Liquid Crystals as Solvents in Nuclear Magnetic Resonance

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1 Introduction

The molecules of solvents generally used in high resolution nuclear magnetic resonance (n.m.r.) do not adopt a preferred orientation when the sample is placed in a magnetic field and in this sense the solvents are isotropic. Analysis of the n.m.r. spectrum of a substance dissolved in such a solvent yields a set of chemical shifts and spin–spin coupling constants.[1] These constants have proved to be invaluable to the organic chemist in the determination of the molecular structure of an unknown compound. However, although the measured spin–spin coupling constants and chemical shifts are isotropic, there are magnetic interactions within a molecule which are anisotropic, that is, their magnitude depends on the orientation of the molecule with respect to the magnetic field. Provided the molecule is undergoing rapid isotropic motion, these interactions do not affect the positions of the lines within a spectrum; they can only influence the widths. If, however, the molecular motion can be restricted so that the molecule adopts a preferred orientation, the positions and number of lines in the spectrum will depend on the anisotropic interactions, and valuable information is gained. As we shall see, it is possible to determine relative bond lengths, bond angles, and signs of spin–spin coupling constants. The nematic mesophases of several liquid crystals[2] have proved to be ideal solvents to restrict the motion of solute molecules.

This Review is intended for the chemist who wishes to understand the physical basis and significance of high-resolution n.m.r. experiments with use of liquid crystals as solvents. While the Review does not treat the subject with complete rigour, it should enable the reader to tackle, with some confidence, the original papers, as well as the excellent article by Buckingham and McLauchlan[3] who deal with the theory in considerable detail. The reader is assumed to be conversant with the article by Bovey;[4] detailed knowledge of the nature of liquid crystals, or the theory of nuclear dipolar coupling is not presupposed.

2 The Dipolar Coupling

The magnitude of an isotropic spin–spin coupling constant (henceforth referred to as the spin–spin coupling constant) measured in n.m.r. depends on the nature

[1] J. W. Emsley, J. Feeney, and L. H. Sutcliffe, 'High Resolution Nuclear Magnetic Resonance Spectroscopy', Pergamon Press, London and New York, vol. 1, 1965.
[2] G. W. Gray, 'Molecular Structure and the Properties of Liquid Crystals', Academic Press, London and New York, 1962.
[3] A. D. Buckingham and K. A. McLauchlan, 'Progress in n.m.r. Spectroscopy', ed. J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Pergamon Press, London and New York, vol. 2, 1967.
[4] F. A. Bovey, *Chem. Eng. News*, 1965, **43**, 98.

of the bonds joining the two nuclei, and this is one reason why n.m.r. is invaluable to the chemist in molecular-structure determinations. However, the two nuclei also interact through space rather like bar magnets and this interaction is known as the dipole–dipole or dipolar coupling.[5] Suppose we measure the nuclear resonance spectrum of two protons A and B having the same chemical shift with the magnetic field, H, pointing along the interproton axis. In the absence of dipolar coupling, the two protons would come into resonance at H_0, but because of the dipolar interactions, the field felt by nucleus B is not equal to H but is instead $H \pm \Delta H$ depending on the orientation of the nuclear spin of A. Thus the protons come into resonance at $H_0 + \Delta H$ and at $H_0 - \Delta H$ and the effect of the dipolar coupling is therefore to split the single line at H_0 into a doublet centred on H_0 with a separation $2\Delta H$.

In general the frequency separation between these lines for two protons is[6]

$$\Delta\nu = \frac{3\gamma^2_{\mathrm{H}}\hbar}{4\pi r^3}\ (3\cos^2\phi - 1) \tag{1}$$

where γ_{H} is the proton gyromagnetic ratio, r is the interproton distance, and ϕ is the angle between this axis and the magnetic field. This formula contains a spin exchange contribution and so requires modification if the dipolar coupling is between two different nuclei, *e.g.*, carbon-13 and hydrogen; the doublet splitting is then given by

$$\Delta\nu = \frac{\gamma_i\gamma_j\hbar}{2\pi r^3_{ij}}\ (3\cos^2\phi - 1) \tag{2}$$

The factor of $\frac{3}{2}$ has vanished because the resonance frequency of nucleus i is different from that of nucleus j (see ref. 6, p. 98).

It is interesting to substitute some numbers into equation (1), for we find the separation $\Delta\nu$ for two protons 1 Å apart to be 360·33 kHz when the field is along the interproton axis. One might therefore expect these large dipolar splittings to dominate the n.m.r. spectrum, for the largest proton spin–spin coupling rarely exceeds 20 Hz. The absence of any large splitting is, however, due to the rapid isotropic Brownian motion of the molecules. This movement means that ϕ is continually changing and to calculate the observed splitting, $\langle\Delta\nu\rangle$, from equation (1) we must take a time average over all molecular orientations, that is,

$$\langle\Delta\nu\rangle = \frac{3\gamma^2_{\mathrm{H}}\hbar}{4\pi r^3}\ \langle 3\cos^2\phi - 1\rangle \tag{3}$$

where the angular brackets $\langle\ \rangle$ are intended to denote an average over all values of ϕ. When we say that a molecule is moving isotropically, we mean that all orientations are equally probable, so $\langle 3\cos^2\phi - 1\rangle$ is zero and the dipolar splitting must vanish. On the other hand, if all molecular orientations are not equally probable, that is the motion is anisotropic, then $\langle 3\cos^2\phi - 1\rangle$

[5] E. R. Andrew, 'Nuclear Magnetic Resonance', Cambridge Univ. Press, 1955, ch. 6.
[6] A. Abragam, 'The Principles of Nuclear Magnetism', Oxford Univ. Press, 1961, p. 217.

would not vanish, and we would observe a splitting of the spectral line. Since the separation of the lines depends on r, we would have a method of measuring both internuclear distances and, indirectly, bond angles.

One obvious way of restricting the motion of a molecule is to freeze the compound and n.m.r. studies of powders, but preferably single crystals, have yielded internuclear distances.[7] The technique is not generally applicable because the dipolar coupling to nuclei in neighbouring molecules often serves to broaden the lines and obscure the splitting. In some instances the molecules are well separated by non-magnetic nuclei, *e.g.*, in inorganic hydrates, and the doublet splitting can then be resolved.[8] The intermolecular dipolar broadening can also be removed if the motion of the molecules is sufficiently rapid; however, to retain the splitting from intramolecular dipolar coupling, the motion must be anisotropic.

An apparently attractive method of restricting the motion of a molecule possessing a dipole moment is to apply a large static electric field to the sample. Under these conditions the molecules would tend to be aligned with their dipole moments parallel to the electric field and the n.m.r. spectrum should reflect this preferred orientation. Buckingham and McLauchlan[9] have shown that the application of an electric field to *p*-nitrotoluene does indeed result in a change in its n.m.r. spectrum. The increase in the separation between certain lines was attributed to an unaveraged dipolar coupling, although this interpretation has been questioned by Sears and Hahn[10] who have employed pulsed n.m.r. techniques. In view of this difficulty and the expected low degree of alignment, it is fortunate that Saupe and Englert[11] have demonstrated the very high degree of alignment that can be obtained by using the nematic mesophase of a liquid crystal as a solvent.

3 Liquid Crystals

A normal organic solid such as benzoic acid melts sharply at a given temperature to give a clear liquid and continued heating does not produce any further change, until charring! However, if the substance is capable of existing as a liquid crystal, the sharp transition at the melting point produces a turbid liquid but on further heating, there is a second phase transition when a clear isotropic liquid is produced. As we shall see, it is the cloudy mesophase or liquid crystalline state which interests us.

Although the properties of the mesophase are well characterised experimentally, no unique theory has been suggested to explain these properties. Indeed two opposing theories have been described; on the one hand, there is the swarm theory suggested by Bose[12] and on the other, Zocher's distortion theory [13]

[7] R. E. Richards, *Quart. Rev.*, 1956, **10**, 480.

[8] Z. M. El Saffar, *J. Chem. Phys.*, 1966, **45**, 4643.

[9] A. D. Buckingham and K. A. McLauchlan, *Proc. Chem. Soc.*, 1963, 144.

[10] R. E. J. Sears and E. L. Hahn, *J. Chem. Phys.*, 1966, **45**, 2753; 1967, **47**, 348.

[11] A. Saupe and G. Englert, *Phys. Rev. Letters*, 1963, **11**, 462.

[12] E. Bose, *Z. Physik*, 1909, **10**, 32.

[13] H. Zocher, *Trans. Faraday Soc.*, 1933, **29**, 945.

Fortunately, both theories give the same result when used to describe the positions of the lines in a magnetic resonance spectrum.[14] Since the distortion theory has been used as a basis for the description of the orientation of molecules in n.m.r. experiments, we shall persist in its use. Three types of liquid crystal have been characterised, and they differ in their local molecular order, although the most important liquid crystal for magnetic resonance experiments is the nematic mesophase. We now describe the general properties of liquid crystals.

The molecules of compounds which form a nematic mesophase are normally long and contain benzene rings, for example, *p*-azoxyanisole, whose nematic range extends from 118° to 135°. The intermolecular forces, together with a cooperative effect, tend to arrange the molecules with their long axes parallel. As the lateral distance between molecules increases, the tendency for the long axes to be parallel decreases; however, in the nematic mesophase, the ordering is considerable, extending over many thousands of molecules. The single degree of local ordering is shown in Figure 1. In the absence of any external restraint,
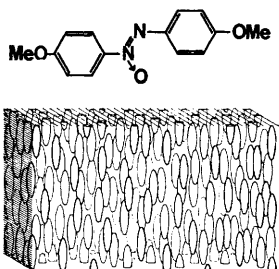

Figure 1 *The local molecular arrangement for a nematic mesophase, for example,* p-*azoxyanisole*

the orientation of the local order in one region of the sample with respect to that in another region is completely random although the direction of order does change continuously (ref. 2, p. 76). When a magnetic field greater than 1000 gauss is applied to the sample, however, the long axes of the molecules tend to become aligned parallel to the magnetic field.[15] It is useful to think of this effect in the following way. The magnetic field interacts with anisotropic components of the magnetic susceptibility, in much the same manner as an electric field interacts with an electric dipole moment, to produce partial alignment. The calculated degree of alignment for a single molecule of, for example, *p*-azoxy-anisole in a field of 20 kG, is extremely small. The anisotropy in the magnetic susceptibility is, however, enhanced by the large degree of local order and this leads to the alignment of molecules in the mesophase. The viscosity of a nematic mesophase is comparable with that of a normal liquid, such as benzene, which implies that the molecular motion is sufficiently rapid to average out the intermolecular dipolar coupling. Although the motion of the solute is also rapid, the

[14] G. R. Luckhurst, *Mol. Cryst.*, 1967, **2**, 363.
[15] W. Maier, *Z. Naturforsch.*, 1947, **2a**, 458.

anisotropic environment is capable of restricting the rotational freedom of the solute, and causing partial alignment.

The molecules in a smectic mesophase are also aligned with their long axes parallel to one another, but the local structure contains an extra degree of order which is illustrated in Figure 2. The additional order makes the structure of the
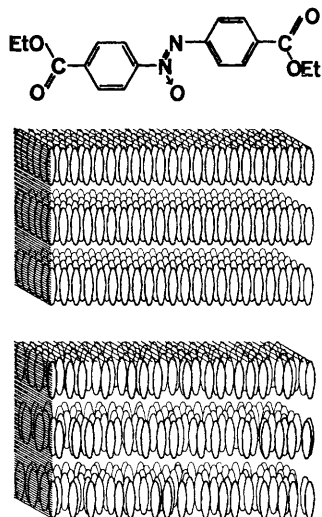

Figure 2 *The local structure of a smectic mesophase, for example, ethyl* **p**-*azoxybenzoate*

smectic mesophase similar to a solid, and as we might expect, the mesophase is rather viscous. By implication, the molecular motion must be relatively slow and so the intermolecular dipolar coupling should broaden the n.m.r. lines; however, no magnetic resonance experiment in which a smectic liquid crystal was used as a solvent has been reported. Again, the molecules making up compounds which form smectic mesophases are rather long and narrow (*e.g.*, salts of oleic acid) and frequently they contain aromatic rings carrying terminal substituents (*e.g.*, ethyl *p*-azoxybenzoate).

Cholesteryl esters form a third type of liquid crystal (the cholesteric mesophase). Although cholesterol itself melts to an isotropic liquid, most of its esters give liquid crystals whose structure is shown in Figure 3. Each molecule is represented by a single line and, within a given layer, the long axes of the molecules are parallel but the direction of alignment changes continuously on passing from one layer to the next. The resulting helical structure is responsible for the high optical activity of the cholesteric mesophase. The reason for the helix is hinted at by the following simple experiment. When right- or left-handed bolts are stacked with their long axes parallel, the threads interact in such a way that the long axes change direction from one layer to the next and a helix results.[16]

[16] E. Sackmann, S. Meiboom, and L. C. Snyder, *J. Amer. Chem. Soc.*, 1967, **89**, 5981
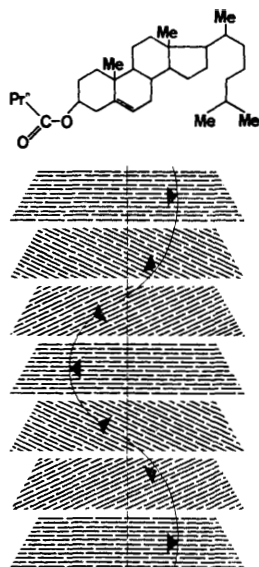
Figure 3 *The helical structure of a cholesteryl liquid crystal, for example, cholesteryl propionate*

Because of the small anisotropy associated with the magnetic susceptibility of predominantly aliphatic compounds and the complex structure of the cholesteric mesophase, it is not possible to say if solutes could be aligned with this mesophase. In fact, electron resonance experiments using cholesteryl propionate as a solvent for vanadyl acetylacetonate have failed to indicate any alignment,[17] suggesting that any anisotropy is averaged to zero by the helical structure. Another experiment with bolts suggests a method of eliminating the twist, for if one stacks bolts with alternate left- and right-handed threads, their axes remain parallel. Indeed appropriate mixing of two cholesteric compounds with opposite rotations produces a solvent which does align benzene when placed in a magnetic field.[16]

Often aqueous solutions of certain soaps (salts of long-chain sulphonic acids) exhibit anisotropic behaviour. The local order is a function of composition and can resemble either that of a smectic or nematic mesophase.[18] The viscosity of the mesophase is often extremely high, and it is surprising that molecules dissolved in them do give high-resolution n.m.r. spectra. It is even more surprising to find that methyl alcohol is highly aligned in such a solvent system.[19] We shall not mention this class of liquid crystal solvent again although they could be particularly valuable for orienting lyophilic solutes.

4 Experimental Methods

Although mixtures of cholesteric mesophases may form a useful class of solvents for alignment experiments, present results suggest that the broad background

[17] G. R. Luckhurst, Thesis, Cambridge, England, 1965, ch. 7.
[18] V. Luzzati, H. Mustacchi, and A. Skoulios, *Discuss. Faraday Soc.*, 1958, **25**, 43.
[19] K. D. Lawson and T. J. Flautt, *J. Amer. Chem. Soc.*, 1967, **89**, 5489.

n.m.r. signal may limit their usefulness in this field. We shall therefore concern ourselves entirely with nematic liquid crystal solvents.

Addition of solutes to a liquid crystal lowers both the melting point and the nematic–isotropic transition temperature, which may often become lower than the m.p.;[20] in other words, no mesophase exists or the mesophase becomes monotropic with respect to the solid. Clearly if the structure of the solute is similar to that of the solvent, it will be possible to add a large amount of solute and under favourable conditions 25 moles % may be dissolved. For this, and indeed other reasons, it is necessary to use a very sensitive n.m.r. spectrometer to measure the spectra. When the spectrometer sensitivity is not sufficient, one can use time-averaging techniques in which many spectra are added to the memory of a computer thus decreasing the random noise while increasing the signal intensity. Unfortunately, although such techniques do produce improved results, they are time-consuming and demand high instrument stability.[21]

The melting points of most nematogenic compounds, especially those which are commercially available, are above room temperature. The solution must therefore be heated in the n.m.r. probe and great care must be taken both to eliminate thermal gradients within the sample and to ensure a constant temperature ($\pm 0.1°$). The necessity arises because the alignment is extremely temperature-dependent,[22] and since the positions of the n.m.r. lines are related to the alignment, they are temperature-dependent. Thus molecules in different regions of the sample would have different n.m.r. transition frequencies and because of molecular motion these frequencies would be modulated and so cause line-broadening.[23] Recent work by Spiesecke and Bellion-Jourdan[24] and by Demus[25] has largely eliminated the need for an instrumental solution to the problem. They find that by mixing suitable nematic liquid crystals they can lower the melting point of the solid mixture to about 30° and still obtain a mesophase.

In conventional n.m.r. spectrometers the sample is rotated about an axis perpendicular to the magnetic field in order to reduce field inhomogeneities. Since the molecules of a nematic mesophase are aligned parallel to the magnetic field, such rotations should destroy the alignment and in the majority of experiments which have been reported the sample was not spun. In certain cases, however, sample rotation has been found to reduce the linewidth although it is not clear whether the improved resolution results from a reduction of magnetic field inhomogeneity or temperature gradients.[26] For successful experiments, the speed of spinning must remain constant and in the region of 5 to 10 c. per second. Because the sample is rotated about the axis parallel to the magnetic field in n.m.r. spectrometers having superconducting solenoids, these instruments may prove to be ideally suited for liquid-crystal studies.

[20] J. S. Dave and M. J. S. Dewar, *J. Chem. Soc.*, 1954, 4616.
[21] L. C. Snyder and S. Meiboom, *J. Chem. Phys.*, 1967, **47**, 1480.
[22] H. C. Longuet-Higgins and G. R. Luckhurst, *Mol. Phys.*, 1964, **8**, 613.
[23] A. Saupe, *Z. Naturforsch.*, 1965, **20a**, 572.
[24] H. Spiesecke and J. Bellion-Jourdan, *Angew. Chem. Internat. Edn.*, 1967, **6**, 450.
[25] D. Demus, *Z. Naturforsch.*, 1967, **22a**, 285.
[26] P. Diehl and C. L. Khetrapal, *Mol. Phys.*, 1968, **14**, 283.

5 Examples of the Theory

By starting with the appropriate spin Hamiltonian and describing the average orientation of the molecule with an ordering matrix[27] or with certain motional constants,[28] it is possible to derive all the results one needs to analyse n.m.r. spectra of solutes in a nematic mesophase. This approach is valuable because it treats the problem with mathematical rigour, but in this Review we shall concentrate on the physical aspects of the problem. These are best dealt with by considering specific examples, although we shall begin by introducing the concept of the ordering matrix developed by Saupe.[27]

A. The Ordering Matrix.—The analysis of the spectra of oriented molecules demands a mathematical description of the orientation and a convenient point to begin is the formula (3) for the average splitting which we write as

$$\langle \Delta \nu \rangle = \frac{3\gamma^2_H \hbar}{4\pi r^3} \langle 3 l_{za} l_{za} - 1 \rangle \tag{4}$$

In this equation we have introduced the direction cosine, l_{za}, which is the cosine of the angle between the two axes, z, the direction of the magnetic field and a, the interproton axis. We now define a quantity S_{aa} by the equation

$$S_{aa} = \tfrac{1}{2} \langle 3 l_{za} l_{za} - 1 \rangle \tag{5}$$

where S is subscribed with two a's because a occurs in both direction cosines. Since the value of $\langle l_{za} l_{za} \rangle$ is a measure of the alignment of axis a with respect to the magnetic field, S_{aa} also gives a measure of the alignment but in a more convenient form. When the motion is isotropic, S_{aa} is zero whereas if a is completely aligned along the z axis, the maximum value of S_{aa} is unity since ϕ is zero. If a is perpendicular to z, the minimum value is $-\tfrac{1}{2}$. The values of S_{bb} and S_{cc} are given by equations analogous to (5). It is possible to define quantities which involve the direction cosines of different axes, for example S_{ab}, and in general

$$S_{ij} = \tfrac{1}{2} \langle 3 l_{iz} l_{jz} - \delta_{ij} \rangle \tag{6}$$

where δ_{ij} is the Kronecker delta, taking the value 1 when i is the same as j and 0 when $i = j$. The S values can be arranged in a square array which is known as the ordering matrix. The properties of the matrix have been discussed elsewhere,[28] and we shall mention just two of these.

The sum of the diagonal elements (the trace of the matrix) is zero and this is proved simply by adding equations for S_{aa}, S_{bb}, and S_{cc} to give

$$S_{aa} + S_{bb} + S_{cc} = \tfrac{3}{2} \{ l_{za} l_{za} + l_{zb} l_{zb} + l_{zc} l_{zc} - 1 \} = 0 \tag{7}$$

since the sum of l^2_{za}, l^2_{zb}, and l^2_{zc} is unity.[29]

Combination of equations (4) and (5) gives

[27] A. Saupe, *Z. Naturforsch.*, 1964, 19a, 161.
[28] L. C. Snyder, *J. Chem. Phys.*, 1965, 43, 4041.
[29] H. Margenau and G. M. Murphy, 'The Mathematics of Physics and Chemistry', D. Van Nostrand Co. Inc., Princeton, New Jersey, 1955, 2nd edn., vol. 1, p. 139.

$$\langle \Delta \nu \rangle = \frac{3\gamma_{\mathrm{H}}^2 \hbar}{2\pi r^3} S_{aa} \tag{8}$$

which is a value for $\langle \Delta \nu \rangle$ in terms of an ordering matrix for an axis system in which one axis is parallel to the interproton vector. Often such an axis system does not reflect the geometry of the molecule which really determines the value of the ordering matrix. It is useful, therefore, to be able to relate an ordering matrix in one axis system a, b, and c to that in another system α, β, and γ. Because S transforms as a second-rank tensor the required relationship is

$$S_{\alpha\alpha} = \sum_{i,j=a}^{c} l_{\alpha i} l_{\alpha j} S_{ij} \tag{9}$$

B. Equivalent Protons.—We begin by considering 1,2,3,5-tetrachlorobenzene which for our purposes can be regarded as a simple two spin system. Because the protons are equivalent, the isotropic n.m.r. spectrum contains a single line. If, however, the spectrum is measured in the nematic mesophase then, because the molecule is oriented with respect to the magnetic field, we would expect to find the single line split into a doublet. The n.m.r. spectrum has been measured in 4,4′-di-n-heptyloxyazoxybenzene,[30] a nematic liquid crystal, and Figure 4
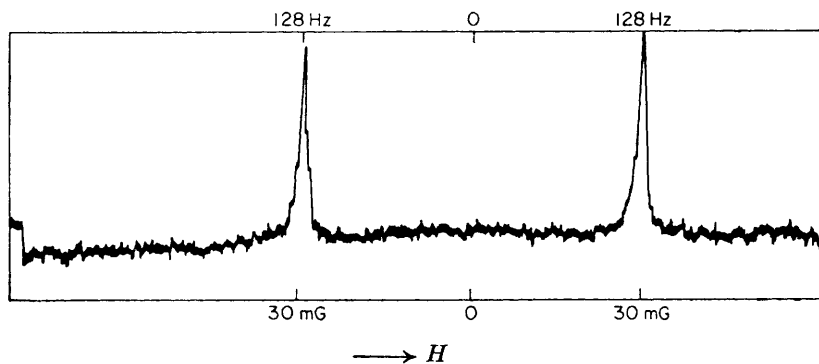

Figure 4 *The anisotropic n.m.r. spectrum of* 1,2,3,5-*tetrachlorobenzene in* 4,4′-*n-heptyloxy-azoxybenzene at* 82° [Reproduced, by permission, from *Z. Naturforsch.*, 1964, **19a**, 172]

shows that we do indeed observe two lines which are separated by 256 Hz. The absence of the solvent spectrum is general and at first sight rather surprising because the n.m.r. spectrum of the isotropic phase is readily observed. The explanation lies in the fact that 4,4′-di-n-heptyloxyazoxybenzene contains 38 protons; there are therefore 2^{38} spin levels, and if each nuclear transition had a different frequency, the n.m.r. spectrum would be far too complex to measure. Fortunately, most of the transitions are multiply degenerate and, in fact, it is fairly easy to observe the n.m.r. spectrum in the isotropic phase. The effect of

[30] G. Englert and A. Saupe, *Z. Naturforsch.*, 1964, **19a**, 172.

aligning the solvent molecules is to introduce a dipolar coupling between the protons, which splits this degeneracy and so reduces the intensity of each peak to such an extent that they vanish in the noise.

According to the theory we have developed, the observed splitting is given by

$$\langle \Delta \nu \rangle = \frac{360 \cdot 33}{r^3} S_{bb} \tag{10}$$

where we have substituted for the constants in equation (9) and $\langle \Delta \nu \rangle$ is given in kHz provided r is measured in Å. In the equation b is the interproton axis and the complete molecular axis system is shown in Figure 5. Provided
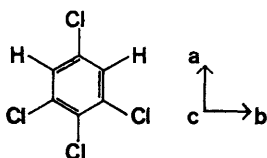

Figure 5 *The molecular axis system for 1,2,3,5-tetrachlorobenzene*

all in-plane orientations of the molecule are equally probable, the ordering matrix will be axially symmetric in the axis system a, b, c. Further since the trace of the S matrix is zero we have

$$S_{aa} = S_{bb} = -\tfrac{1}{2} S_{cc} \tag{11}$$

Substitution of the interproton distance of $4 \cdot 30$ Å into equation (10) combined with equation (11) yields a value of $0 \cdot 113$ for S_{cc}. Unfortunately, the simple n.m.r. experiment does not yield the absolute magnitude of the splitting and so we cannot determine the sign of S_{cc} except when S is greater than $\tfrac{1}{2}$. It must then be positive since the minimum value of S is $-\tfrac{1}{2}$. Other experiments show that planar molecules tend to be aligned with their planes parallel to the magnetic field and so we can be sure S_{cc} is negative.

Since S is both temperature- and concentration-dependent, the measurement of the n.m.r. spectra of molecules in liquid crystals provides an excellent technique for studying solvent–solute interactions. For example, Spiesecke[31] has measured the spectra of acetonitrile, and its isonitrile isomer in various liquid-crystal solvents under identical conditions. In three different solvents the nitrile is always more aligned than the isonitrile. It is tempting and reasonable to think that larger molecules will be more aligned than smaller ones; Spiesecke's result is then surprising, since the isonitrile is longer than the nitrile. Clearly other interactions are involved and liquid-crystal measurements should prove useful in their investigation.

When a molecule contains n equivalent protons, the isotropic n.m.r. spectrum consists of a single line whereas the anisotropic spectrum contains n equally spaced lines with a binomial distribution of intensities. Thus the spectrum of

[31] H. Spiesecke, Euratom, Italy, personal communication.

1,3,5-trichlorobenzene in 4,4′-di-n-hexyloxyazoxybenzene has three lines with intensities 1 : 2 :1 and a separation of 346 Hz between each line;[30] this is shown in Figure 6. If we assume that the ordering matrix for 1,3,5-trichlorobenzene is
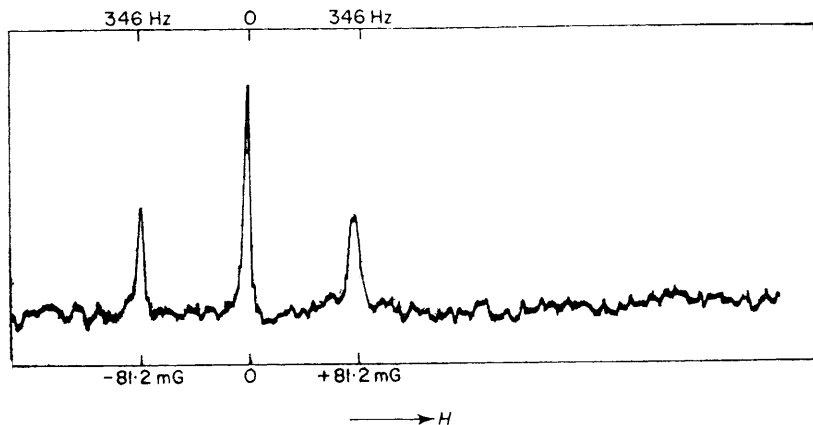

Figure 6 *The anisotropic spectrum of 1,3,5-trichlorobenzene in 4,4′-di-n-hexyloxyazoxybenzene at 80°* [Reproduced, by permission, from *Z. Naturforsch.*, 1964, 19a, 172]

axially symmetric, the average splitting is also given by equation (10). By using this together with the same interproton distance of 4·30 Å, it is calculated that S_{cc} is 0·153 where c is perpendicular to the molecular plane. Because of the different experimental conditions used in the determinations, the difference in the values of S_{cc} for the two solutes is not surprising.

C. Non-equivalent Protons.—The first published high resolution n.m.r. spectrum of a compound oriented in a nematic mesophase was that of benzene dissolved in 4,4′-di-n-hexyloxyazoxybenzene.[11] Since benzene possesses six 'equivalent' protons one might at first sight expect the anisotropic spectrum to contain six lines with binomial intensities 1 : 5 :10 :10 : 5 :1. Figure 7 shows this supposition to be false, for the spectrum contains a multitude of lines. The solution to this apparent dilemma is contained in the word 'equivalent'. 1,3,5-trichlorobenzene is shown in Figure 8 and from the diagram we can see that proton 1 is separated from protons 2 and 3 by the same distance and because the ordering of all inter-proton axes is the same, the 1–2 interaction is identical with the 1–3 and the 2–3. Proton 1, therefore, interacts equally with the other protons in the molecule, and we describe this by saying the protons are equivalent. In benzene, however, the 1–2 separation is different from the 1–3 which is also different from the 1–4. Thus proton 1 is not equally coupled to the other protons in benzene. It is easy to extend this argument to all the other protons and because each proton is coupled to at least one other proton to an extent which is not equal to its coupling to any other, the protons are non-equivalent. Musher[32] has given a more rigorous

[32] J. I. Musher, *J. Chem. Phys.*, 1967, **46**, 1537.

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Figure 7 *The anisotropic spectrum of benzene in 4,4'-di-n-hexyloxyazoxybenzene at 85°. The theoretical reconstruction is given for J_{meta} both positive (full lines) and negative (broken lines); clearly J is positive [Reproduced, by permission, from Z. Naturforsch., 1965, 20a, 572]*
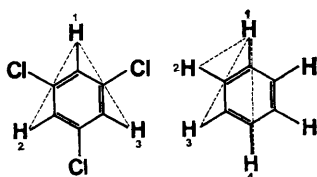
Figure 8 *The equivalence of the protons in* 1,3,5-*trichlorobenzene and benzene*

definition of equivalence and this has been shown to be identical[33] for nuclei with spins $I = \frac{1}{2}$ to that given earlier by Englert and Saupe.[30] Application of the concept of equivalence is a useful aid to the interpretation of both isotropic and anisotropic n.m.r. spectra and has been employed in the partial analysis of the spectrum of ethyl iodide dissolved in 4,4′-n-hexyloxyazoxybenzene.[34]

The anisotropic n.m.r. spectrum of benzene has been completely analysed by use of computer techniques,[35] and as one might expect the spectrum does contain a large amount of information. Indeed it is possible to determine the absolute magnitudes of the *ortho* and *meta* spin–spin coupling constants; Saupe[23] has arrived at identical conclusions by using group-theoretical methods. The next section indicates how the sign of the spin–spin coupling constant can be determined from anisotropic n.m.r. spectra.

D. The Sign of the Spin–Spin Coupling Constant.—The conceptual basis of the technique is best understood by considering a specific example and the determination of the sign of J_{CH} in acetonitrile is particularly illuminating. The n.m.r. spectrum of acetonitrile aligned in 4,4′-di-n-hexyloxyazoxybenzene has been measured[36] and the high degree of alignment of such a relatively small molecule may indicate a specific solute–solvent interaction. The molecule contains three equivalent protons and the anisotropic spectrum shown in Figure 9 consists of the expected 1:2:1 triplet with a spacing of 3495 Hz. We are interested in the sign of J_{CH}, and since the natural abundance of a carbon isotope with a nuclear spin is small, the methyl carbon was enriched with carbon-13, which has spin $\frac{1}{2}$. The effect of the carbon-13–proton coupling is to split each line in the original three-line spectrum into a doublet. Because the enrichment was not complete, the spectrum given in Figure 9 also contains a 1:2:1 triplet coming from molecules without carbon-13.

The magnitude of the proton dipolar splitting is given by

$$\langle \Delta \nu \rangle = \frac{-3\gamma^2_{H}\hbar}{4\pi r^3} S_{cc} \tag{12}$$

where r is the interproton distance and c is an axis parallel to the length of the

[33] A. Saupe and J. Nehring, *J. Chem. Phys.*, 1967, **47**, 5459; J. I. Musher, *ibid.*, p. 5460.
[34] C. M. Woodman, *Mol. Phys.*, 1967, **13**, 365.
[35] L. C. Snyder and E. W. Anderson, *J. Amer. Chem. Soc.*, 1964, **86**, 5023.
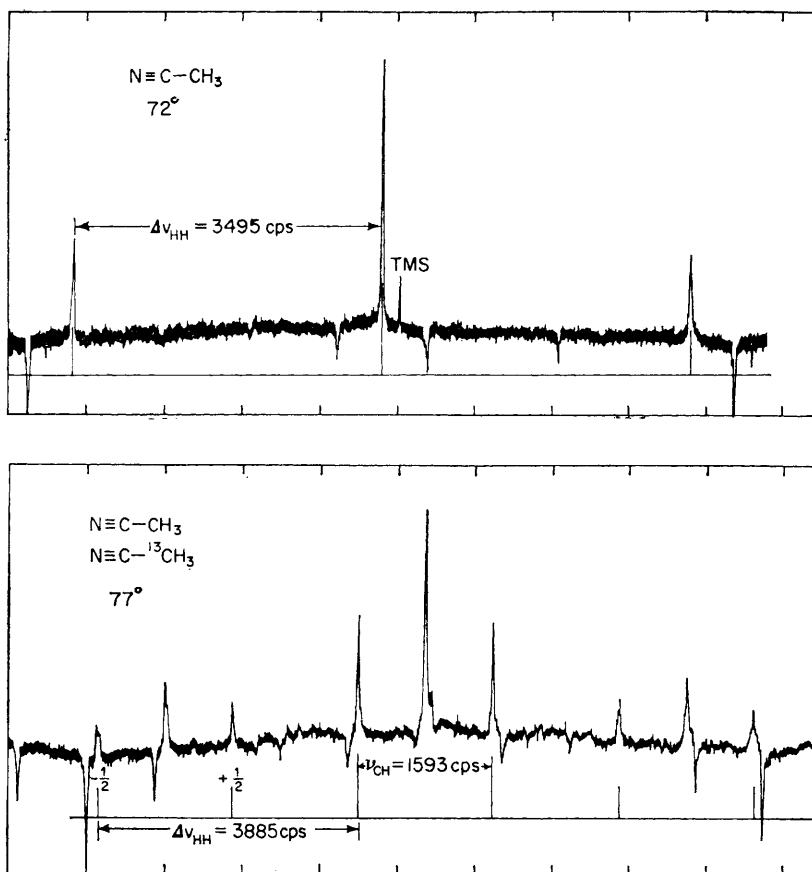[36] G. Englert and A. Saupe, *Mol. Cryst.*, 1966, **1**, 503.

Figure 9 *The anisotropic n.m.r. spectra of acetonitrile and* [2–^{13}C]*acetonitrile in 4,4'-di-n-hexyloxyazoxybenzene* [Reproduced, by permission, from *Mol. Cryst.*, 1966, **1**, 503]

molecule. It is important to note that since the three protons are equivalent, the splitting does not depend on the magnitude of the proton spin–spin coupling.[32,33] This is not the case for the carbon-13–proton splitting, for the nuclei cannot be equivalent and so the splitting is the sum of the spin–spin and the dipolar coupling

$$\langle \Delta\nu \rangle_{CH} = J_{CH} + \frac{\gamma_C \gamma_H \hbar}{\pi R^3} S_{\alpha\alpha} \tag{13}$$

where R is the internuclear distance, α is parallel to the internuclear axis, and the dipolar splitting was calculated from equation (2) because the nuclei are not identical. The element $S_{\alpha\alpha}$ is readily related to the ordering matrix in the orthogonal axis system a, b, c through equation (9), and is

$$S_{\alpha\alpha} = \frac{S_{cc}}{2} \{ 3l_{\alpha c}l_{\alpha c} - 1 \} \tag{14}$$

where l_{xc} is the direction cosine between the carbon–hydrogen bond and the length of the molecule [N.B., the axial symmetry of the ordering matrix was used in deriving equation (14)]. It is straightforward to relate l_{xc} to the internuclear distances R and r to give

$$\langle \Delta\nu \rangle_{CH} = J_{CH} + \frac{\gamma_C \gamma_H \hbar}{2\pi R^3} \left\{ 2 - \frac{r^2}{R^3} \right\} S_{cc} \tag{15}$$

To proceed further, we must substitute numbers into equation (15); $\langle \Delta\nu \rangle_{CH}$ is 1593 Hz and J_{CH}, measured by raising the temperature of the sample above the nematic–isotropic transition point, is 136·5 Hz. The value of S_{cc} calculated from the proton–proton splitting of 3091 Hz (the value given in Figure 9 is incorrect[37]) and an interproton distance of 1·805 Å is 0·1009. Although this calculation does not yield the sign of S_{cc}, we can be sure it is positive by analogy with the positive sign found for acetylenic compounds[31] by use of a technique to be described in section 6. The value of S_{cc} together with $R = 1·108$ Å allows us to calculate the last term in equation (15) to be 1459·9 Hz and, putting the numbers together, we find 1593 Hz must equal 1459·9 $\pm$ 136·5 Hz, an equation which can only be satisfied if J is positive, as predicted by theory.[38] An identical result has been found by studying both the proton and fluorine spectra of methyl fluoride dissolved in a liquid crystal,[39] although the analysis is more complex. In the case of benzene itself the absolute signs of J came from a full analysis of the spectrum. The analysis reveals that the spectrum contains two types of line, those whose positions depend on the partially averaged dipolar splitting and those whose positions depend also on the spin–spin coupling constants. By fitting the positions of the first class of line, the relative bond lengths and the degree of alignment can be determined. With this knowledge, the positions of the second class are fitted simply by varying the J's thus determining their absolute magnitudes.

E. Molecular Geometry.—The dipolar splitting which is observed in anisotropic n.m.r. spectra depends on two factors, the degree of orientation, S, and the internuclear distance, r. If liquid-crystal solvents are to be used to determine bond lengths, we must have some way of measuring S. The most obvious and accurate way of making this measurement is to have an internal molecular standard. In other words, we determine the dipolar splitting for two protons with a known internuclear distance and use this to calculate S. Armed with the value for the alignment we can calculate the r from the observed dipolar splittings for the other magnetic nuclei.

The basis for such a determination is well illustrated by our previous analysis of the splittings observed in [2-^{13}C]acetonitrile. Equations (12) and (15) show that both the proton–proton splitting and the proton–carbon-13 splitting

[37] A. Saupe, University of Freiburg, Germany, personal communication.
[38] D. M. Grant and M. Barfield, 'Advances in Magnetic Resonance', ed. J. S. Waugh, Academic Press, New York, 1965, vol. 1.
[39] R. A. Bernheim and B. J. Lavery, *J. Amer. Chem. Soc.*, 1967, **89**, 1279.

(adjusted for J_{CH}) are proportional to S_{cc}. By eliminating S_{cc}, we find equation

$$\frac{\langle \Delta \nu \rangle_{CH} - J_{CH}}{\langle \Delta \nu \rangle_{HH}} = \frac{2r^3}{3R^3} \frac{\gamma_C}{\gamma_H} \left\{ \frac{r^2}{R^2} - 2 \right\} \tag{16}$$

and can determine the ratio r/R. The HCH bond angle is simply $2 \sin^{-1} r/R$ and values have been determined for this from the anisotropic n.m.r. spectra of several methyl compounds;[40] the results of these measurements are given in the Table.

Table

Compound	Solvent*	Bond angle from n.m.r.	Bond angle from microwave	Ref.
CH_3CN	I	$109° \; 2' \pm 2'$	$109°16'$	a
	II	$108°56' \pm 2'$		
CH_3NC	—	$109°45'$ †	$109°7'$	b
CH_3OH	II	$110° \; 3' \pm 8'$	$109° \; 2' \pm 45'$	c
CH_3I	I	$111°42' \pm 2'$	$111°25'$	d

* I is 4,4'-di-n-hexyloxyazoxybenzene and II is 4-n-octyloxybenzoic acid.
† Ref. 31.

a L. F. Thomas, E. I. S. Sherrad, and J. Sheridan, *Trans. Faraday Soc.*, 1955, **51**, 619; *b* C. C. Costain, *J. Chem. Phys.*, 1958, **29**, 864; *c* P. Venkateswarlu and W. Gordy, *J. Chem. Phys.*, 1955, **23**, 1200; *d* S. L. Miller, L. C. Aamodt, G. Dousmanis, C. H. Townes, and J. Kraitchman, *J. Chem. Phys.*, 1952, **20**, 1112.

The Table shows that the n.m.r. technique is capable of greater accuracy than microwave methods. In comparing the two sets of data, one must realise that while the n.m.r. results were obtained in the liquid phase, the microwave results are for molecules in the gas phase. Indeed, one of the strengths of the liquid-crystal technique is its ability to determine molecular geometries in the liquid phase. The small differences in the bond angles may be attributed to the difference in the nature of the phase. An alternative explanation is hinted at by the measurement of the anisotropic spectra of spherically symmetric molecules. Snyder and Meiboom[41] have measured the n.m.r. spectra of tetramethylsilane and neopentane in 4,4'-di-n-hexyloxyazoxybenzene. Since these molecules are not expected to be aligned by a nematic liquid crystal, it is surprising to find that the spectra consist of a 1:2:1 triplet, and not a single line. The splitting undoubtedly comes from the dipolar coupling between the protons in a particular methyl group. It is thought that the methyl group is distorted by the neighbouring liquid-crystal molecules, and if the splitting is to be observed the distortion must depend on the orientation of the methyl group with respect to the field.

In the preceding sections we have been mainly concerned with first-order

[40] A. Saupe, G. Englert, and A. Povh, *Adv. Chem. Ser.*, 1967, **63**, 51.
[41] L. C. Snyder and S. Meiboom, *J. Chem. Phys.*, 1966, **44**, 4057.

n.m.r. spectra; that is, those in which the spacings between the lines are multiples of the coupling constants in the spin Hamiltonian. Let us now consider 3,5-dichlorobenzoic acid, whose anisotropic n.m.r. spectrum has been measured in 6-n-hexyloxy-2-naphthoic acid.[42] The solute is similar to 1,3,5-trichlorobenzene which was considered earlier, but now the ordering matrix is not axially symmetric because the carboxyl groups of both solute and solvent form hydrogen bonds,[43] so that the 1–4 axis is more aligned than the 2–6. This added degree of alignment spoils the first-order analysis and instead of a 1:2:1 triplet the spectrum contains eight lines. The analysis of the line separations is straightforward, and it is fairly easy to obtain analytic expressions in terms of the dipolar coupling constants, which are themselves given by equations similar to (12).
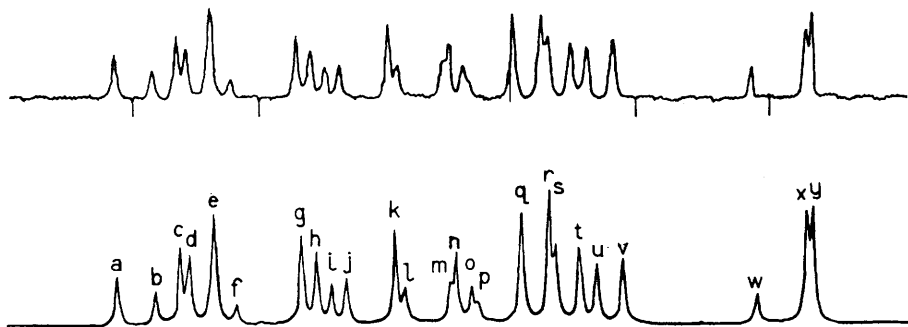

Figure 10 *A comparison of the experimental and theoretical n.m.r. spectrum of cyclopropane in a nematic mesophase. Since the spectrum is symmetrical, only the low-field half is given* [Reproduced, by permission, from *J. Chem. Phys.*, 1967, **47**, 1480]

When the molecule contains many protons interacting differently, it is not possible to obtain analytic expressions for the line separations and computer techniques must be used to obtain the coupling constants. A particular *tour de force* of the liquid-crystal technique has been the determination of the geometry of cyclopropane[21] by measuring the n.m.r. spectra of molecules not containing carbon-13 and of those which do. The many magnetic interactions within cyclopropane have been successfully analysed as one can see from Figure 10 where the theoretical spectrum is compared with the experimental one. Although the geometry determined by n.m.r. is in satisfactory agreement with that obtained from gas-phase electron diffraction, the analysis of the dipolar coupling constants to obtain the bond lengths emphasised an interesting point.[44]

The dipolar couplings, obtained from the spectrum, are of course proportional to $1/r^3$. Such a simple relationship, however, neglects the vibrations of the molecule and strictly speaking the dipolar coupling is proportional to an average over all vibrations, *i.e.*, to $\langle 1/r^3 \rangle$. It is convenient to write r, which is

[42] G. Englert and A. Saupe, *Z. Naturforsch.*, 1965, **20a**, 1401.
[43] J. C. Rowell, W. D. Phillips, L. R. Melby, and M. Panar, *J. Chem. Phys.*, 1965, **43**, 3442.
[44] J. A. Ibers and D. P. Stevenson, *J. Chem. Phys.*, 1958, **28**, 929.

the separation at any given time, as the sum of the equilibrium internuclear distance, r_e and an extension δr. The function we require is $\langle 1/(r_e + \delta r)^3 \rangle$ and provided $\langle \delta r \rangle / r_e$ is small we can expand this quantity as a power series in $\langle \delta r \rangle / r_e$ to give

$$\langle 1/(r_e + \delta r)^3 \rangle = \frac{1}{r_e{}^3} \left\{ 1 - \frac{\langle \delta r \rangle}{r_e} + \frac{6 \langle \delta r^2 \rangle}{r_e{}^2} - .. \right\} \qquad (17)$$

Provided r_e is defined as the average value of r, then $\langle \delta r \rangle$ vanishes and the dipolar coupling is proportional to $(1/r_e{}^3)[1 + 6(a/r_e{}^2)]$ where a is the root-mean-square vibrational displacement. Both X-ray and electron diffraction techniques measure $\langle r_e + \delta r \rangle$ which is just the equilibrium separation, and the values for n.m.r. will be related to these by

$$r_{\mathrm{nmr}} = r_e \left\{ 1 - 2 \left(\frac{a}{r_e} \right)^2 \right\} \qquad (18)$$

The calculation of a for a given vibration is an extremely difficult task and vibrational effects may be a potential source of error in the use of n.m.r. to measure bond lengths. Fortunately, in the case of cyclopropane, the discrepancies are rather small, in agreement with estimates[45] of a/r_e for a methylene group of 0·1. Strictly the dipolar coupling is proportional to the average value of $1/r^3$ and S but when the molecule is rigid, the effect of vibrations on S is negligible. If, however, the molecule is non-rigid, such as n-pentane, we should also have to allow for the dependence of S on the internal motion of the molecule.

The examples of structure determination which have been discussed were useful in (*a*) establishing the validity of the liquid crystal technique and (*b*) showing the small effect on molecular dimensions on passing from the gas to the liquid phase. As one might hope, the technique is being applied to unknown structures and a particularly fruitful field would seem to be organometalic complexes. For example, one would like to know whether the protons in cyclobutadiene iron tricarbonyl shown in Figure 11 are arranged in a square or rectangular con-
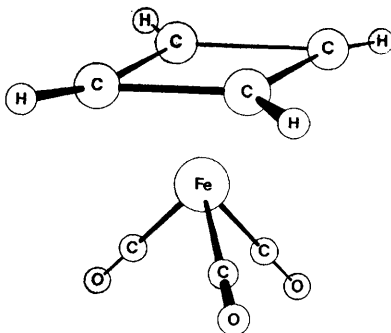

Figure 11 *The structure of cyclobutadiene iron tricarbonyl*

[45] O. Bastiansen, F. N. Fritsch, and K. Hedberg, *Acta Cryst.*, 1964, **17**, 538.

figuration. This is an ideal problem for liquid-crystal n.m.r. and the spectrum of the complex has been recorded in 4,4'-di-n-hexyloxyazoxybenzene.[46] The spectrum is not first order and contains eight lines, as one would expect for a square configuration, although the intensities of the lines are not in complete agreement with theory. If the departure of the intensities from their theoretical values is ascribed to a small distortion of the ring, the ratio of unequal sides is found to be 0.9977 ± 0.0045, that is, the departure from a square configuration is very small.

6 The Chemical Shift Tensor

The previous sections have shown how anisotropic n.m.r. spectra are dominated by the nuclear dipolar coupling. However, the chemical shift can also be anisotropic and this anisotropy will be observed in the spectra as a shift in the positions of the lines. Consider a single nucleus whose chemical shift tensor is σ_{ab} where a, b, and c form a molecule fixed-axis system. The chemical shift, σ, measured from the isotropic spectrum is one third of the trace of σ_{ab} but in the nematic mesophase the chemical shift, $\langle \sigma \rangle$, is given by

$$\langle \sigma \rangle = \sum_{i,j=a}^{c} \sigma_{ij} \langle l_{zi} l_{zj} \rangle \tag{19}$$

This can be rewritten by use of the ordering matrix defined in equation (6) as

$$\langle \sigma \rangle = \sigma + \frac{2}{3} \sum_{i,j=a}^{c} \sigma_{ij} S_{ij} \tag{20}$$

Under certain conditions equation (20) can be used to determine the signs of the elements of the ordering matrix. Consider the acetylenic proton in methylacetylene. The symmetry of the molecule demands that both S_{ab} and σ_{ab} are axially symmetric about the long axis a. Equation (20) can therefore be written as

$$\langle \Delta\sigma \rangle = \frac{2}{3} S_{aa}(\sigma_{aa} - \sigma_{bb}) \tag{21}$$

where $\langle \Delta\sigma \rangle$ is the difference in the chemical shift for the anisotropic and isotropic spectra. It is important to realise that the sign of $\langle \Delta\sigma \rangle$ follows immediately from experiment, and if the sign of $(\sigma_{aa} - \sigma_{bb})$ is known the sign of S_{aa} can be determined. The difference $(\sigma_{aa} - \sigma_{bb})$ can be calculated with some certainty and is positive for acetylenic protons.[47] Since $\langle \Delta\sigma \rangle$ is positive, the ordering matrix element, S_{aa} must also be positive,[36] implying that methylacetylene is aligned with its long axis parallel to the magnetic field.

The derivation of equation (19) contains a hidden assumption for it treats the

[46] C. S. Yannoni, G. P. Caesar, and B. P. Dailey, *J. Amer. Chem. Soc.*, 1967, **89**, 2833.
[47] J. A. Pople, *Proc. Roy. Soc.*, 1957, *A*, **239**, 541.

molecule as if it were rotating in an isotropic potential. Clearly such an approximation is not valid for the anisotropic fields created by the liquid-crystal solvent are responsible for the alignment. The anisotropy is expected to produce a change $\Delta^\circ\sigma$ in the chemical shift even if the tensor were isotropic.[48] There are two contributions to $\Delta^\circ\sigma$; the first results from the change in the volume susceptibility of the sample when the solvent passes from the isotropic to the nematic mesophase. (The volume susceptibility determines the value of the magnetic field inside the sample.) The other contribution depends on the anisotropy of the solvent effects often encountered in n.m.r. Since the total magnitude of the two effects is difficult to calculate, the use of liquid crystals may not yield reliable values for the anisotropy in the chemical shift tensor. Although such comments cast doubt on the value of $(\sigma_{aa} - \sigma_{bb})$ determined for the acetylenic proton in methylacetylene, they do not affect the conclusion that S_{aa} is positive.

[48] A. D. Buckingham and E. E. Burnell, *J. Amer. Chem. Soc.*, 1967, **89**, 3341.