NUCLEAR MAGNETIC RESONANCE

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The nuclear resonance spectra of solids are usually broad; this broadening may arise from interaction between the magnetic moments of the nuclei by dipolar coupling or by a scalar spin–spin coupling, or from interaction between nuclear electric quadrupole moments and electric field gradients in the solid.

In solids containing nuclei grouped in very simple configurations, the dipolar broadening may give nuclear magnetic resonance spectra with interesting line shapes from which structures and distances can be derived[1]. The range of problems suitable for this type of study is, however, very limited.

Broadening of nuclear magnetic resonance by nuclear scalar coupling has, so far, been observed in only a few cases. The widths of the thallium resonances in thallium salts have been used by Freeman, Gasser and Richards[2] to infer information regarding the chemical binding in these crystals.

Nuclei for which $I > \frac{1}{2}$ usually possess an electric quadrupole moment, and in a solid the interaction between this and an electric field gradient often produces a very large splitting of the nuclear magnetic resonance lines. Important information about the crystal structure can often be obtained[3] from a measurement of these splittings, but, because the effect depends on the angle between the electric field gradient and the applied magnetic field, it is necessary to use large single crystals for this work. In powders, a range of angles occurs, and the electric quadrupole interaction then appears merely as a broadening of the resonance which is often so great as to make the signal unobservable.

Molecular motion can reduce these interactions between the nuclei to a greater or lesser extent, and a study of the variation of line width with temperature can provide information regarding this molecular motion[4].

In liquids and solutions the molecular motion is so vigorous that the contributions of dipolar and electric quadrupole interactions to the line width are greatly reduced, so that finer details which arise from weaker interactions can be observed. It seems probable that the greatest range of chemical applications of nuclear magnetic resonance spectra will depend on measurements on liquids, solutions and gases.

Nuclear resonance spectra of liquids are often complex; the sharp components of the spectrum arise from the chemical shifts and the spin–spin coupling between the nuclei. The chemical shift is caused by the magnetic moments induced by the applied magnetic field in the electrons of the molecule, so that in a given applied magnetic field the resonance occurs at a position characteristic of the chemical environment of the nucleus. The theory of magnetic shielding in molecules has been given by Ramsey[5], but it is unfortunately not possible to make *a priori* calculations except for the simplest molecule. The empirical and semi-empirical[6,7] uses of these shifts have almost endless applications to chemical problems, however.

The spin coupling between the nuclei in a molecule is transmitted through the electrons involved in chemical bonds between the nuclei. The multiplicity of lines caused by this interaction is easy to interpret when the chemical shifts are large compared with the coupling constants, and provides valuable information about the ways in which the chemical groupings are linked together[6,7]. When the coupling constants are comparable with the chemical shifts between the nuclei concerned, however, relatively sophisticated methods may be required in order to analyse the spectrum. Methods by which this may be done are given by Pople, Schneider and Bernstein[6], by Waugh and Dobbs[8], Fessenden and Waugh[9], Castellano and Waugh[10] and others.

The theory of spin–spin coupling in molecules has been given by Ramsey[11], and although the theory can be applied rigorously only for very simple systems, considerable progress has been made with approximate methods. Coupling between protons probably arises mainly from the so-called Fermi[12] "contact" interactions, and theories based on this assumption have been developed using both the molecular-orbital[13] and valence-bond[14] methods. The valence-bond method has so far proved to be the most successful; it has made possible not only correct order of magnitude calculations of coupling constants, but also the correct explanation of the variation of coupling constant with bond angle. For example, Karplus[14] has shown that the H—C—C—H coupling constant should vary markedly with the dihedral bond angle. In most ethane derivatives there is free rotation about the C—C bond so that the mean coupling constant of 6–7 c/s is then observed. In heavily substituted ethanes, however, rotation about the C—C bond may be sufficiently restricted to allow the coupling constants in the *trans* and *gauche* forms to be observed separately; Sheppard and Turner[15] have shown that, in a number of compounds of this kind, the results obtained are in accord with the theory of Karplus. If there is an equilibrium between the *trans* and *gauche* forms of such an ethane, one would expect the apparent coupling constant to vary with temperature as the proportions of the two forms change. This has been observed[16], and the results used to estimate the heat change of this transformation. The changes of coupling constant with temperature are usually very small and accurate measurements are required. An example is shown in *Figure 1*[17], from which it is seen that there is also a strong solvent effect on the *trans–gauche* equilibrium; this is being studied at Oxford by Mr P. Higham.

Most of the chemical work so far has made use of the nuclear resonance spectra of hydrogen, fluorine and phosphorus nuclei. There are, of course, many other nuclei with magnetic moments, but the signals obtained from them are often weak and sometimes broadened by electric quadrupole interactions. These spectra can, nevertheless, provide much useful information in a great variety of ways, just as can high resolution spectra.

For example, Gasser and Richards[18] have studied the cobalt resonances in $Co(H_2O)_6^{3+}(NO_3^-)_3$ to which had been added a large excess of ethylenediamine (en). The cobalt resonance due to the $Co(H_2O)^{3+}$ ion gradually becomes weaker and is replaced by another resonance due to the cobalt *tris*ethylenediamine ion. By following the rate of this reaction as a function of temperature, the activation energy was found to be 22 kcal/mole. The cobalt resonance of sodium cobaltinitrite solution shows two chemically shifted components with intensities in the ratio of 8 : 1. As the temperature is changed, the relative intensities vary in a reversible manner, indicating a chemical equilibrium[18] with a heat of reaction of 8·4 kcal/mole. This equilibrium may correspond with changes from structures of the type Co—NO_2 to Co—ONO. The nitrogen resonance in these solutions also has two components[19] which, at room temperature, have an intensity ratio of 3 : 2. The second cobalt resonance, therefore, probably arises from ions of the approximate proportion $Co(NO_2)_3(ONO)_3$ or $Co(NO_2)_4(ONO)_2$.

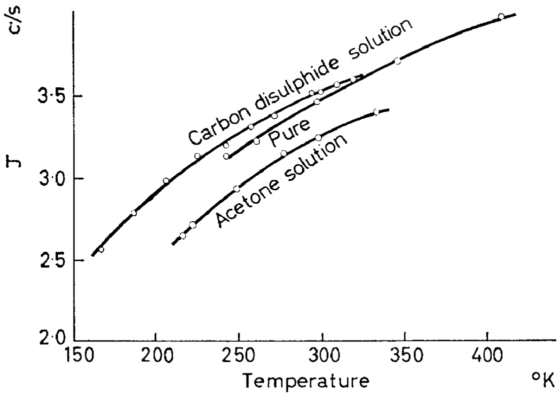


Figure 1. Temperature dependence of the CH—CH coupling constant in 1,1,2-trichloropropane

Another important property of a nuclear resonance transition is the spin-lattice relaxation time, T_1. Spin-lattice relaxation is stimulated by fluctuations of magnetic field near the Larmor frequency and by nuclear electric quadrupole interactions. The fluctuations of magnetic field may be the appropriate frequency component of the fields due to rotation of the molecule, the intramolecular contribution, or to motion of nearby molecules, the intermolecular contribution.

The intramolecular contribution to relaxation can include:

(*a*) the fluctuating magnetic fields set up by other nuclei in the rotating molecule;

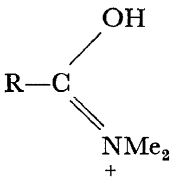
(*b*) the effect of anisotropic chemical shifts which, as the molecule rotates, modulate the applied magnetic field;

(*c*) magnetic moments set up by the rotational motion of the molecule as a whole.

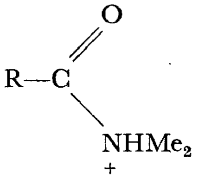
In 1956, Nederbragt and Reilly[20] pointed out that the relaxation times of the protons in alkylbenzenes were quite different from those in the aromatic ring. It seems likely that a further study of such effects may bring to light correlations which would be of value in the interpretation of spectra. A study of the relative contributions of intra- and intermolecular effects to nuclear relaxation can provide detailed information regarding molecular collisions. A notable start on this problem has been made by Bovey[21], Mitchell and Eisner[22], and Gutowsky and Woessner[23].

An example of how the effect of nuclear quadrupole coupling on relaxation times can be useful is provided by some work on the nitrogen resonances of amides[24].

When a strong acid is added to an amide, a proton is added to form a positive ion; the addition of the proton could occur at the oxygen:



or at the nitrogen:



Infra-red studies of systems of this kind have been taken by Spinner[25] to support strongly *N*-protonation, whereas high resolution proton resonance measurements[26] support *O*-protonation.

When *N*-protonation occurs, the nitrogen atom achieves a more symmetrical electrical environment than in the amide, but *O*-protonation would produce a less symmetrical environment. The nuclear electric quadrupole coupling constant depends on the electric field gradient at the nucleus, and in a liquid it strongly influences the spin-lattice relaxation time. The effect is often so great and T_1 is so short that the nuclear resonance line width is dominated by it; the shorter the relaxation time the broader the line. The width of the absorption line can then be taken as a measure of $1/T_1$.

It can be readily shown[6] that, when the relaxation time is dominated by quadrupole effects,

$$\frac{1}{T_1} \sim e^4 q^2 Q^2 \eta$$

Where eq is the electric field gradient, Q is the nuclear quadrupole moment and η is the viscosity. The width of the nuclear resonance line can therefore be plotted against the viscosity of the liquid to give a straight line of slope proportional to the quadrupole coupling constant. *Figure 2*[24] shows this plot for mixtures of *N*-dimethylformamide and glycerol. When acid is added to this amide, the viscosity increases, and so the line width is recorded for various mixtures of *N*-dimethylformamide and trifluoroacetic acid and plotted in *Figure 2* as a function of viscosity. It is seen that the line width in the presence of acid is much higher than with glycerol at the same viscosity. This shows that addition of acid increases the electric quadrupole coupling constant and favours *O*-protonation of the amide.

Spin-lattice relaxation times are greatly affected by the presence of paramagnetic materials, and a detailed study of these effects can yield fascinating information about the interactions between the nuclei and the unpaired electrons. In systems of this kind it is also often possible to observe the *Overhauser effect*, which occurs when nuclear and electron resonances in the same system are simultaneously excited. When the electron resonance is saturated, dramatic changes can occur in the nuclear resonances, leading sometimes to enhancements of the intensity and sometimes to reversal of the intensity by one or two orders of magnitude.

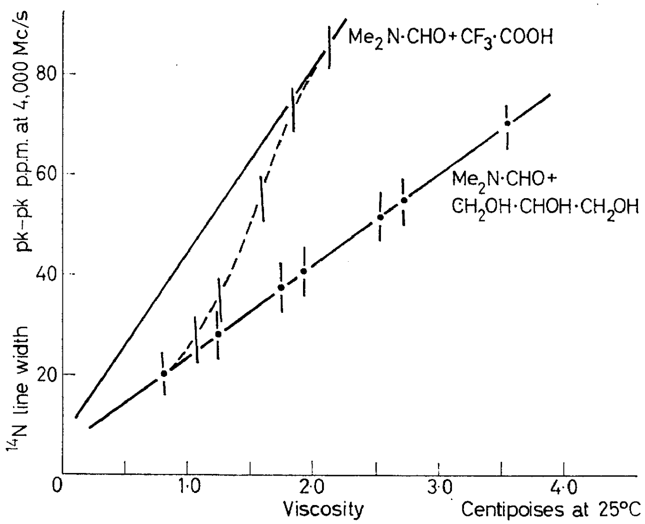


Figure 2. Viscosity plotted as a function of width of nuclear resonance line for mixtures of *N*-dimethylformamide and either glycerol or trifluoroacetic acid

An immediate application of this effect would be to enhance nuclear resonance signals which are otherwise too weak to be observed. A particularly interesting possibility is the study of ^{13}C resonance spectra in natural abundance. These resonances can be observed by conventional methods[27], but are very weak; if the intensity could be increased by 10 to 100 times, an enormous field of studies in organic chemistry would become available.

The interaction between nuclei and electrons can occur in many ways[28], and different forms of interaction give different types of behaviour when the double resonance experiment is performed. From the experimental results it is, therefore, possible to infer the types of interaction between nuclei and electrons which are most important for that system, and the way in which they are modified by the addition of other substances.

The mechanism of the Overhauser effect may be illustrated by two simple examples. When polyethylene is irradiated with high energy radiation, free radicals are formed which are stable in the polymer at room temperature.

The unpaired electrons are weakly coupled with the protons so that the energy levels are as shown in *Figure 3.* Δ is the separation of the electron energy levels in the applied magnetic field and δ is the corresponding spacing for the nuclei. The letters S and I refer to the electron and nuclear spin quantum numbers respectively. The normally permitted transitions are 1–3 and 2–4, but the coupling between the electrons and the nuclei causes the transitions 1–4 and 2–3 to become allowed. If we excite transition 1–4 very strongly, by applying microwaves of the appropriate frequency, and allow relaxation to occur by the permitted transition 4–2, we are, in effect, pumping nuclei from the lower $(+\frac{1}{2})$ energy level into the upper $(-\frac{1}{2})$ level. This increase in population of the $(-\frac{1}{2})$ level at the expense of the $(+\frac{1}{2})$ level results in a strong and reversed nuclear resonance signal. On the other hand, if we saturate transition 2–3 and permit relaxation by transition 3–1, we shall pump the nuclei from the upper to the lower level; the increased population in the $(+\frac{1}{2})$ level gives a strongly enhanced nuclear resonance signal. These striking effects are illustrated in *Figure 4* for this system[29].

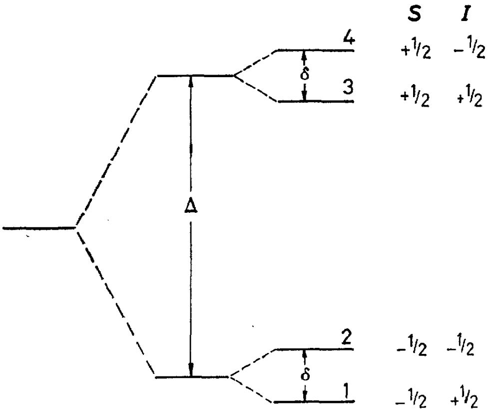


Figure 3. Illustration of the Overhauser effect.

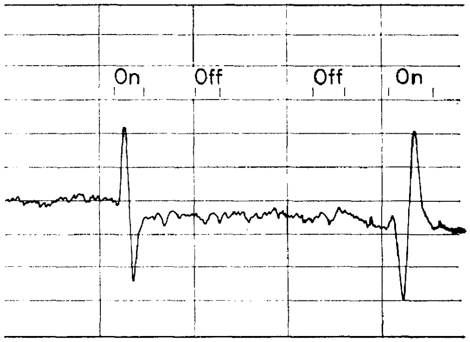


Figure 4. Nuclear resonance signals from polyethylene irradiated with high energy radiation

As the electron resonance transition is traversed, we first excite transition 2–3 and observe an enhanced nuclear resonance signal, and then on the other side of the electron resonance line we excite transition 1–4 and observe a reversal of the nuclear resonance signal. These changes of the intensity of the nuclear resonance signal are plotted in *Figure 5(a)*.

In normal circumstances, the spin-lattice relaxation time of the protons in the polyethylene is determined by the paramagnetic free radicals. When an electron resonance is saturated, however, some of the electron magnetization is removed, so that T_1 for the protons is expected to become longer. This change is shown in *Figure 5(b)*.

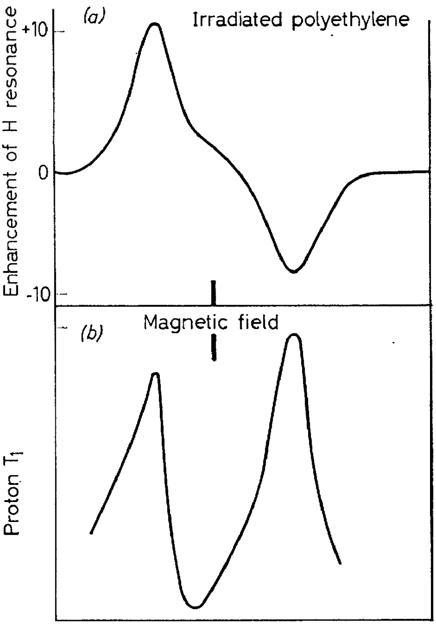


Figure 5 (a). The intensity of the nuclear resonance signal from polyethylene plotted as a function of the frequency of the exciting radiation; (*b*) simultaneous changes in the spin-lattice relaxation time (T_1) of the protons in the irradiated polyethylene

A different kind of interaction occurs in solutions of Frémy's salt,

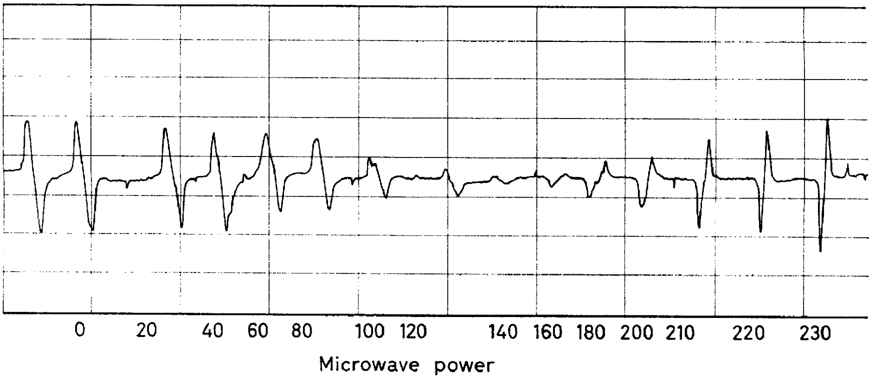


Figure 6. Nuclear resonance signals obtained from 0·1M aqueous Frémy's salt (air-saturated) with increasing microwave power of the exciting radiation

$NO(SO_3K)_2$[30], where the nuclei and electrons are coupled together by a time-dependent dipolar interaction. The energy levels are as in *Figure 3*, except that δ varies with time during the collisions. In this case all possible transitions become allowed, but it turns out that the dominant relaxation mechanism is the 3–2 transition. If we saturate the allowed 1–3 transition, and relaxation occurs by 3–2, then nuclei are pumped from the lower to the upper level and a strongly reversed signal is obtained. The effect on the nuclear resonance signal of increasing the microwave power is shown in *Figure 6*; the signal decreases in intensity to zero and then increases again with the sign reversed.

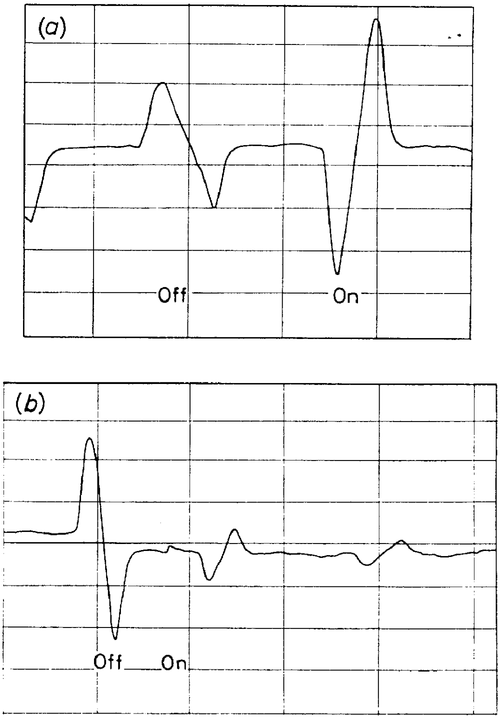


Figure 7. Nuclear resonance signals from irradiated 0·1M aqueous Frémy's salt saturated with (*a*) nitrogen and (*b*) oxygen

The addition of a third species which affects the relative transition probabilities between these levels will produce a corresponding change in the Overhauser effect. For example, dissolved oxygen facilitates transitions 4–3, 2–1 and 3–1 and 4–2, and so, for a given microwave power, reduces the negative enhancement of the signal. In *Figure 7*(*a*) the reversal of the nuclear polarization is shown in a nitrogen-saturated solution of Frémy's salt. In *Figure 7*(*b*), the corresponding signal is shown for an oxygen-saturated solution. The nuclear resonance signal is no longer reversed but merely made weaker.

I feel sure that a detailed study of these fascinating effects will, in the future, widen still further the field of applications of nuclear resonance to chemical problems.

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