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Theoretical and Physical Aspects of Nuclear Shielding

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1 Introduction

This Chapter covers the same ground as the first Chapter of Volume 8 and the first part of the first Chapter of Volume 9, with slightly different emphasis according to the nature and distribution of original papers published during the review period June 1st 1979 to May 31st 1980. The theoretical formulation of shielding tensor components and questions of gauge invariance have been covered admirably by W. T. Raynes in past volumes of this Series and are not repeated here. Treated for the first time are the theoretical aspects of chiral shifts and the dependence of isotope shifts on structure.

2 Calculations of Nuclear Shielding

A. General Theory.—In this review period there has been a renewed interest in the current-density approach to nuclear shielding.[1,2] The local shielded field $\boldsymbol{B}_{\text{eff}}(\boldsymbol{r}_0)$ at the nucleus located at $\boldsymbol{r}_0$ is

$$\boldsymbol{B}_{\text{eff}}(\boldsymbol{r}_0) = (1-\boldsymbol{\sigma})\boldsymbol{B}_0 = (1-\boldsymbol{\sigma})B_0\boldsymbol{n} \tag{1}$$

where $\boldsymbol{n}$ is a unit vector in the direction of the magnetic field. The shielding field $\boldsymbol{B}'(\boldsymbol{r}_0) = -\boldsymbol{\sigma}\boldsymbol{B}_0$ and the induced magnetic moment $\boldsymbol{m}$ are related to the current density $\boldsymbol{j}$ by

$$\boldsymbol{B}'(\boldsymbol{r}_0) = \int \frac{(\boldsymbol{r}-\boldsymbol{r}_0)\times\boldsymbol{j}}{|\boldsymbol{r}-\boldsymbol{r}_0|^3}\,\mathrm{d}V \tag{2}$$

and

$$\boldsymbol{m} = \tfrac{1}{2}\int \boldsymbol{r}\times\boldsymbol{j}\,\mathrm{d}V \tag{3}$$

In the semi-classical method of calculating magnetic shielding and magnetizability, the quantum-mechanical charge-density distribution of a molecule (obtained by some SCF procedure, for example) is input into the classical equations of motion of an electron density $e\rho(\mathbf{r})$. It has previously been shown[3] that the current density can be calculated from the classical equations of motion of the electron density by

$$\boldsymbol{j} = (e^2\mu_0/m_e)\,B_0(\boldsymbol{r}\times\boldsymbol{n}+\nabla U) \tag{4}$$

where e, μ_0, and m_e are the usual physical constants and U is the 'velocity potential' introduced by Salzer and Schmeidel.[3] The paramagnetic current density is asso-

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[1] K. Salzer, *Ann. Phys. (Leipzig)*, 1979, **36**, 91.
[2] C. J. Jameson and A. D. Buckingham, *J. Phys. Chem.*, 1979, **83**, 3366.
[3] K. Salzer and H. Schmiedel, *Ann. Phys. (Leipzig)*, 1977, **34**, 415.

ciated with $\rho(\boldsymbol{r})\nabla U$, whereas the diamagnetic current density is associated with $\rho(\boldsymbol{r}\times\boldsymbol{n})$. The equation of continuity for the currents induced by the external magnetic field

$$\operatorname{div}\boldsymbol{j} = \operatorname{div}[\rho(\boldsymbol{r}\times\boldsymbol{n}+\nabla U)] = 0 \tag{5}$$

must be satisfied.

One might solve this equation by finding parametrized classes of functions U (variational method).[4] Recently, Salzer developed a method of numerical solution of this partial differential equation and used the H_2 molecule as a test case.[1] His shielding tensor for H_2 is in very good agreement with the results by Raynes *et al.*[5] In molecules with complicated electron density functions, in which cases the adjustment of the variation function for the velocity potential U is difficult, the advantages of Salzer's procedure become evident. By use of a finer grid of points in those regions where the density function is rapidly changing, the numerical method can be applied to any charge-density distribution.

In another approach, the current density is expanded as a series in the magnetic field

$$\boldsymbol{j} = \boldsymbol{j}^{(0)}+\lambda\boldsymbol{j}^{(1)}+\lambda^2\boldsymbol{j}^{(2)}+\ \ldots \tag{6}$$

The magnetic shielding density function $\boldsymbol{\sigma}^{\mathrm{N}}(\boldsymbol{r})$ is defined by

$$\boldsymbol{\sigma}^{\mathrm{N}}(\boldsymbol{r})\cdot\boldsymbol{B} = \frac{-(\boldsymbol{r}-\boldsymbol{r}_0)\times\boldsymbol{j}}{|\boldsymbol{r}-\boldsymbol{r}_0|^3} \tag{7}$$

where $\boldsymbol{j}^{(0)}$ is zero for a diamagnetic molecule and $\boldsymbol{j}^{(1)}$ is calculated using the coupled Hartree–Fock formulation.[6]

The shielding density function is a surface in four-dimensional space. It is the analogue of the polarizability density function and the charge density. Upon integration these density functions yield the nuclear shielding, the polarizability, and the total number of electrons, respectively. Maps of surfaces that are plots of charge density on a particular plane in the molecule-fixed axes have been found to be useful in discussions of bonding and force constants. In the same way, shielding density maps could be used in discussions of chemical shifts. Shielding density maps have been calculated and discussed for the H atom, the F^- ion, and the H and F nuclei in HF molecule.[2] Shielding changes upon bond formation involving these species are interpreted in terms of density difference maps.

A fundamental relationship between the electronic $\boldsymbol{g}$ tensor of a molecule and the nuclear magnetic shielding tensor has been shown by Hegstrom.[7] A theoretical formulation of the $\boldsymbol{g}$ tensor in its most general form is presented. The $\boldsymbol{g}$ tensor arises in the interaction $\mu_{\mathrm{B}}\boldsymbol{S}\cdot\boldsymbol{g}\cdot\boldsymbol{B}$ between the total electron spin of a molecule $\boldsymbol{S}$ and the external field $\boldsymbol{B}$. Hegstrom shows that it can be written for a diatomic molecule AB as

$$\boldsymbol{g} = g_{\mathrm{e}}(1-<p_{\mathrm{e}}{}^2/2m_{\mathrm{e}}>)\mathbf{1}+\boldsymbol{g}_{\mathrm{aniso}}+(g_{\mathrm{e}}-1)\sum_{\mathrm{N}\,=\,\mathrm{A,B}} Z_{\mathrm{N}}\boldsymbol{\sigma}_{\mathrm{N}}. \tag{8}$$

The first term is an isotropic correction to the free-electron g factor (g_{e}) arising from the relativistic mass increase of the electron, the second term is a small anisotropic correction, and the third term arises from the spin–orbit coupling terms. Z_{N} is the

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[4] B. M. Ludwig and J. Voitlander, *Z. Naturforsch., Teil A*, 1970, **25,** 867.
[5] W. T. Raynes, A. M. Davies, and D. B. Cook, *Mol. Phys.*, 1971, **21,** 123.
[6] G. H. F. Diercksen and R. McWeeny, *J. Chem. Phys.*, 1966, **44,** 3554.
[7] R. A. Hegstrom, *Phys. Rev. A*, 1979, **19,** 17.

nuclear charge and $\boldsymbol{\sigma}_N$ is the nuclear shielding tensor. The theory is applied to the calculation of the electronic $\boldsymbol{g}$ tensors for the $^2\Sigma$ ground states of the simplest paramagnetic molecule, $H_2{}^+$, and its isotopic relatives HD^+ and $D_2{}^+$. The components of the nuclear magnetic shielding tensor are calculated as functions of internuclear distance, tabulated, and compared with previous calculations. Finally, an interesting relationship between the second-order part (paramagnetic term) of the nuclear magnetic shielding tensor and the second-order part of the *electron* spin–rotation tensor is pointed out. This is exact for a one-electron molecule and may lead to useful approximations for a many-electron molecule. Note that for diamagnetic molecules the relationship between the second-order part of the nuclear magnetic shielding tensor and the *nuclear* spin–rotation tensor has been in wide use for many years as a means of obtaining an experimental measure of the former from accurate measurements of the latter. Such relationships between different magnetic properties are extremely useful because they provide consistency checks for experimental measurements of the different properties as well as for the corresponding theoretical calculations.

B. *Ab Initio* Calculations.—Coupled Hartree–Fock perturbation theory has been applied by Lazzeretti and Zanasi to evaluate second-order magnetic properties of the HCl, H_2S, PH_3, and SiH_4 molecules.[8] An efficient procedure for processing only symmetry distinct two-electron integrals in the coupled H–F algorithm is introduced, which leads to sizeable gains in computer time (roughly 3 to 12 times faster for the entire procedure than was achieved for previous calculations). This allows the use of very large basis sets, with particular attention to the polarization functions for the second row atoms. The paramagnetic contribution to nuclear shielding is dramatically dependent on the quality of the basis sets. With the improvement of basis sets the paramagnetic terms become more accurate and a higher degree of gauge dependence for the total shielding is achieved. The results for ^{35}Cl and ^{31}P can be compared with experiment and the agreement is good. The results for ^{1}H show good agreement with experiment except for PH_3. Keil and Ahlrichs[9] reported coupled Hartree–Fock calculations of nuclear magnetic shielding in LiH, HF, and PH_3 in its C_{3v} and D_{3h} structure using a 'well-polarized' basis. The average ^{31}P shielding increases by 11.7 p.p.m. in going from the C_{3v} to the D_{3h} structure. Results of all-electron *ab initio* calculations of ^{31}P magnetic shielding are compared in Table 1 with experimental (spin–rotation-derived) results and also with calculations using a pseudo-potential for the K and L shells. It is clear that the pseudo-potential approach leads to some error when compared with an all-electron calculation using the same set of valence shell functions.[10] It is also clear that a flexible basis set with improved polarization functions on the heavy atom gives much better results.[8, 9]

An *ab initio* calculation of the ^{31}P shielding in the phosphate group has been carried out.[14] Since the ^{31}P nuclear shielding is widely used as a tool for the study of

[8] P. Lazzeretti and R. Zanasi, *J. Chem. Phys.*, 1980, **72,** 6768.
[9] F. Keil and R. Ahlrichs, *J. Chem. Phys.*, 1979, **71,** 2671.
[10] J. Ridard, B. Levy, and Ph. Millie, *Mol. Phys.*, 1978, **36,** 1025.
[11] S. Rothenberg, R. H. Young, and H. F. Schafer, *J. Am. Chem. Soc.*, 1970, **92,** 3243.
[12] T. D. Gierke and W. H. Flygare, *J. Am. Chem. Soc.*, 1972, **94,** 7277.
[13] P. O. Davis, R. M. Neumann, S. C. Wofsy, and W. Klemperer, *J. Chem. Phys.*, 1971, **55,** 3564.
[14] F. R. Prado, C. Giessner-Prettre, B. Pullman, and J. P. Daudey, *J. Am. Chem. Soc.*, 1979, **101,** 1737.

Table 1 *Comparison of the results of some calculations of the* ^{31}P *nuclear shielding tensor for the* PH_3 *molecule at its equilibrium configuration, all values in* p.p.m., *gauge origin on* P, *with the spin–rotation-derived experimental value*

	Ref. 11	*Pseudo pot. Ref.* 10	*Ref.* 10	*Ref.* 9	*Ref.* 8	*Expt.*[a]
$\sigma_{xx}{}^{d}$	981.52	979.5	981.53	981.35	981.85	983
$\sigma_{zz}{}^{d}$	979.99	977.9	979.93	979.96	980.36	985
σ^{d}	981.01	978.9	980.99	980.89	981.35	984
$\sigma_{xx}{}^{p}$		−319.0	−339.14	−378.80	−391.03	−370
$\sigma_{zz}{}^{p}$		−341.8	−364.15	−416.21	−429.31	−421
σ^{p}		−326.6	−347.48	−391.27	−403.79	−387
σ_{xx}		660.5	642.39	602.55	590.82	612
σ_{zz}		636.1	615.78	563.75	551.05	564
σ_{av}		652.3	633.51	589.62	577.56	597

[a] Derived by Gierke and Flygare[12] using spin–rotation constants from Ref. 13.

the backbone of nucleic acids and of the polar head of phospholipids, *ab initio* calculations of ^{31}P shielding in model compounds of the biological phosphate groups are important. One of the applications of ^{31}P n.m.r. that is of interest is the determination of the population of the *gauche–gauche* conformer (rotation angles about the P–O ester bonds both approximately 60°). Such an estimation is possible only if the chemical shift difference between the pure *gauche–gauche* (*gg*) and the pure *gauche–trans* (*gt*) conformations is known. While a mononucleotide with a pure *gg* phosphate group is known, there is no equivalent stable rigid compound with a *gt* phosphate group. For this reason theoretical calculations are necessary. The computations were carried out for $X_2PO_4^-$ anions, with one or both X = Me, H.[14] The authors conclude that: (*a*) the geometry of the conformers seems to be the principal factor in the determination of the ^{31}P chemical shielding, as it is for the energy difference between the two conformers, (*b*) the value of the chemical shift, $\sigma_{gg}-\sigma_{gt}$ is most probably in the range −3.5 to −6.5 p.p.m., and (*c*) the paramagnetic component is the determining term for the calculated chemical shift variations. These calculations are able to reproduce correctly the order of magnitude of the anisotropy of the shielding tensor, $\Delta\sigma = \sigma_{33} - \frac{1}{2}(\sigma_{22} + \sigma_{11}) = 174$ p.p.m., as well as the orientation of each of its principal axes that have been measured for diester phosphates.[15]

During this review period probably the most accurate calculations of first-order properties of the molecules N_2 and CO have been reported.[16,17] The results of configuration interaction calculations of the diamagnetic shielding for these molecules by Amos are compared with SCF and approximate calculations in Table 2. It has been known that the method of Flygare *et al.*[12] gives very good agreement with *ab initio* calculations insofar as the isotropic average of σ^{d} is concerned, although it is somewhat less accurate in the prediction of the anisotropy of σ^{d}. In Table 2 we see that the average σ^{d} by all three methods are in agreement to within a few tenths of a p.p.m.

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[15] J. Herzfeld, R. Griffin, and R. Haberkorn, *Biochemistry*, 1978, **17**, 2711.

[16] R. D. Amos, *Mol. Phys.*, 1980, **39**, 1.

[17] R. D. Amos, *Chem. Phys. Lett.*, 1979, **68**, 536.

Table 2 *Diamagnetic contribution to chemical shielding, in* p.p.m., *with gauge origin at the nucleus of interest, at three levels of calculation*

	Aprox.[a]	*SCF*	*CI*	
^{15}N in N_2	348.9	338.42[18]	339.31[16]	$\sigma_{\parallel}^{d}$
$R = 2.07$ au	401.6	407.19	407.36	$\sigma_{\perp}^{d}$
	384.0	384.27	384.68	σ_{av}^{d}
^{13}C in CO	280.4	271.15[19]	271.26[17]	$\sigma_{\parallel}^{d}$
$R = 2.132$ au	349.0	354.16	354.13	$\sigma_{\perp}^{d}$
	326.1	326.49	326.51	σ_{av}^{d}
^{17}O in CO	418.7	411.12[19]	410.83[17]	$\sigma_{\parallel}^{d}$
	456.2	461.72	461.73	$\sigma_{\perp}^{d}$
	443.7	444.85	444.76	σ_{av}^{d}

[a] Method of Flygare *et al.*[12]

Ab initio calculations of the electric field dependence of nuclear magnetic shielding and magnetizability are reported.[20] The components of the tensors $\boldsymbol{\sigma}^{(1)}$ and $\boldsymbol{\sigma}^{(2)}$ (discussed in an earlier volume[21]) that describe the linear and quadratic electric field dependence of the nuclear magnetic shielding, were computed for H_2 and HF molecules using a gauge-invariant double-finite-perturbation SCF approach.

C. Semi-empirical Calculations.—In this review period we have seen a number of intermediate neglect of differential overlap calculations of nuclear shielding. Dobosh, Ellis, and Chou have extended their earlier INDO models used to calculate chemical shifts for carbon, to proton shifts, the major change being the inclusion of all three-centre integrals in the calculation of the shielding tensors.[22] The parametrization had to be changed once again, using ^{13}C chemical shifts for a representative set of molecules (methane, ethane, ethylene, acetylene). The proton calculations appear to hold promise for examining small effects such as conformational and substituent effects on proton shielding. MINDO/3 calculations of ^{19}F and ^{11}B shielding in a variety of compounds show highly overestimated ^{11}B results and a standard deviation of 69.7 p.p.m. in the comparison with experimental ^{19}F chemical shifts over a range of 700 p.p.m.[23] It is to be concluded that the MINDO/3 method is not suitable for shielding calculations. CNDO/S and INDO/S methods are specifically parametrized to account for excited states and are expected to have a better likelihood of success in calculating second-order properties. For ^{13}C in several compounds containing cumulative double bonds, these two methods give standard deviations of 23 and 22 p.p.m. in comparison with experimental chemical shifts.[24] Since the range of chemical shifts studied was 187 p.p.m., the correlation is really not better in a relative sense than the aforementioned ^{19}F MINDO/3 calculations, although the absolute deviations are much smaller here. Semi-empirical calculations of nuclear shielding using magnetically active excitation energies from ultra-

[18] E. A. Laws, R. M. Stevens, and W. N. Lipscomb, *J. Chem. Phys.*, 1971, **54**, 4269.
[19] R. M. Stevens and M. Karplus, *J. Chem. Phys.*, 1968, **49**, 1094.
[20] M. Zaucer and A. Azman, *Z. Naturforsch., Teil A.*, 1979, **34**, 1279.
[21] C. J. Jameson and J. Mason, in 'Nuclear Magnetic Resonance', ed. G. A. Webb (Specialist Periodical Reports), The Chemical Society, London, 1979, Vol. 9, p. 1.
[22] P. A. Dobosh, P. D. Ellis, and Y. C. Chou, *J. Magn. Reson.*, 1979, **36**, 439.
[23] M. Jallali-Heravi and G. A. Webb, *J. Mol. Struct.*, 1979, **55**, 113.
[24] C. Collier and G. A. Webb, *Org. Magn. Reson.*, 1979, **12**, 659.

violet spectroscopy and photoelectron spectroscopy can be used to interpret ^{13}C shielding differences.[25] By regrouping the terms in the diamagnetic and paramagnetic contributions to shielding, one could consider (*a*) 'local' terms, which are large, and (*b*) distant contributions, which effectively cancel. It has been suggested[25] that instead of lumping together all terms other than those involving orbitals centred on the nucleus in question (A):

$$\sigma^{A} = \sigma_{d}(\text{on A}) + \sigma_{p}(\text{on A}) + \sum_{\text{all B}} \sigma(\text{on A and B}) \qquad (9)$$

one could simply *assume* that *nearest* neighbours (L) matter but all others give cancelling contributions:

$$\sigma^{A} = \sigma_{d}(\text{on A and L}) + \sigma_{p}(\text{on A and L}). \qquad (10)$$

This is the 'atom-plus-ligand' approach.[25] The first term is defined as having been calculated by using Flygare's method,[12] including only nearest neighbours. When this term is subtracted from absolute shieldings defined by the ^{13}CO spin–rotation measurement, one can get an empirical measure of the second term. It is the second term that is presumed to correlate inversely with excitation energies for families of compounds. There are indeed some correlations found in series of alkenes and fluoroalkenes, but as would normally be expected, the interpretations are not so simple.[25]

As has been mentioned above, semi-empirical methods involve parametrization of some part or other of the calculation. In calculations involving the sum-over-states approach as opposed to the coupled Hartree–Fock approach, there is always the problem of having to use a limited number of states or use an average excitation energy. However, there is a model system that can be used to mimic real molecules, and which provides an exactly solvable quantum-mechanical system in an external magnetic field. The anisotropic harmonic oscillator is such a model system.[26] The environment of a nucleus in a diatomic or linear polyatomic molecule is simulated by placing the nucleus along the long axis of the ellipsoid. The environment of a nucleus in benzene is simulated by placing the nucleus in the plane perpendicular to the short axis. Harris and Swope show that the magnetic shielding tensor of a nucleus in the presence of a charged anisotropic harmonic oscillator may be reduced to quadrature. The sum over states in the paramagnetic terms collapse to one term for the harmonic oscillator because when l_x or l_y operates on the ground state the resulting state is proportional to one of the excited states of the oscillator. Thus one may remove the energy denominator of that state and use completeness. In other words, the use of an average energy is *exact* for the harmonic oscillator. The nucleus is put where it is to donate a spin but not to interact coulombically with the electron. Thus the absolute magnitudes of shielding calculated with this model cannot be expected to be accurate. However, the ratios of the components to one another such as σ_{xx}/σ_{zz}, or $\sigma_{\text{in-plane}}/\sigma_{zz}$ are quite good for both H_2 and benzene. Even though the model is purely geometric, it exemplifies the diamagnetic character of the shift in fields perpendicular to the plane of the molecule. The physical effect is easily understood in terms of angular momentum conservation in this model system, and there is no necessity to invoke aromaticity or other attributes.

In this review period renewed interest in the 'ring-current' concept and its

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[25] J. Mason, *J. Chem. Soc., Faraday Trans. 2*, 1979, **75**, 607.

[26] R. A. Harris and W. C. Swope, *Mol. Phys.*, 1979, **38**, 287.

relationship to the concept of 'aromaticity' is capped by the review of these ideas by Mallion.[27] Proton chemical shifts in benzene, in the poly-condensed hydrocarbons, and in large monocyclic polyenes have been widely interpreted in terms of the ring-current concept (we prefer to call it a model), first put into quantum-mechanical form by London.[28] Despite controversy and criticism of the basis of the concept,[29—32] it has been widely used over the years since its introduction, and unfortunately, has been intertwined in the literature with another non-observable, aromaticity. Mallion comments on the philosophical and practical difficulties with the use of both concepts.[27] From the point of view of nuclear shielding, one should consider a ring current merely in terms of its association with some part of nuclear magnetic shielding, given that one may choose to partition σ in some way so as to have a contribution due to "ring currents" and the rest. Of course this partitioning is purely artificial, since there is as yet no unambiguous way of segregating the parts. An all-electron calculation of σ using a coupled Hartree–Fock scheme, for example, does not allow for such a separation, since the one and two electron integrals involve all the orbitals. Thus, the use of the ring-current model necessarily involves approximate calculations, usually an assumption of σ–π separation. Blustin[33] assumes a model in which there is a localized bond structure for the π electrons and a partitioning of σ as follows:

$$\sigma = \sigma(\text{local}) + \sigma(\text{non-local}) \tag{11}$$

The perimeter bonds in the ring system are distinguished from the remaining internal bonds and the molar susceptibility of each type of bond is defined by reference to experimental values for naphthalene and pyrene molecules; σ(non-local) is then calculated by the use of McConnell's approximation, which relates σ(non-local) to the anisotropy in the magnetic susceptibility.[34] The local contributions are assumed to be the same in each case and are thus defined by using benzene as the reference molecule. The results of these very simple calculations on 65 protons in condensed hydrocarbons show deviations of less than 0.20 p.p.m. for 82% of the protons, which appears to surpass in accuracy the best ring-current results available.[35] Blustin concludes that (*a*) a simple criterion for aromaticity can be given (which does not concern us here) and (*b*) the results indicate that it is not necessary to associate a special ring-current attribute to π electrons in an aromatic system.[33] Of course, it may be argued that it is precisely these non-local contributions that are being included in a ring-current model, since empirical values for magnetic susceptibilities are used in Blustin's calculations of non-local contributions.

Other workers partition σ in a different way:

$$\sigma = \sigma_0 + \sigma(\text{ring currents}) + \sigma(\text{local anisotropic}) \tag{12}$$

where σ_0 is defined to be a constant such as to include all other contributions to

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[27] R. B. Mallion, *Pure Appl. Chem.*, 1980, **52,** 1541.
[28] F. London, *J. Phys. Radium (Paris)*, 1937, **8,** 397.
[29] J. I. Musher, *Adv. Magn. Reson.*, 1966, **2,** 177.
[30] J. I. Musher, *J. Chem. Phys.*, 1967, **46,** 1219.
[31] J. M. Gaidis and R. West, *J. Chem. Phys.*, 1967, 1218.
[32] P. W. Atkins and J. A. N. F. Gomes, *Mol. Phys.*, 1976, **32,** 1063.
[33] P. H. Blustin, *Mol. Phys.*, 1980, **39,** 565.
[34] H. M. McConnell, *J. Chem. Phys.*, 1957, **27,** 226.
[35] H. G. Ff. Roberts, *Mol. Phys.*, 1974, **27,** 843.

reproduce the proton chemical shift of benzene relative to TMS.[36] This has been applied by Vogler to calculations of ^{1}H chemical shifts of cyclic polyenes with outer (at the periphery of the molecule) as well as inner protons: [14]- and [18]-annulene[37] and of kekulene and similar compounds.[38] He finds that local anisotropy contributions are greater for the inner than for the outer protons.

Other papers reporting semi-empirical calculations of nuclear shielding were unfortunately available to this author only in the form of abstracts and will be mentioned only very briefly. Aminova *et al.*[39,40] calculated proton shielding constants in compounds containing phosphorus, *e.g.*, PH_3 and $P(CH_3)_3$. ^{13}C shielding calculations have been reported by some Japanese workers.[41,42] ^{13}C and ^{31}P shielding calculated using a modified CNDO/S method, in which orbital exponents were regarded as dependent on the electronegativity difference between directly bonded atoms, have been reported and are in good agreement with experimental chemical shifts and anisotropies.[43]

3 Physical Aspects of Nuclear Shielding

A. Anisotropy of the Shielding Tensor.—From the ^{1}H n.m.r. spectra in a single crystal of hexagonal ice at liquid-nitrogen temperature, the following conclusions were drawn.[44] The magnetic shielding tensors are the same for all protons and they are axially symmetric around the O–H . . . O direction. The tensor components with respect to water are 16 ± 0.5 p.p.m. along the symmetry axis and -12.5 ± 0.5 p.p.m. perpendicular to this axis. The isotropic shift is -3 p.p.m. with respect to water at room temperature. Combined multiple pulse n.m.r. and off-magic-angle sample spinning techniques have been used to obtain the carboxylic acid proton shielding tensor in 2,6-dimethylbenzoic acid in the randomly oriented solid.[45] The values reported are $\sigma_{\perp} = -18.5$ p.p.m., $\sigma_{\parallel} = -4.2$ p.p.m. relative to TMS.

Shielding tensors measured in crystals are sometimes inconsistent with the symmetry of the isolated molecules. This is only to be expected since the shielding tensor measured in crystals reflects the symmetry of the nuclear environment, which is usually dominated by the molecular symmetry but may be substantially altered by the crystal site symmetry. Small intermolecular shielding contributions can have a substantial effect upon the observed shielding tensor, especially if the anisotropy of the isolated molecule shielding tensor itself is small. A good example is that of the proton shielding tensors measured in single crystals of pyromellitic acid dianhydride.[46] The experimental results give the least shielded direction close to the normal of the aromatic ring, but the other two principal shielding directions do not conform to the D_{2h} symmetry of the molecule. The deviations are ascribed to intermolecular shielding contributions that can be calculated on the basis of a

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[36] M. Barfield, D. M. Grant, and D. Ikenberry, *J. Am. Chem. Soc.* 1975, **97,** 6956.
[37] H. Vogler, *J. Mol. Struct.*, 1979, **51,** 289.
[38] H. Vogler, *Tetrahedron Lett.*, 1979, 229.
[39] R. M. Aminova, M. B. Zuev, and I. D. Morozova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1979, **10,** 2190.
[40] R. M. Aminova, R. G. Islamov, I. Ts. Lyast, and A. A. Musina, *Zh. Strukt. Khim.*, 1979, **20,** 175.
[41] W. Inamoto and S. Masuda, *Kagaku No Ryoiki*, 1979, **33,** 4.
[42] I. Ando, M. Kondo, A. Nishioka, and S. Watanabe, *Bull. Chem. Soc. Jpn.*, 1979, **52,** 2474.
[43] P. Bernard-Moulin and G. Pouzard, *J. Chim. Phys. Phys.-Chim. Biol.*, 1979, **76,** 708.
[44] W. K. Rhim, D. P. Burum, and D. D. Elleman, *J. Chem. Phys.*, 1979, **71,** 3139.
[45] R. E. Taylor, R. G. Pembleton, L. M. Ryan, and B. C. Gerstein, *J. Chem. Phys.*, 1979, **71,** 4541.
[46] S. Aravamudhan, U. Haeberlen, H. Irngartinger, and C. Krieger, *Mol. Phys.*, 1979, **38,** 241.

magnetic dipole model. The secondary field produced at the site of the proton under consideration due to the diamagnetic currents induced in the neighbouring molecules by the applied field is considered as arising from magnetic point dipoles situated at the neighbouring molecules. The moments are determined from the corresponding components of the susceptibility tensor of the molecules. The resulting difference between the measured shielding tensor and the calculated intermolecular contribution is found to conform well to the D_{2h} symmetry of the molecule. Thus, this difference can be identified, with reasonably good accuracy, with the proton shielding of an isolated pyromellitic acid dianhydride molecule: σ_{33}(normal to molecular plane) $= -6.16$ p.p.m. and σ_{11}(along the C–H bond) $= -1.86$ p.p.m. and σ_{22}(along the long axis of the molecule) $= 0.40$ p.p.m. relative to a spherical sample of water. Note that the least shielded direction is along the normal to the plane. This is usually described by the ring-current model. What is considered surprising in this shielding tensor is the relative magnitudes of the in-plane components.

The ^{13}C shielding tensor of non-rotating benzene was measured in a successful application of a low-temperature probe assembly, which permits high-power cross-polarization and decoupling experiments at temperatures as low as 10 K.[47] The principal values of the carbon shielding tensor are σ_{33}(normal to the plane) $= 127.7 \pm 3.0$ p.p.m., σ_{11}(along C–H bond) $= -88.2 \pm 3.2$ p.p.m. and, $\sigma_{22} = -12.0 \pm 2.0$ p.p.m. with respect to liquid benzene. The most shielded element being perpendicular to the molecular plane and the least shielded in the direction of the C–H bond, is found in the substituted benzenes as well.

The shielding anisotropy of ^{19}F has been measured in CF_4 and in F^- ion in a liquid crystal. Line-shape analysis of the ^{19}F n.m.r. spectrum of the CF_4 molecule enclathrated in the heavy water clathrate hydrate yields $\Delta\sigma = 138 \pm 4$ p.p.m. for the difference between shielding components parallel and perpendicular to the C–F bond.[48] Spin–rotation constants calculated from this shielding anisotropy are found to be in good agreement with results obtained by molecular-beam methods. The magnitude of the shielding anisotropy of the F^- anion (which should be zero for the free ion) as well as its sign in lyotropic liquid crystals change according to the composition of the sample.[49] Anisotropies ranging from $+6.6$ to -19.4 p.p.m. were measured. The interactions causing shielding anisotropy are suspected to be electrostatic in origin. Similarly, intermolecular interactions with cesium ion in the lamellar phase of the l-monooctanoin–water–caesium chloride system lead to anisotropy in the shielding of the $^{133}Cs^+$ ion.[50] These induced anisotropies are a measure of the intermolecular contribution to shielding anisotropies obtained in oriented molecules that must be presumed to be always present. Appropriate caution must be exercised in using anisotropies obtained in liquid-crystal media.

Shielding anisotropies for ^{31}P have been reported in this review period for triphenylphosphine and the corresponding oxo, thioxo, and selenoxo compounds.[51] The results are compared in Table 3 with previous results for phosphorus in similar compounds. There is a striking increase in $\Delta\sigma$ in going from the three-co-

[47] M. Linder, A. Höhener, and R. R. Ernst, *J. Magn. Reson.*, 1979, **35**, 379.
[48] S. K. Garg, D. W. Davidson, and J. A. Ripmeester, *J. Magn. Reson.*, 1979, **36**, 325.
[49] O. Söderman, A. Khan, and G. Lindblom, *J. Magn. Reson.*, 1979, **36**, 141.
[50] N.-O. Persson and G. Lindblom, *J. Phys. Chem.* 1979, **83**, 3015.
[51] J. B. Robert and L. Wiesenfeld, *J. Magn. Reson.*, 1980, **38**, 357.

Table 3 *Anisotropy of the* ^{31}P *nuclear magnetic shielding tensor*[a] *in* p.p.m.

X		X = P(CH$_3$)$_3$	X = PPh$_3$	X = PF$_3$
Lone pair	$\Delta\sigma$	7.63 ± 0.5[52]	23[51]	181 ± 5[54]
	$\sigma_\parallel$	409 ± 5	379	357 ± 5
	$\sigma_\perp$	401 ± 5	356	175 ± 5
O	$\Delta\sigma$	173.6 ± 0.5[52]	280[51]	284 ± 15[55]
	$\sigma_\parallel$	424 ± 5	516	594 ± 15
	$\sigma_\perp$	250 ± 5	236	260 ± 15
S	$\Delta\sigma$	111.6 ± 0.5[52]	112[51]	461 ± 10[54]
	$\sigma_\parallel$	386 ± 5	390	610 ± 5
	$\sigma_\perp$	274 ± 5	278	149 ± 5
Se	$\Delta\sigma$	99 ± 15[53]	103[51]	
	$\sigma_\parallel$	414	392	
	$\sigma_\perp$	314	289	

[a] $\Delta\sigma$ is the measured quantity. The absolute shielding values $\sigma_\parallel$ and $\sigma_\perp$ are calculated based on the PH$_3$ shielding tensor, which is assumed to be known accurately,[12, 13] see Table 1

ordinate to the tetra-co-ordinate phosphorus compounds. ^{31}P n.m.r. spectra of highly oriented DNA fibres have been observed for three different conformations, the A, B, and C forms of DNA.[56] DNA in aqueous solution has generally been assumed to adopt the same conformation as is present in DNA fibres at high relative humidities (B form). The results are interpreted consistently in terms of the presence of significant variations in the backbone conformation of DNA, the magnitude of the variation in phosphodiester orientations is thought to be as large as ±20° from an average conformation. The results are consistent with the assumption that the magnitude and orientation of the shielding tensor with respect to the atomic co-ordinates of the phosphodiester group are virtually identical for all conformers of DNA in the fibre. The elements of the shielding tensor for ^{31}P in DNA are σ_{33}(along helical axis) = 103 p.p.m., $\sigma_{11} = -76$ p.p.m., $\sigma_{22} = -16$ p.p.m. relative to trimethyl phosphate.[57]

The ^{207}Pb shielding tensor in a single crystal of Pb(NO$_3$)$_2$ has been measured[58] and found to be axially symmetric. $\sigma_\parallel - \sigma_\perp = 53 \pm 5$ p.p.m. and $\sigma_{av} = 601 \pm 8$ p.p.m. relative to an infinitely dilute aqueous solution of Pb(NO$_3$)$_2$. If one considers Pb(NO$_3$)$_2$ to be an ionic crystal, the anisotropic shielding must be due to intermolecular contributions. However, since the anisotropy is rather large, it can only be explained by a small covalent character to the bonding in Pb(NO$_3$)$_2$.

B. The Effects of Rotation and Vibration.—Molecular electronic properties such as nuclear shielding depend on the rotational and vibrational states of the molecule. The property may be observed for a particular vibrational and rotational state, or

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[52] A. J. Montana, N. Zumbulyadis and B. P. Dailey, *J. Am. Chem. Soc.*, 1977, **99**, 4290.
[53] J. P. Albrand, A. Cogne, and J. B. Robert, *Chem. Phys. Lett.*, 1977, **48**, 524.
[54] A. J. Montana, N. Zumbulyadis, and B. P. Dailey, *J. Chem. Phys.*, 1976, **65**, 4756.
[55] P. K. Bhattacharyya and B. P. Dailey, *Mol. Phys.*, 1974, **28**, 1.
[56] H. Shindo, J. B. Wooten, B. H. Pheiffer, and S. B. Zimmerman, *Biochemistry.*, 1980, **19**, 518.
[57] H. Shindo, *Biopolymers*, 1980, **19**, 509.
[58] O. Lutz and A. Nolle, *Z. Phys. B*, 1980, **36**, 323.

for a given vibrational state averaged over all J and M_J states, as is common in molecular spectroscopy in the vapour phase or in molecular beams. In n.m.r. however, the spectroscopic time scale is such that one observes an average over all rovibrational states. Thus, the shielding in the limit of the isolated molecule will be perceived to change with temperature as the populations of the rovibrational states change with temperature.

A general treatment of the variation of any molecular electronic property with vibration and rotation, within the Born–Oppenheimer approximation, has been given.[59] The property P is expanded as a power series in the reduced normal co-ordinates:

$$P = P_e^{(0)} + \sum_{i=1}^{N} P_i^{(1)} q_i + \sum_{i,j=1}^{N} P_{ij}^{(2)} q_i q_j + \sum_{i,j,k=1}^{N} P_{ijk}^{(3)} q_i q_j q_k + \ldots \qquad (13)$$

where $P_e^{(0)}$ is the value of the property at its equilibrium configuration. $P_i^{(1)}$, $P_{ij}^{(2)}$, *etc.*, are electronic properties which describe the sensitivity of P to small displacements from equilibrium, and q_i, q_j, *etc.*, are reduced normal co-ordinates that can be used to describe the relative geometry. The expectation value of P for a given rovibrational state, $P_{vJ\tau}$

$$P_{vJ\tau} = P_0^{J\tau} + \sum_{i=1}^{N} A_i^{J\tau}(v_i + \tfrac{1}{2}) + \sum_{i \leq j}^{N} B_{ij}(v_i + \tfrac{1}{2})(v_j + \tfrac{1}{2}) \qquad (14)$$

is provided together with general formulae for A_i and B_{ij} for the general case of an asymmetric rotor, which are expressed explicitly in terms of the derivatives $P_i^{(1)}$, $P_{ij}^{(2)}$, $P_{ijk}^{(3)}$ . . ., and molecular constants such as cubic force constants, moments of inertia, and harmonic frequencies. The $P_{ij}^{(2)}$ terms have yet to be included; this involves the use of a second-contact transformation, in which quartic force constants will undoubtedly appear. Isotope effects are due to changes in the molecular constants upon isotopic substitution, which in turn appear in a non-cancelling fashion in the expectation value formula.

N.m.r. results showing the effects of vibration and rotation for ^{11}B, ^{13}C, ^{15}N, ^{19}F, and ^{31}P nuclei in various molecules have been summarized.[60] These are temperature-dependent shieldings observed in the gas phase in the zero-pressure limit (to eliminate intermolecular interactions, which also affect shielding). The largest shifts are exhibited by ^{19}F. (The order is roughly F_2, NF_3, ClF, CF_3CF_3, SF_6, CF_3Br, PF_3, CF_3Cl, CF_3H, POF_3, CF_4, SiF_4, BF_3, and CH_3F.) Only a limited number of molecules containing ^{31}P (PF_3, POF_3, PF_5, PH_3), ^{15}N ($\underline{N}NO$, $N\underline{N}O$), ^{13}C (CO_2,[61] CO, CH_4), and ^{11}B (BF_3) have been reported. Quantitative interpretation of the results is possible in a small number of molecules (F_2, ClF, CF_4, SiF_4, BF_3, CO, HBr,[62] and HCl[63]).

C. Isotope Effects.—The largest body of data on isotope shifts in n.m.r. is that of ^{2}D-induced isotope shifts in the spectra of various nuclei. Because the fractional mass change is greatest in the substitution of ^{1}H by ^{2}D (except of course, for ^{3}T), these isotope shifts have been large and easy to observe. However, a hydrogen atom

[59] G. Riley, W. T. Raynes, and P. W. Fowler, *Mol. Phys.*, 1979, **38**, 877.
[60] C. J. Jameson, A. K. Jameson, and S. Wille, *J. Phys. Chem.*, 1979, **83**, 3372.
[61] K. Jackowski and W. T. Raynes, *J. Chem. Soc., Chem. Commun.*, 1979, 863.
[62] W. T. Raynes and B. P. Chadburn, *J. Magn. Reson.*, 1973, **10**, 218.
[63] W. T. Raynes and B. P. Chadburn, *Mol. Phys.*, 1972, **24**, 853.

offers little variety in the bonding situations it finds itself in, since it is unlikely to form multiple bonds or have co-ordination numbers greater than 1. With the increasing number of studies of ^{18}O-induced isotope shifts in ^{13}C and ^{31}P n.m.r. spectra, we at last have a family of data that can be correlated with bond order, hybridization, and perhaps other parameters used to describe structure. Several interesting papers on ^{18}O-induced isotope shifts, reported during this review period, provide data that can begin to be correlated with structure. The results are summarized in Tables 4 and 5. The phosphates in which the isotope effects were measured are shown below:

Table 4 ^{18}O-*induced* ^{13}C *isotope shifts,* p.p.m. *per* ^{18}O, *tabulated as* $\sigma_{\text{heavy}} - \sigma_{\text{light}}$

Bond Order (C^*–^{18}O)	*Hybridization of* C*		
	sp^3	*sp*^{2}	*sp*
3			metal carbonyls 0.040[64,65]
2		0.042—0.048[66,67] aldehydes 0.045—0.052[66,67] ketones 0.028—0.036[66] amides 0.033—0.039[66] esters	
1	0.019—0.035[66-68] alcohols 0.025[67] ethers 0.024—0.032[66,67] esters	0.016[67] phenol 0.016—0.018[67] ethers 0.010—0.015[66] esters	

Table 5 ^{18}O-*induced* ^{31}P *isotope shifts in phosphates,* p.p.m. per ^{18}O[a]

	Bond Order P*–^{18}O	*End* P*	*Backbone* P*
End ^{18}O	2	0.0354 (1)[69]	
	1.5	0.0293 (2)[69]	0.0281—0.0285 (6)[70]
	1.33	0.0236 (3*a*)[69] 0.025 (3*b*)[71] 0.0215—0.0220 (3*c*)[70]	
	1.25	0.0206 (4)[71-73]	
Backbone ^{18}O	1.0	0.022 (5)[74,75] 0.0215—0.022 (5)[70]	0.0163—0.0172 (7)[70]

[a] See numbered structures in text

[64] D. J. Darensbourg and B. J. Baldwin, *J. Am. Chem. Soc.*, 1979, **101,** 6447.

[65] D. J. Darensbourg, *J. Organomet. Chem.*, 1979, **174,** C70.

[66] J. C. Vederas, *J. Am. Chem. Soc.*, 1980, **102,** 374.

[67] J. M. Risley and R. L. Van Etten, *J. Am. Chem. Soc.*, 1980, **102,** 4609.

[68] J. M. Risley and R. L. Van Etten, *J. Am. Chem. Soc.*, 1979, **101,** 252.

[69] G. Lowe, B. V. L. Potter, B. S. Sproat, and W. E. Hull, *J. Chem. Soc., Chem. Commun.*, 1979, 733.

[70] M. Cohn and A. Hu, *J. Am. Chem. Soc.*, 1980, **102,** 913.

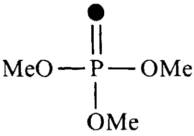
[71] G. Lowe and B. S. Sproat, *J. Chem. Soc., Chem. Commun.*, 1978, 565.

[72] O. Lutz, A. Nolle, and D. Staschewski, *Z. Naturforsch., Teil A*, 1978, **33,** 380.

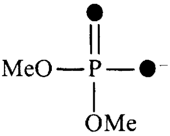
[73] M. Cohn and A. Hu, *Proc. Natl. Acad. Sci. USA*, 1978, **75,** 200.

[74] G. Lowe and B. S. Sproat, *J. Chem. Soc., Perkin Trans 1*, 1978, 1622.

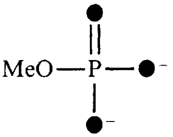
[75] G. Lowe and B. S. Sproat, *J. Chem. Soc., Chem. Commun.*, 1978, 783.


$\mathrm{MeO{-}\overset{\overset{\bullet}{\|}}{\underset{\underset{OMe}{|}}{P}}{-}OMe}$

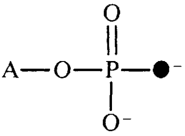
(1)


$\mathrm{MeO{-}\overset{\overset{\bullet}{\|}}{\underset{\underset{OMe}{|}}{P}}{-}\bullet^{-}}$

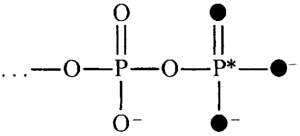
(2)


$\mathrm{MeO{-}\overset{\overset{\bullet}{\|}}{\underset{\underset{\bullet^{-}}{|}}{P}}{-}\bullet^{-}}$

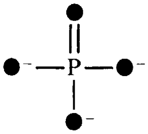
(3*a*)


$\mathrm{A{-}O{-}\overset{\overset{O}{\|}}{\underset{\underset{O^{-}}{|}}{P}}{-}\bullet^{-}}$

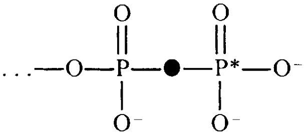
(3*b*)


$\mathrm{\ldots{-}O{-}\overset{\overset{O}{\|}}{\underset{\underset{O^{-}}{|}}{P}}{-}O{-}\overset{\overset{\bullet}{\|}}{\underset{\underset{\bullet^{-}}{|}}{P^{*}}}{-}\bullet^{-}}$

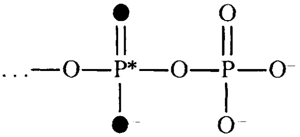
(3*c*)


$\mathrm{\bullet^{-}{-}\overset{\overset{\bullet}{\|}}{\underset{\underset{\bullet^{-}}{|}}{P}}{-}\bullet^{-}}$

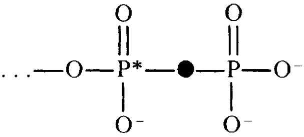
(4)


$\mathrm{\ldots{-}O{-}\overset{\overset{O}{\|}}{\underset{\underset{O^{-}}{|}}{P}}{-}\bullet{-}\overset{\overset{O}{\|}}{\underset{\underset{O^{-}}{|}}{P^{*}}}{-}O^{-}}$

(5)


$\mathrm{\ldots{-}O{-}\overset{\overset{\bullet}{\|}}{\underset{\underset{\bullet^{-}}{|}}{P^{*}}}{-}O{-}\overset{\overset{O}{\|}}{\underset{\underset{O^{-}}{|}}{P}}{-}O^{-}}$

(6)


$\mathrm{\ldots{-}O{-}\overset{\overset{O}{\|}}{\underset{\underset{O^{-}}{|}}{P^{*}}}{-}\bullet{-}\overset{\overset{O}{\|}}{\underset{\underset{O^{-}}{|}}{P}}{-}O^{-}}$

(7)

Except for the orthophosphate ion(4) and the methyl phosphates (1,2,3*a*) all of the ^{18}O-induced ^{31}P isotope shifts were measured in nucleotides.

It can be seen from Table 4 that there is an important dependence of ^{18}O-induced ^{13}C isotope shift on the C*–^{18}O bond order. Given sp^2 hybridization on the carbon of interest, the higher bond order corresponds to a larger shift. There is an evident dependence on hybridization; the isotope shift appears to increase with increasing *p* character on the carbon of interest. (Incidentally, this has been noted elsewhere,[76] since the ratio of Larmor frequencies ω_T/ω_H depends on the carbon–hydrogen bond hybridization.) In addition, there is some dependence on electronegativity of substituents on the carbon. None of these is surprising of course, since the ^{13}C absolute shielding itself is known to vary with hybridization and substituent electronegativity. Since the bond extensions and the bond-angle deformations over which the shielding average is carried out are minor perturbations of the absolute shielding at the equilibrium configuration, the same variables that affect the absolute shielding affect the isotope shift. In addition, there are dynamic variables, the factors which affect the magnitude of average bond extensions and angle deformations. The order of the bond connecting the nucleus of interest and the atom where isotopic substitution occurs will affect the magnitude of average bond displace-

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[76] J. P. Bloxsidge, J. A. Elvidge, J. R. Jones, R. B. Mane, and M. Saljoughian, *Org. Magn. Reson.*, 1979, **12**, 574.

ment. In addition, the nature of the average over vibrations must be different when the nucleus of interest or the heavy atom is buried in the molecular backbone than when it is peripheral. These are dynamic effects that are expected to manifest themselves in isotope shifts. The work summarized in Tables 4 and 5 is an auspicious beginning to the study of the effect of structure on isotope shifts in n.m.r.

Because of isotope effects on the chemical equilibrium constant, a phenomenon which is well understood, there are additional effects on the n.m.r. spectrum caused by isotopic substitution. Since the equilibrium constant for a conformational equilibrium is different for different isotopically related molecules, the relative concentrations of conformers vary.[77–80] These are equilibrium isotope effects and quite apart from the intrinsic isotope effects discussed above.

D. Intermolecular Effects.—One of the intermolecular effects on nuclear shielding that is subtle and expected to be small, is that due to the differing interactions between two sets of chiral molecules. Nuclei that are equivalent (interchangeable by C_n, $\infty > n > 1$) are or course, isochronous,[81] that is, they have identical average nuclear shielding values. Nuclei that are enantiotopic (interchangeable by S_n) and in an achiral environment are likewise isochronous.[82] Nuclei that are diastereotopic are not interchangeable by any symmetry operation and are therefore intrinsically anisochronous. In an environment of optically inactive molecules the corresponding nuclei of an enantiomeric pair of molecules have the same time-averaged shielding; however, in an optically active solvent they have different average shieldings. We can easily understand this in terms of binary interactions. A chiral solute molecule R_A and its enantiomer S_A form diastereomeric pairs $R_A \ldots R_B$ and $S_A \ldots R_B$ with chiral solvent molecule R_B. Because stereospecific interactions between such solute and solvent molecules at short range lead to a *correlated* intermolecular geometry, corresponding nuclei in S_A and R_A in the diastereomeric pairs will experience different shielding *via* the usual mechanisms operating in intermolecular effects on shielding (*e.g.*, magnetic anisotropy, electrical, and dispersive effects) leading in many instances to an experimentally significant magnetic shielding non-equivalence. This expectation has in fact been the basis for the use of n.m.r. for the direct determination of optical purity and of absolute configurations.[83–85] Observed chiral shifts are of the order of 0.025 p.p.m. for ^{1}H,[86] 0.036 p.p.m. for ^{19}F,[87] and 0.164–0.685 p.p.m. for ^{15}N.[88]

While the non-equivalence resulting from conventional dispersive, *etc.*, interactions (which Stiles calls chirality independent shielding) are readily understood (see, for example, Raynes, Buckingham, and Bernstein[89]), the question arises as to the

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[77] F. A. L. Anet, V. J. Basus, A. P. W. Hewett, and M. Saunders, *J. Am. Chem. Soc.*, 1980, **102,** 3945.

[78] J. W. Faller, H. H. Murray, and M. Saunders, *J. Am. Chem. Soc.*, 1980, **102,** 2306.

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[80] J. J. Led and S. B. Petersen, *J. Magn. Reson.*, 1979, **33,** 603.

[81] A. Abragam, 'The Principles of Nuclear Magnetism', Oxford, 1961, p. 480.

[82] K. Mislow and M. Raban, *Top. Stereochem.*, 1967, **1,** 1.

[83] W. H. Pirkle and S. D. Beare, *J. Am. Chem. Soc.*, 1969, **91,** 5150.

[84] J. Reuben, *J. Chem. Soc., Chem. Commun.*, 1979, 68.

[85] G. M. Whitesides and D. W. Lewis, *J. Am. Chem. Soc.*, 1970, **92,** 6979.

[86] T. G. Burlingame and W. H. Pirkle, *J. Am. Chem. Soc.*, 1966, **88,** 1837.

[87] W. H. Pirkle, *J. Am. Chem. Soc.*, 1966, **88,** 1837.

[88] R. Dyllick-Brenzinger and J. D. Roberts, *J. Am. Chem. Soc.*, 1980, **102,** 1166.

[89] W. T. Raynes, A. D. Buckingham, and H. J. Bernstein, *J. Chem. Phys.*, 1962, **36,** 3481.

existence and magnitude of chirality dependent shielding of a sensor nucleus by a chiral perturbing group in the long-range limit, at a sufficiently large separation that there are no geometric correlations between a chiral solute molecule and a chiral solvent molecule.[90]

Two chiral shielding mechanisms have been proposed, which persist even in the absence of stereospecific interactions.[90, 91] The first mechanism is based on dispersive interactions associated with simultaneous electric dipolar and magnetic dipolar interactions between the chiral molecules, which leads to shielding of every nucleus in one enantiomer of A and deshielding at every nucleus in the other.[90] This shielding falls off as R^{-6} (R is the distance between the sensor nucleus and the chiral perturbing group) and is proportional to the pseudo-scalar mean values of the site chirality strengths at the corresponding nuclei and the rotatory strengths of the perturbing group. A second mechanism is based entirely on purely electric dipole interactions between molecules, and involves multiplication of pseudoscalar products of electric dipole transition moments on each molecule.[91] The sign of each scalar triple product reflects the chirality of the molecule in question. Hence, like the first mechanism, the chiral shieldings are equal in magnitude but opposite in sign. This contribution falls off as R^{-9}. While Stiles' analysis reinforces symmetry arguments predicting that finite anisochrony persists even in the absence of stereospecific molecular interactions, an order of magnitude estimate of the size yields an effect at least four orders of magnitude weaker than the conventional dispersive shielding of the same nucleus by the same perturbing group. Only the diamagnetic component of these shielding mechanisms has been considered by Stiles. It is possible, although not likely, that the paramagnetic component is orders of magnitude larger.

Intermolecular effects on nuclear shielding measured in the gas phase have been reported for ^{19}F and ^{31}P in NF_3, PF_3, POF_3, and PF_5,[60] and for ^{13}C in CO_2.[61] In the expansion of nuclear magnetic shielding in powers of density

$$\sigma(T,\rho) = \sigma_0(T)+\sigma_1(T)\rho+\sigma_2(T)\rho^2+\ \dots \qquad (15)$$

where ρ is the density of the pure gas, $\sigma_1(T)$ is the second virial coefficient of nuclear shielding and $\sigma_0(T)$ is the temperature-dependent shielding in the isolated molecule (already discussed in Section 3B). When observing a given nucleus in a molecule X in a gaseous mixture, there are as many terms $\sigma_1(\mathrm{X,A})\rho_{\mathrm{A}}$ as there are molecular species A interacting with X, including X itself. σ_1 has been found to be negative in all systems studied so far, and includes the bulk susceptibility contribution $\sigma_{1\mathrm{b}} = -2\pi\chi_{\mathrm{m}}/3$ for measurements in cylindrical samples with the axis perpendicular to the direction of the field. The magnitudes of σ_1 for various nuclei are compared in Table 6. Studies of density dependence of ^{1}H shielding in organic solvents (measured as a pressure dependence over a range of 1 kbar) show high frequency shifts with increasing density;[92] this is the same direction as has been observed in the gas phase.

Ab initio calculations of nuclear shielding in the H_2–He interacting pair[93] and ^{7}Li

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[90] P. J. Stiles, *Chem. Phys. Lett.*, 1976, **43,** 23.
[91] P. J. Stiles, *Aust. J. Chem.*, 1979, **32,** 1375.
[92] K. Endo, Y. Hazama, K. Okabayashi, I. Tonoike, and K. Suzuki, *Chem. Phys. Lett.*, 1979, **61,** 336.
[93] J. P. Riley, I. H. Hillier, and W. T. Raynes, *Mol. Phys.*, 1979, **38,** 353.

Table 6 *Range of σ_1 values for various nuclei*[60]

Nucleus	$\lvert\sigma_1\rvert$, p.p.m. amagat^{-1}
^{1}H	0—0.008
^{11}B	0.0085 in BF_3
^{13}C	0.022—0.0105
^{15}N	0.0026—0.02
^{19}F	0.006—0.07
^{31}P	0.0023—0.266
^{129}Xe	0.166—0.75

shielding in Li^+ interacting with H_2O, NH_3, or CH_3OH[94] provide some insight into the two extreme cases, on the one hand weak van der Waals forces, and on the other formation of strong complexes with binding energies of the order of up to 123 kcal mol^{-1}. The chemical shifts between ^7Li in the Li^+CH_3OH, Li^+OH_2, and Li^+NH_3 complexes are in fair agreement with the ^7Li chemical shifts measured in infinitely dilute solutions of Li^+. The shielding appears to be largely diamagnetic in origin, the paramagnetic term is rather small. Since the number of molecules in the first hydration shell of the Li^+ ion is generally thought to be 4, the authors also calculated the ^7Li nuclear shielding in the $Li^+(OH_2)_n$ ($n = 1,4$) complexes and the $Li^+(NH_3)_n$ complexes. The results show that the experimental chemical shifts are correctly reproduced when all the ligands in the first solvation shell are included in the calculation. One has to be cautious in comparing theoretical results with chemical shifts measured in solutions. In this particular case, the effects of the counterion are eliminated by extrapolation to infinite dilution. It is not indicated whether the experimental chemical shifts used are corrected for bulk susceptibility differences between the solvents.

The effects on nuclear shielding of density changes in the solvent accompanying changes in temperature are usually unjustifiably neglected. These are not necessarily small. From the known magnitudes of the dependence of nuclear shielding on density (σ_1) from measurements in the gas phase, and the known magnitudes of the dependence of liquid densities on temperature, one can estimate that these neglected effects can be rather large. For comparison, the temperature dependence of the mass magnetic susceptibility of liquids is found to be due entirely to changes in densities with temperature.[95] One hopes that the intermolecular effects can be neglected compared to the magnitudes of shielding changes that are usually of interest in structural or chemical dynamics (usually temperature dependent) studies. An indication that such is not usually the case in studies of hindered rotation by n.m.r. has been reported recently.[96] The free energy of activation for hindered internal rotation of dimethylacetamide was measured by ^1H n.m.r. in the gas phase and found to be 15.64 ± 0.1 kcal mol^{-1}. All the activation data previously found for this molecule in solution *exceed* the value measured in the gas phase. Even in the non-polar solvent iso-octane it is significantly higher (by 1.7 kcal mol^{-1}), while other more polar solvents increase the barrier even further.[97, 98] A similar result was

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found in another vapour-phase n.m.r. study of hindered rotation. The intermolecular contribution to the barrier is 2 kcal mol^{-1} in liquid dimethylnitrosamine.[99] It is probably generally true that barriers to internal rotation are lower in gases than they are in liquids.

Intermolecular effects are also usually neglected in magnetic shielding studies employed in the determination of equilibrium constants for molecular complex formation ($A + D = AD$). The usual experiment involves measuring the shielding of the acceptor A as a function of total donor concentration in a number of different A- and D-containing solutions. The usual analysis involves the assumption that the shielding of A and AD remain constant in the presence of varying concentrations of donor! An attempt to effect a partial remedy for this problem is presented by Stamm *et al.*,[100] who refer to the intermolecular effects on shielding, apart from the specific complex formation, as 'additional unspecific shielding' and assume this to be linearly dependent on donor concentration for both A and AD. The assumption of linear dependence is probably not too bad (an ideal solution approximation for A in solvent D and for AD in solvent D), although there have been some reports of non-ideal behaviour (non-linear change in shielding with mole fraction in a binary solution).[101]

Linear electric-field effects on ^{1}H and ^{13}C nuclear shielding have been discussed and the field-gradient contribution to the theory[89, 102, 103] reconsidered.[104] Electrostatic field effects (intramolecular fields in these recent applications) introduced by Buckingham as a shielding contribution for protons,[102] has been increasingly used to interpret ^{13}C shielding as well. In this review period the theory has been applied to ^{13}C shifts, especially to quaternary carbon atoms,[105] and also to ^{1}H and ^{13}C shifts in carbohydrates.[104] The theory meets with moderate success even with molecular structures assumed from crystal data in the rationalization of shifts induced by variation of pH.[104]

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