

Chiral Shielding in Nuclear Magnetic Resonance Spectroscopy

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Abstract

A novel van der Waals shielding mechanism is discussed which contributes to the magnetic shielding non-equivalence of optical isomers of one chiral species in the presence of a second optically active species. It is more direct than standard mechanisms which invoke stereospecific association of the interacting molecules but appears to be of marginal experimental significance.

One of the more interesting but poorly understood chemical aspects of n.m.r. spectroscopy is the dependence of nuclear shielding in chiral molecules on the chiralities of the surrounding molecules.¹⁻⁴ In an environment of optically inactive molecules the corresponding nuclei of an enantiomeric pair resonate at the same frequency and are said to be isochronous.² Symmetry arguments indicate that they become diastereotopic² and therefore anisochronous² in a chiral environment. Intermolecular forces which discriminate between diastereoisomers^{5,6} lead to slightly different angular correlations and intermolecular distances in the diastereomeric pairs. In conjunction with standard magnetic anisotropy,⁷ electrostatic⁸ and dispersive⁹ shielding mechanisms these differential geometric correlations can account for the order of magnitude of the observed magnetic shielding non-equivalences.^{3,10} It is relevant, however, to ask whether experimentally significant magnetic shielding non-equivalence would persist if stereospecific interactions could be neglected. In this context it should be noted that in an isotropic liquid there are no geometric correlations between a chiral solute molecule and a chiral solvent molecule sufficiently remote from the solute.

Let us consider the diastereomeric pairs $R_A...R_B$ and $S_A...R_B$. A chiral shielding mechanism has been reported¹¹ which, even in the absence of stereospecific inter-

¹ Pirkle, W. H., *J. Am. Chem. Soc.*, 1966, **88**, 1837.

² Mislow, K., and Raban, M., *Top. Stereochem.*, 1967, **1**, 1.

³ Pirkle, W. H., and Beare, S. D., *J. Am. Chem. Soc.*, 1969, **91**, 5150.

⁴ Whitesides, G. M., and Lewis, D. W., *J. Am. Chem. Soc.*, 1970, **92**, 6979.

⁵ Craig, D. P., and Mellor, D. P., *Top. Curr. Chem.*, 1976, **63**, 1.

⁶ Schipper, P. E., *Chem. Phys.*, 1977, **26**, 29.

⁷ McConnell, H. M., *J. Chem. Phys.*, 1957, **27**, 226; Stiles, P. J., *Chem. Phys. Lett.*, 1975, **30**, 259;

Perram, J. W., and Stiles, P. J., *Proc. R. Soc. London, Ser. A*, 1976, **349**, 125.

⁸ Buckingham, A. D., *Can. J. Chem.*, 1960, **38**, 300; Batchelor, J. G., *J. Am. Chem. Soc.*, 1975, **97**, 3410.

⁹ Rummens, F. H. A., 'Van der Waals Forces and Shielding Effects' (Springer: Berlin 1975).

¹⁰ Morozov, L. L., Fedin, E. I., and Kabachnik, M. I., *Russ. J. Phys. Chem.*, 1974, **48**, 6.

¹¹ Stiles, P. J., *Chem. Phys. Lett.*, 1976, **43**, 23.

actions, leads to shielding of every nucleus in one enantiomer of A and deshielding at every nucleus in the other. This mechanism is based on dispersive interactions associated with simultaneous electric dipolar and magnetic dipolar interactions between the chiral molecules. It was noted, however, that the magnitude of such shielding is too small to account for observed magnetic shielding non-equivalences.

Schipper⁶ recently described a new dispersive force which discriminates energetically between diastereomeric pairs of molecules. We show here that there is a related chiral shielding mechanism which like the mechanism previously described does not rely on stereospecific interactions between molecules. It differs from the former, however, in that the interactions between molecules are purely of electric dipole character.

For simplicity we confine our attention to chiral shielding associated with the diamagnetic component of the total shielding in non-degenerate molecular ground states. The theoretical development is similar to that outlined in ref.¹¹ Consider nucleus N_A in molecule A of the composite system AB consisting of the chiral sensor species A and the chiral perturbing molecule B. Its diamagnetic shielding (in SI units) takes the form¹²

$$\sigma(N_A) = \left(\frac{\mu_0}{4\pi}\right) \left(\frac{e^2}{3m_e}\right) \int \psi^{AB}_0 \sum_{i=1}^n r_{Ni}^{-1} \psi^{AB}_0 d\tau \quad (1)$$

where ψ^{AB}_0 is the wavefunction of the ground state of the composite system, $n = n(A) + n(B)$ is the total number of electrons, e is the proton charge, m_e the electronic mass and r_{Ni} the distance between electron i and the nucleus N_A . When the molecules are infinitely separated

$$\psi^{AB}_0 = \psi^A_0 \psi^B_0$$

the product of the individual ground states. If, however, they interact at a distance R through the electric dipole (μ_A)–electric dipole (μ_B) term

$$V^{AB} = (4\pi\epsilon_0)^{-1} [(\mu_A \cdot \mu_B)/R^3 - 3(\mu_A \cdot R)(\mu_B \cdot R)/R^5] \quad (2)$$

in the Hamiltonian of the composite system the ground-state wavefunction ψ^{AB}_0 can be expanded as a linear combination of products of the form $\psi^A_a \psi^B_b$. The term of interest here is obtained by expanding ψ^{AB}_0 in (1) to third order¹³ in the perturbation (2). The upper limit n is approximated by $n(A)$ and isotropic orientation averaging is performed for each molecule. The average chiral shielding at nucleus N_A emerges as

$$\begin{aligned} \bar{\sigma}_c(N_A) = & -\frac{2}{3(4\pi\epsilon_0)^3 R^9} \sum_{a,a',a'',b,b'} \left[\frac{(\mu_A^{0a} \cdot \mu_A^{aa'} \times \mu_A^{a'0}) \sigma_d^{00}(N_A)}{(E_A^A + E_B^B)^2 (E_A^A + E_B^B)} \right. \\ & \left. - \frac{(\mu_A^{0a} \cdot \mu_A^{aa'} \times \mu_A^{a''0}) \sigma_d^{a''0}(N_A)}{(E_A^A + E_B^B)(E_A^A + E_B^B) E_A^{a''}} \right] (\mu_B^{0b} \cdot \mu_B^{bb'} \times \mu_B^{b'0}) \end{aligned} \quad (3)$$

where $\mu_A^{aa'}$ is the electric dipole transition moment

$$\int \psi^A_a \mu_A \psi^A_{a'} d\tau_A$$

¹² Ramsey, N. F., *Phys. Rev.*, 1950, **78**, 699.

¹³ Dalgarno, A., in 'Quantum Theory' (Ed. D. R. Bates), Vol. 1, Ch. 5 (Academic Press: New York 1961).

between vibronic states a and a' in molecule A, $E_a^A = h\nu_{a0}^A$ is the energy difference between the a^{th} state of A and its ground state, $\sigma_d^{00}(\text{N}_A)$ is the diamagnetic component of the isotropic shielding at nucleus N in the isolated species A,

$$\sigma_d^{a''0}(\text{N}_A) = \left(\frac{\mu_0}{4\pi}\right)\left(\frac{e^2}{3m_e}\right)\int\psi_{a''}^A\sum_{i=1}^{n(A)}r_{\text{Ni}}^{-1}\psi_0^A\text{d}\tau_A \quad (4)$$

and the summation in (3) extends over all excited vibronic states in the two molecules.

Expression (3) for chiral shielding involves multiplication of pseudo-scalar products of electric dipole transition moments on each molecule. The sign of each scalar triple product reflects the chirality of the molecule in question. Thus the chiral shieldings at nucleus N_A when the left- and right-handed isomers of A interact with a particular enantiomer of B are equal in magnitude but opposite in sign. When each diastereomeric pair has an intermolecular separation R the magnitude of the associated anisochrony is $2|\bar{\sigma}_c(\text{N}_A)|$. The result (3) reinforces symmetry arguments which predict that finite anisochrony persists even in the absence of stereospecific molecular interactions. An order of magnitude estimate of the size of this form of chiral shielding can be based on the first term in (3). Let molecules A and B be identical and possess only two electronically excited states 50000 cm^{-1} and 75000 cm^{-1} above the ground state. We assume that the transition moments μ^{0a} , $\mu^{aa'}$ and $\mu^{a'0}$ are each of magnitude 4.8 Debye units ($1\text{ D} = 3.336 \times 10^{-30}\text{ C m}$) and are polarized in the molecule-fixed x , y and z directions respectively. If the intermolecular separation R is 1.0 nm the new term is of the order $10^{-10}\sigma_d^{00}$ where σ_d^{00} is the normal diamagnetic shielding associated with the sensor nucleus. At this separation the chiral shielding (3) in R^{-9} is similar in magnitude to the R^{-6} contribution described earlier¹¹ and is too small to be experimentally significant. At shorter intermolecular distances the new term in R^{-9} is much bigger and may therefore contribute marginally to observed magnetic shielding non-equivalence of nuclei in heavy atoms for which σ_d^{00} is large. At short range, however, the assumption of uncorrelated intermolecular geometry is unwarranted and once geometric correlations are admitted standard shielding mechanisms⁷⁻⁹ take precedence.