]. The high values of the axial–axial constant (row 4) constitute one of the principles underlying the conformational studies of substituted cyclohexanes and similar problems in more complex compounds[37]. In those cases where the splitting of the hydroxyl proton signal indicated in row 8 is observed experimentally, it indicates unambiguously the absence of proton mobility; the disappearance of the multiplet structure of the signal permits the measurement of the rate of proton exchange (see Section XIII).

The constants J_{ab} for unsaturated compounds are given in rows 10–26 of Table 3. Here the most interesting finding appears to be the theoretically predicted[38] rule $J_{trans} > J_{cis}$, which has always been confirmed experimentally. This rule is invaluable in the study of the stereochemistry of the reactions of olefinic hydrogen atoms[39]. It is a special case of the dependence of J_{ab} on the angle between the half-planes containing the bonds CH_a and CH_b, investigated by Karplus[38]. This relation also constitutes a useful method for stereochemical investigations in most cases where the C–C bond is intermediate between a single and a double bond[40]. The useful relations in the series of conjugated cyclic compounds do not require further comment.

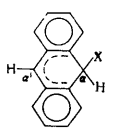
The interaction constants $J(^{13}C-H)$ play a major role in structural analysis by the NMR method. If the principal carbon isotope carbon-12 had a magnetic moment the ^1H NMR spectra would have been much more complex than is actually observed. Fortunately only the nucleus of carbon-13, the natural concentration of which is 1.1%, has a spin of 1/2. Therefore when the sensitivity of the spectrometer is enhanced, the proton resonance spectra show the so called ^{13}C satellites: doublet signals due to molecules in which the light carbon isotope is replaced by the heavy isotope. In the centre of this spin–spin doublet there is a signal two hundred times more intense and corresponding to protons joined to carbon-12. It has been found that the $J(^{13}C-H)$ splitting makes it possible to distinguish clearly the hybridisation of the carbon atom to which the given proton is linked. According to Muller and Pritchard[41], the values of $J(^{13}C-H)$ for methane, ethylene, and acetylene are respectively 125, 156, and 250 Hz. These three points together with the origin of coordinates (fourth point) lie quite accurately on a straight line when the $J(^{13}C-H)$ values are plotted against the amount of s character. This observation gave rise to an extensive literature. One may quote as a good example the work in

Table 3. Spin–spin proton coupling constants (from data issued by the Varian Company).

No.	Type	J_{ab}, Hz	J_{ab}, Hz typical	No.	Type	J_{ab}, Hz	J_{ab}, Hz typical
1		from +5 to -30	from −12 to −15	19	$H_a-C\equiv CH_b$	from −2 to −3	
2	CH_a-CH_b (free rotation)	6–8	7	20	$-CH_a-C\equiv C-CH_b-$	2–3	
3		0–1	0	21	 3-memb. 4-memb. 5-memb. 6-memb. 7-memb.	0–2 2–4 5–7 8–11 10–13	
4	 $a-a'$ $a-e'$ $e-e'$	6–14 0–5 0–5	8–10 2–3 2–3	22	 *J* (*ortho*) *J* (*meta*) *J* (*para*)	6–10 1–3 0–1	9 3 ~0
5	 (*cis* or *trans*)	0–7	4–5	23	 *J* (2–3) *J* (3–4) *J* (2–4) *J* (3–5) *J* (2–5) *J* (2–6)	5–6 7–9 1–2 1–2 0–1 0–1	5 8 1.5 1.5 1 ~0
6	 (*cis* or *trans*)	6–10	8	24	 *J* (2–3) *J* (3–4) *J* (2–4) *J* (2–5)	1.3 (?) −2.0 3.1–3.8 0–1 1–2	1.8 3.6 ~0 1.5
7	 (*cis* > *trans*)	2–8	3–5	25	 *J* (2–3) *J* (3–4) *J* (2–4) *J* (2–5)	4.9–6.2 3.4–5.0 1.2–1.7 3.2–3.7	5.4 4.0 1.5 3.4
8	CH_a-OH_b (no exchange)	4–10	5	26	 *J* (1–2) *J* (1–3) *J* (2–3) *J* (3–4) *J* (2–4) *J* (2–5)	2–3 2–3 2–3 3–4 1–2 1.5–2.5	
9		1–3	2–3	27		44–81	
10		5–8	6	28		7–13	
11		12–18	17	29		0	
12		0–3	−2	30		200–300	
13		6–12	10	31		7–80	
14		0–3	1–2	32		0–25	
15		4–10	7	33		1–8	
16		from −0.5 to −3.0	−1.5	34		12–40	
17		from −0.5 to −3.0	−2	35		*o* 6–10 *m* 5–6 *p* 2	
18		9–13	10	36		*o* 20 *m* 0–7 *p* 0–12	



which it was shown unambiguously on the basis of the values of the $J(^{13}C-H)$ constants that in the molecule of dihydroanthracene[42]



the α-atom of the benzene ring is sp^3-hybridised:

$$J_{\alpha}(^{13}C-H) = 127\,Hz,\quad J_{\alpha'}(^{13}C-H) = 163\,Hz.$$

Measurements of the constants for the spin–spin coupling between protons and ^{29}Si, $^{117(119)}Sn$, Pb, $^{203(205)}Tl$, and ^{199}Hg nuclei are widely used in the chemistry of organometallic compounds. Typical values of these constants are listed in Table 4. An interesting example of the importance of these data is provided by the work of Nesmeyanov et al.[43] It was found that in the spectrum of C_5H_5Tl the signal due to the cyclopentadienyl protons is a narrow singlet with a chemical shift typical for compounds of this type without the slightest trace of spin–spin interaction with thallium nuclei.

At the same time Table 1 shows that thallium has no non-magnetic isotopes and it is evident from Table 3 how strong the spin–spin $J(Tl-C-H)$ interaction usually is. The singlet nature of the PMR signal of C_5H_5Tl indicates complete exclusion of the spin–spin coupling. This is important evidence confirming the generally accepted view[44] concerning the mechanism of the spin–spin coupling, to which the Fermi contact interaction makes the main contribution. Such interaction is non-zero only when there is an appreciable electron density at both nuclei. Only *s* electrons can come into contact with the nucleus and therefore when the chemical bond involves pure *p* or *d* states, the absence of spin–spin interaction is to be expected. Univalent thallium forms a bond with the cyclopentadienyl ring via a 6*p* electron and the admixture of the *s* state to this chemical bond from thallium does not exceed 10^{-3} according to the data of the experiment quoted, since otherwise signs of splitting in the PMR signal would have been noticeable. Similar observations were made in the study of organophosphorus compounds. The constant $J(^{31}P-C-H)$ for tricoordinate phosphorus in the fragment $^{31}P-CH_2$ is several times smaller than for pentacoordinate phosphorus, which can be reasonably related to the tendency towards lone pair formation and the corresponding decrease of the *s* character of the $P^{III}-C$ bond.

Table 4. Metal–proton spin–spin coupling constants.

No.	Type	J(M-H), Hz	No.	Type	J(M-H), Hz
1	SiH_4	202	9	$Sn(CH_3)_4$	54
2	SiH_3F	229	10	$Sn(CH_3)_3Cl$	60
3	SiH_3I	240	11	$Sn(CH_3)_2Cl_2$	71
4	SiH_2F_2	282	12	$Sn(CH_3)Cl_3$	100
5	$SiHF_3$	381	13	$^{205}Tl(CH_3)_3$	251
6	$Si(CH_3)_4$	~6	14	$^{205}Tl(C_2H_5)_3$	$J(Tl-CH_2)=198$
7	$^{119}Sn-(CH_2-CH_3)_4$	$J(SnC-H_3)=\pm 71$ $J(Sn-CH_2)=\pm 32$			$J(Tl-CH_3)=396$
8	(A)H, (B)H, C=C, Sn(CH=CH$_2$)$_3$, H(C)	$J(Sn-H_A)=91$ $J(Sn-H_B)=183$ $J(Sn-H_C=98$	15	4-HgCl, 5, 2, O	$J(Hg-H_2)=40$ $J(Hg-H_4)=75$ $J(Hg-H_5)=28$
			16	OCH_3, $CH-CH_2-HgCl$, HC_3	$J(Hg-H_\alpha)=223$ $J(Hg-H_\beta)=338$ $J(Hg-H_\gamma)=0$

Spin–spin interaction with nuclei which have spins $I > 1/2$ leads to appreciable changes in the NMR spectra. Apart from a magnetic moment, such nuclei also have a quadrupole electric moment. The interaction of the nuclear quadrupole moment with an inhomogeneous electric field fluctuating as a result of thermal motion, which must exist in the specimen, leads to rapid reorientation of the nucleus, i.e. constitutes an additional mechanism of nuclear magnetic relaxation. Depending on the contribution of this mechanism, the spin–spin multiplets associated with the nuclei participating in the interaction with the quadrupolar nucleus can be either altogether "diffuse", or significantly broadened, or can comprise a set of sharp peaks of virtually the normal type.

The contour of the signals obtained is sometimes unexpectedly freakish. We may quote several examples. The simplest[45] is provided by deuterium exchange in 2-methylpentane; the 1,2-methyl protons in $(CH_3)_2-CH-(CH_2)_2CH_3$ give rise to a distinct doublet with a splitting of 6.62 Hz. In 2-deutero-2-methylpentane $(CH_3)_2-CD-(CH_2)_2CH_3$ the signal due to the $(CH_3)_2$ group proved to be a triplet with intensity ratios of 1 : 1 : 1 and a splitting of about 1 Hz. The form of this signal demonstrates unambiguously that deuterium is precisely in the position indicated. The ratio of the spin–spin interaction constants $J(CH_3-CD)/J(CH_3-CH) = 0.1512 \pm 0.008$, which agrees well with the ratio $\gamma_D/\gamma_H = 0.1535$.

^{14}N nuclei also have a spin $I = 1$, i.e. should give rise to 1 : 1 : 1 triplets. However, the high magnetic moment leads to an even more effective quadrupole relaxation of the ^{14}N nuclei; these nuclei execute such rapid transitions that the width of the signals of the protons linked to ^{14}N via a spin–spin interaction also increases markedly. Then the PMR signal is sometimes absent altogether. Thus in formamide the signals of the NH_2 protons are clearly visible only on saturation of the ^{14}N resonance[46].

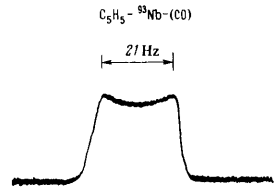


Figure 5. PMR signal of cyclopentadienyl protons in cyclopentadienylniobium tetracarbonyl.

It is important to emphasise that for ^{14}N the 1 : 1 : 1 ratios indicate only the integral line intensities. The observed pattern is altered by the different peak widths: the outer lines of the triplet correspond to levels with a shorter lifetime and therefore they are 40% wider and correspondingly lower than the central peak.

^{11}B and ^{35}Cl are typical examples of nuclei with a spin $I = 3/2$. In accordance with the possible number of states of the 3/2 spin in a magnetic field, such nuclei should give rise to a quartet. Indeed the ^{19}F NMR signal of the B–F group in 3-fluorobarene proved to be a quartet with intensity ratios of 1 : 1 : 1 : 1, all the peaks having approximately the same integral intensity and width. The NMR spectra of compounds with spin–spin coupling between the ^1H, ^{19}F, ^{31}P, and ^{35}Cl nuclei do not show this type of pattern: the quadrupole relaxation of the nuclei obliterates the multiplet and a single averaged peak is observed. The ^{93}Nb nucleus has a spin $I = 9/2$. Spin–spin coupling with such a nucleus leads to the formation of a decaplet all the components of which have the same integral intensity. However, in a multilevel system of this kind the probability of transitions is such that the extreme peaks of the multiplets are longest-lived and hence have the highest amplitude[47]. A typical spectrum is presented in Fig. 5. Evidently quadrupole relaxation in the Nb nucleus leads to a broadening of the multiplet components such that only a characteristic outline with maxima at the edges remains. After dividing the distance between the maxima by the number of intervals between the peaks, we obtain an approximate estimate $J(Nb-C-H) \simeq 2$ Hz.

XIII. CHEMICAL EQUILIBRIUM AND CONFORMATIONAL TRANSITIONS

Nuclear magnetic resonance proved to be a very sensitive and reliable method for detecting tautomeric equilibria, prototropy and exchange processes, intramolecular motion, etc. The reasons for the effectiveness of the method for these phenomena have already been given in essence when discussing the question of the magnetic equivalence of the methyl and methylene protons in the ethyl group. If the rate of a process whereby a given nucleus is transferred from a situation A to a situation B is high compared with the frequency range $\Delta\nu_{AB}$ which separates the ν_A and ν_B peaks in the spectrum, the effective field acting upon the nucleus becomes averaged. Therefore instead of two peaks only one is observed and its width is close to the natural width of the NMR line, i.e. is determined by the spin–spin relaxation time T_2. By reducing the temperature, it is possible to ensure that the residence time τ in each state (let $\tau_A = \tau_B = \tau$) is comparable to T_2. This leads to a broadening of the observed peak. Further retardation of the process leads to the "spreading" of the line over the entire frequency range $\Delta\nu$, and, when the latter is sufficiently wide, the line becomes virtually unobservable. Finally, when the given process ceases completely, two distinct peaks with frequencies ν_A and ν_B will of course arise in the spectrum and their width will again be determined by T_2. When the temperature is raised somewhat relative to the point corresponding to such "freezing out" of the exchange process, we yet again note signs of broadening of the peaks: the new widths, as in the previously discussed case of the other end of the temperature range, will be $T_2^{-1} + \tau^{-1}$. All these processes can be described mathematically in detail with the aid of Bloch's equations. However, for the purpose of the present review, the overall pattern of the changes with temperature observed in the NMR spectra of certain systems has been outlined adequately above.

The simplest example of the equilibrium of the type described is the keto–enol tautomerism, the study of which by nuclear magnetic resonance revealed a number of fundamental facts. Here the starting point was the investigation of acetylacetone[48], which at room temperature proved to be a mixture of the keto- and enolic forms in proportions of 4 : 1. It is important to stress that the detection of tautomers and the measurement of their concentration can be achieved with the aid of NMR much more reliably than by any other method, since each form is associated with a particular set of lines. Thus the enolic form of acetylacetone and similar compounds is characterised by the formation of a strong intramolecular hydrogen bond; a six-membered ring system of conjugated bonds is formed. In such systems there is a very marked shift of the hydroxyl proton signal towards weaker fields: from 13 to 20 p.p.m. on the δ scale. The signal of the methylene protons of the keto-form is displaced approximately by 10 p.p.m. towards stronger fields; the two signals can be very reliably distinguished. In more complex molecules there is a tendency for the enolic form to predominate at low temperatures. Thus 4-acetoacetylphenyl ether[49] shows no signs of the presence of the keto-form up to 100°C and only in the melt at 150°C does the ketone content reach 20%. The rate of interconversion of the equilibrium forms is low, since the corresponding peaks of the OH and CH_2 protons are broadened by no more than 1 Hz. These data provide a rough estimate of the height of the barrier inhibiting the ketone $\rightleftharpoons$ enol interconversion. It is significant that the estimate based on the Arrhenius equation, which is invariably invoked in all more accurate investigations in this field, is $\nu = \nu_0 \exp(-U/kT)$. Here the frequency ν_0 can be reasonably compared with intermolecular vibrations, i.e. is close to 10^{13} Hz. In other words ν_0 is the number of attempts at bond dissociation. The observed frequency ν of the ketone $\rightleftharpoons$ enol transitions represents the number of successful attempts at overcoming the barrier inhibiting the transition from one tautomeric form to another. For high-resolution NMR spectra, the observed frequency may be assumed to be $\nu \simeq 1$ Hz. Thus, let us suppose that at a low temperature in the absence of equilibrium $\nu = 0$ and the line width is > 1 Hz. Then the specimen is heated to a temperature T_C at which the line broadens approximately by 1 Hz due to the limited lifetime of a given tautomer. Under these conditions, the barrier is

$$U = kT_c \ln 10^{13} \simeq 55T_c, \qquad (21)$$

where U is the height of the barrier in cal mole^{-1} and T_C the temperature on the Kelvin scale. For 4-acetoacetylphenyl ether, Eqn. (21) gives $U \simeq 20$ kcal mole^{-1}. It has been shown[50] that the accuracy of this estimate is ±3 kcal mole^{-1}.

As a rule, owing to the reduced strength of the hydrogen bond, the keto-enol tautomeric process is accompanied by prototropy, which leads to an additional temperature dependence of the hydroxyl proton NMR line width[51].

The prototropy also obeys the Arrhenius equation, in which the frequency factor and the activation energy can be readily determined from the NMR spectra recorded at different temperatures. In fact, an increase in line width of the order of 1–2 Hz can be readily detected in PMR spectra at low temperatures. This means that, for an activation energy $\Delta E \simeq 2$ kcal mole^{-1} which is frequently encountered, one can observe with certainty at a temperature of about 200°K proton exchange processes with a frequency factor $\nu_0 = e^5 = 140$ Hz. It is quite impossible to observe such weak processes by other methods.

An extensive literature has been published on the problem of *cis*- and *trans*-enolisation. A rigorous experimental examination of this problem proved to be possible only with the aid of NMR. A series of investigations by Kabachnik and coworkers[52,53] made it possible to study the kinetics and mechanism of the conversion of a *trans*-enol into the *cis*-enol. It was demonstrated convincingly that in solutions the *cis*-enol is more favoured by energy factors than the *trans*-enol.

In organometallic chemistry NMR made it necessary to postulate new types of tautomerism. Thus cyclopentadienyl derivatives of germanium and silicon show an unusual pattern of temperature changes in their NMR spectra. A single narrow signal due to the protons of the cyclopentadienyl ring accompanied by narrow ^{13}C satellites with a splitting of the completely normal kind is observed at high temperatures, while at low temperatures the typical pattern of cyclopentadiene involved in σ-addition is obtained. The question arises how to represent the structure of such a molecule in the intermediate temperature range where the form of the PMR spectrum clearly indicates that the protons of the cyclopentadienyl ring participate in a dynamic process, which averages out the immediate environment. At least two explanations can be proposed. A widely held view is that of Piper and Wilkinson[54], according to which at high temperatures there is rapid metallotropic migration along the perimeter of the cyclopentadienyl ring, at low temperatures the rate of this migration is vanishingly small, and in the range corresponding to the dynamic

process the rate of migration is comparable to the chemical shift between the signals of protons involved in sp^2- and sp^3-hybridisation. In other words, according to Piper and Wilkinson, a change of temperature alters only the quantitative measure of the observed phenomenon: the sharp difference between the high-temperature and low-temperature PMR spectra may be accounted for by a more or less fortuitous factor: at high temperatures the rate (frequency) of migration is greater than the chemical shift, while at low temperatures it is lower.

Another explanation is almost self-evident: one can relate the narrow singlet arising at high temperatures to centrosymmetric addition of the cyclopentadienyl ring to the metal (C_{5V}-bonding). Then the intermediate temperature range corresponds to a sandwich–σ-bond transition in which the interconversion of the σ and C_{5V} molecules (tautomerism) takes place, its rate diminishing as the temperature is reduced, in parallel with the increasing concentration of the σ-molecules. When the temperature is reduced sufficiently, only the stable σ molecules remain in solution.

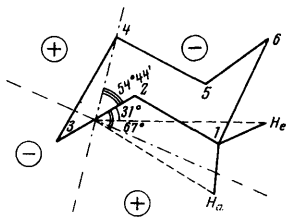


Figure 6. Location of the axial (H_a) and equatorial (H_e) protons in cyclohexane relative to the C_2-C_3 bond in different screening zones.

In principle nuclear magnetic resonance permits a valid choice between the two explanations of the experimental data.

The most widely known example of conformational changes observed with the aid of NMR is provided by the cyclohexane spectrum. The axial and equatorial hydrogen atoms in this molecule are located in different ways relative to the dipole associated with the magnetic anisotropy of the C_2-C_3 bond (Fig. 6). Therefore at low temperatures, at which this molecule may be regarded as rigid, the PMR spectrum is a doublet: the axial protons are screened to a greater extent and their signal is displaced towards weaker fields by 0.2×10^{-6}. On raising the temperature, the inversion of the cyclohexane ring begins and the PMR doublet signal is gradually converted into a singlet, in accordance with the laws already described. At room temperature the rate of inversion is relatively low and the cyclohexane signal is significantly broadened. The shift Δ_{ae} between the signals of the axial and equatorial protons and the available information about molecular geometry permit the calculation of the magnetic anisotropy of the C–C bond. The data thus obtained are significantly more accurate than the estimates of magnetic anisotropy based on magnetochemical concepts[55]. Nuclear magnetic resonance is one of the most effective methods for the investigation of conformations and there is an extensive literature on its application in this field[37,56-58].

XIV. STUDIES ON CRYSTAL STRUCTURES

High-resolution nuclear magnetic resonance is very actively employed in organic chemistry. Until recently low-resolution NMR was largely employed in inorganic chemistry and yielded a number of first class results concerning the fine details of the crystal lattice structure and also the details of thermal motion in the solid state, which are quite unobtainable by other methods.

Diffusion and vibrations of crystallised water molecules[59], the mechanism of the ferroelectric transition[60], the retarded motion in molecular crystals[61], and the exact determination of the coordinates of light atoms[62] are typical examples of problems successfully investigated by low-resolution NMR.

NMR chemical shifts in the solid state are difficult to observe: they are usually hundreds and thousands of times smaller than the observed line width. In Section VI it was already stated that in solids $T_1 \gg T_2$, in contrast to liquids where $T_1 \simeq T_2$. This inequality is caused both by higher values of T_1 and lower values of T_2 compared with the liquid state.

The decrease of the spin–spin relaxation time T_2 implies that the energy exchange processes in the nuclear spin system are very rapid. This entails a corresponding increase in line width. The increase of the spin–lattice relaxation time T_1 implies a sharp reduction in energy transfer from the nuclear spin system to the lattice. In other words, the magnetic nuclei form in the crystal lattice a highly isolated physical system; heat exchange between the lattice and the nuclei is strongly hindered. Therefore it is possible to introduce the concept of the spin temperature (see Section IV). The NMR line form for the crystal cannot be predicted in the general case. Bloch's equations are inapplicable to solids for a simple reason. They have been formulated essentially for a single nucleus and the problem of line form in the spectra of solids must be treated on the basis of statistical laws. In fact, the random motion of molecules in a liquid or gas leads to complete averaging of the intermolecular contribution to the local magnetic field; for an exact description of the phenomenon of nuclear magnetic resonance, it is quite sufficient to take into account only the phase differences between the magnetic moment of an arbitrary nucleus and the vector of the rotating magnetic field H_1 applied to the specimen.

On the other hand, in a solid the radiofrequency field H_1 is much smaller than the local magnetic field H_{loc} caused by the mutual effects of the nuclear magnetic moments fixed in the crystal. Therefore the line form cannot be a function of only H_1 and simple parameters such as T_1 and T_2; it depends fundamentally on the detailed distribution of the nuclear magnetic moment in the crystal structure and in a rigorous approach requires the examination of the specimen as a whole. The difficulties in the theoretical treatment of this problem have not as yet been overcome.

However, Van Vleck[63] showed that, when the crystal structure of the specimen is known, it is possible to find certain numerical characteristics of the line form—the so called moments. If the deviation of the magnetic field from the condition of exact resonance is denoted by the symbol h, the line form is described by a function $g(h)$. It is easy to show that $g(h)$ is symmetrical relative to the point $h = 0$. The nth order moment of the function $g(h)$ is defined as

$$\Delta\overline{H^n} = \int_{-\infty}^{+\infty} g(h)\, h^n dh. \qquad (22)$$

Since the function $g(h)$ is even, all the odd moments (n = 1, 3, 5) become zero and only the even moments need to be calculated. The Van Vleck formula is most widely used in practice for the calculation of the second moment:

$$\Delta H^2 = \frac{9}{4} \cdot \frac{1}{N} \mu^2 \sum_k^n \sum_i r_{ik}^{-6} (3\cos^2\theta_{ik} - 1)^2, \qquad (23)$$

where r_{ik} is the distance between the ith and kth nuclei in the unit cell, n the number of types of crystallographically non-equivalent nuclei in the unit cell, and θ_{ik} the angle between the direction of the constant magnetic field H_0 and r_{ik}.

Comparisons of Eqns. (22) and (23) shows that NMR permits a structural analysis whereby the coordinates of the magnetic nuclei can be determined with high accuracy. The analysis can be carried out by the method of trial and error[64]. Suppose that we have a hypothetical structure A_1 in which specific trial values can be attributed to the distances r_{ik} and the angles θ_{ik}. Then, for any orientation of the single crystals in the field H_0, it is possible to calculate by Eqn. (23) the second moment $\Delta\overline{H}^2_{1c}$. Having recorded the real NMR signal for the same orientation of the crystal, it is possible to evaluate by Eqn. (22) the experimental value ΔH^2_{1e}. When the two numbers are highly inconsistent, it is necessary to revise the hypothetical structure, i.e. to employ for the calculation a new structure A_2, etc. until in the pth stage of the procedure satisfactory agreement between $\Delta\overline{H}^2_c$ and $\Delta\overline{H}^2_e$ is obtained. McCall and Hamming[62] showed that the process described permits the determination of 15 independent structural parameters for a triclinic structure. With increase in the symmetry of the structure, the number of independent parameters is of course smaller and in the simple cubic structure it reduces to a single parameter—the lattice constant. Therefore McCall and Hamming suggested, instead of the method of trial and error, a direct procedure for the structural analysis of single crystals by the NMR method: not more than 15 (depending on the symmetry of the crystal) measurements of the second moment are made. According to Eqn. (23), this set of numbers leads to 15 (or less) equations with 15 unknowns. The solution of this set permits, in principle, the determination of all the required structural parameters. However, Lundin and coworkers[60] and Dereppe et al.[64] showed that the McCall algorithm is unstable relative to unavoidable experimental errors and its practical application does not yield unambiguous results; practically useful conclusions can be derived only by improving the method of calculation significantly. Kitaigorodskii[65] stated that the NMR method can be very useful in the concluding stages of the X-ray diffraction analysis of single crystals. It has been shown[66] that, in order to arrive at a sufficiently reliable result, it is necessary to alter significantly the method of measurement and the experimental values of the second moment must be evaluated by an electronic computer. The accuracy of the structural analysis of single crystals by the NMR method would be indisputable if a rigorous theory of the NMR line shape for solids were available. Provotorov[67] has obtained important results in studies in this direction. Unfortunately it is not yet possible to give a rigorous theoretical explanation even of the almost self-evident fact of the rapid "decay" of the wings of the lines (at distances 2–3 times greater than the line width at half height). The creation of a theory predicting the behaviour of the line, if only at the wings, would convert the low-resolution NMR method into a regular method for improving the accuracy of the results of the X-ray structural analysis of crystals containing hydrogen and fluorine.

In many cases the magnetic nuclei in the crystal form physically isolated pairs or triplets. These cases have been examined by Pake[68] and Powles and Gutowsky[69] respectively. A typical example of the existence of isolated pairs is provided by water of crystallisation. Here the NMR signal proved to be a doublet in which the distance between the components is given by

$$\Delta H = \frac{3}{2}\gamma\hbar r^{-3}(3\cos^2\theta - 1),$$

where the notation has the same significance as in Eqn. (23). For water molecules, r = 1.5 Å and $\Delta H_{max} \simeq 20$ G. Methyl groups are a typical example of nuclear triplets isolated in the crystal. It has been shown[70] that methyl groups at rest separated by distances greater than 3 Å give rise to a complex multiplet spectrum, the form of which changes with the orientation of the single crystal in the magnetic field.

The magnitude of the splitting observed in the spectrum of an isolated group may depend markedly on temperature. The explanation is that, when internal motions arise in the specimen, there is a possibility of additional averaging of the local field at the nucleus under consideration; when the motion is sufficiently rapid, instead of the multiplier $3\cos^2\theta - 1$ having a particular value, it is necessary to calculate its average value over the reorientation period. As in the discussion of the analogous questions in Section XIII, here one must regard as "sufficiently rapid" those motions whose rate exceeds significantly the interval between the observed multiplet components expressed in frequency units. Thus a broad NMR signal is observed for a rigid lattice (low temperatures), while at a high temperature the higher rate of internal motions appreciably diminishes the distance between the components of the NMR signal. A smooth structureless NMR line also consists of separate component pairs. Therefore on raising the temperature, with the consequent appearance of fairly rapid internal motions in the crystal, the single broad NMR line becomes narrower.

The events described are fully analogous to the changes occurring in high-resolution NMR spectra associated with chemical exchange (see Section XIII) but with the difference that the distances between the components and their width in the low-resolution spectrum are greater by a factor of several thousands, since their origin is different. Therefore, as the internal motions are "unfrozen", the characteristic changes in the low-resolution spectrum occur at frequencies $\nu_c \simeq 10^3$–10^4 Hz and not approximately 1 Hz as in the high-resolution spectra. Such a marked change in critical frequencies leads to an appreciable modification of the coefficient in Eqn. (21). If T_c is the temperature at which the width of the low-resolution signal begins to change, the height of the corresponding energy barrier is approximately[50]

$$U(\text{cal mole}^{-1}) = 37\ T_c(^\circ\text{K}). \qquad (24)$$

A somewhat higher accuracy may be achieved by using a more complex expression:

$$U = kT_c \times 2.5 \lg \frac{n}{\Delta} \sqrt{\frac{kT_c}{2J}}, \qquad (25)$$

where n is the multiplicity of the barrier, Δ the NMR line width for $T \leqslant T_c$, J the moment of inertia of the molecule with respect to the reorientation axis, and k the Boltzmann constant.

This formula does not entail a greater experimental complexity—it is only necessary to consider additional information about the specimen. An explanation of the

validity of the strikingly simple formulae (21) and (24) also follows from the form of Eqn. (25): all the parameters describing the structure of the specimen in a specific form are included in the logarithmic term and, when reasonable assumptions are made about the range of their variation, their effect on the final result is small.

The method described by Levich et al.[17] is widely used in the calculation of energy barriers; it requires extremely laborious experiments and frequently leads to contradictory results due to the inadequate accuracy of the measurements.

The sensitivity of broad-band NMR for slow motions led to the discovery in a number of crystals of unexpected displacements and reorientations of large molecules[71]. A word of warning against a common error is appropriate here. The results of the experiments are expressed in terms of curves representing the variation of the width and the second moment of the line with temperature. At certain temperatures these curves show distinct jumps, corresponding to changes by a factor of several units, which are sometimes interpreted as sudden "unfreezing" of a particular type of internal motion. In fact these points correspond to only one type of event: the frequency of the motion under consideration, which varies smoothly with temperature, becomes equal to the width of the NMR line (or the distance between its components); a real phase transition can coincide only fortuitously with the jump in the temperature variation of the NMR line width.

If the crystal has a rigid lattice, in which the thermal motion is confined to small oscillations about equilibrium positions, the NMR line width hardly changes up to fusion, where the width diminishes by a factor of tens of thousands and a high-resolution spectrum is produced. In crystals containing fluorine the chemical shifts are sometimes so great that in modern apparatus (with a field $H_0 = 23\,400$ Oe) they can be observed also in crystals, i.e. in broad-band spectra[72].

XV. PROSPECTS FOR THE IMMEDIATE FUTURE

The question arises of the way in which the NMR method will develop further and the contribution which such development may make to chemistry. It is risky to attempt an answer to these questions but certain trends in present day developments are so clear that their extrapolation to the immediate future and beyond is quite valid.

As in any physical method, the experimental technique is of decisive importance. The available working frequencies, i.e. the strength of the magnetic field H_0, will continue to increase. Electromagnets with a ferromagnetic 28 200 gauss core (120 MHz for protons) and superconducting 51 200 gauss solenoids (220 MHz for protons) are now used in practice. One may expect that "ordinary" (with iron) 35 000 gauss magnets (150 MHz for protons) and highly strengthened fields in iron-free solenoids will be produced. The advantages of such developments were dealt with in adequate detail in Sections VIII and X. Briefly, these involve an increase in the sensitivity and reliability of the method, since the spectra will be simpler. The range of applications will be extended. However, devices with powerful and ultrapowerful magnetic fields will remain rare and will be available only to large complex research centres.

A second important trend in the development of instrumentation will be miniaturisation and improvement in the reliability and simplicity of operation as well as a reduction in price of NMR spectrometers for every day analytical investigations in the chemical laboratory. The results already achieved in 1968 by the firms Perkin-Elmer (P-12 spectrometer), Varian (T-60 spectrometer), and JEOL ("Minimar" spectrometer) show that the construction of a simpler and more reliable NMR spectrometer, no more expensive than the present day gas–liquid chromatographs, is quite realisable.

The automation of analytical investigations by the NMR method constitutes an extremely important task. This is part of the general problem of the automation of research. The Varian and JEOL companies have achieved decisive advantages in this field. It has been shown that in the near future one may expect a large scale employment in chemical research of automated analytical laboratories comprising mass spectrometers, NMR and infrared spectrometers, and other essential devices, the sequence and conditions of the operation of which (including the most complex types of techniques) will be specified by computing and controlling devices, in accordance with the problem formulated by the chemist and based on the fundamental physical relations specified in the program for the device and also on the results of previous solutions of similar problems. The creation of such automated systems will free qualified specialists from routine day to day analyses and will reduce to a minimum the likelihood of an erroneous assignment of spectral lines, will greatly enhance the labour productivity of chemists specialising in synthesis and also spectroscopists. At present the range of applications of high-resolution NMR is somewhat restricted by the requirement of a low viscosity of the specimen. Here revolutionary changes are close at hand. Waugh and coworkers[73,74] showed that it is possible to devise a system where pulses of a radiofrequency field H_1 are applied to the specimen in such a way that the dipole–dipole interaction of the nuclei in the crystal lattice will be reduced to zero with a decrease of the chemical shift by a factor of only $\sqrt{3}$. Consequently it will be possible to obtain the NMR spectra of solids. It is found that the resolving power of the NMR method for solids will be even greater than for liquids and for crystals of ultimate purity may reach 10^{-11}–10^{-12}. The consequences of the large scale employment of this technique by chemists and physicists are difficult to assess; there is no doubt that important discoveries will be made, which will have the most far-reaching influence on both quantum chemistry and the physics of the solid state.

The pulse technique also requires the obligatory application of computers for the interpretation of results. Pulse NMR spectrometers will be increasingly used also in kinetic liquid-phase investigations. The studies described in Section XIII on the kinetics of slow chemical reactions were made using conventional NMR spectrometers. A pulse spectrometer allows the recording of the spectrum tens and hundreds of times faster and thus gives rise to the possibility of investigating fairly rapid processes. This brief list of the immediate prospects for the NMR method shows that its importance in chemistry will increase. The converse influence is also evident—namely the requirements of chemical laboratories to a large extent determine the range of interests of specialists developing the theory of the NMR method and improving its technique. Experience obtained in the "old" branches of spectroscopy shows that such mutual enrichment can continue for many decades. Predictions for such a long period must necessarily be rather vague.

One may also hope that the logic underlying the theoretical concepts will be enriched and their power will be enhanced; such a favourable course of events may occur following the joint interpretation of the vast and occasionally overlapping experimental data accumulated in various

branches of radiospectroscopy (NMR, NQR, ESR), in studies based on the Mössbauer effect, β-spectroscopy, optical spectroscopy, etc.

The following are the simplest examples of such overlapping: information on electron density $|\psi(0)|^2$ at the nucleus obtained from experiments on the Mössbauer effect and measurements of the spin–spin coupling constants the nuclei of the same metals in NMR spectroscopy; data on the magnetic anisotropy of bonds accumulated by the NMR method and information concerning the deviations of these bonds from spherical symmetry obtained by the NQR method; rigorous linear relations between the spin–spin coupling constants and chemical shifts and between spin–spin coupling constants and acidity; correlation between NMR chemical shifts and the vibration frequencies of the corresponding bonds; comparison of NMR chemical shifts with those in β-ray spectra. These and many other facts constitute a wide range of experimental parameters, which may serve as a basis for the creation of a reliable theoretical apparatus which will predict exactly even the exceptionally small effects measured in NMR spectroscopy which play such an important role in chemistry.

The significantly many-sided nature of the tasks which arise in attempts at a rigorous treatment of problems of the chemical bond shows that success in the development of the theory may be achieved using the empirical facts indicated above within the framework of the technique based on finite Fermi systems [75].

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