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PREFACE

Volume 17 of Annual Reports consists of state of the art accounts of five rather distinct areas of NMR spectroscopy.

The review on Theoretical Aspects of Isotope Effects on Nuclear Shielding by Prof. C. J. Jameson and Dr. J. Osten, is a welcome complement to the account by Dr. P. E. Hansen in Volume 15 of this series. It is a pleasure to include the account on Relaxation Processes in Synthetic Polymers by Dr. F. Heatley which is the first time that this particular area of NMR has been visited in the present series.

The other three reports cover fields of NMR which have been treated *inter alia* in earlier volumes. The continuing burgeoning of the literature in these areas has resulted in complete chapters being required to provide adequate current coverage. Prof. J. D. Satterlee deals with the NMR of Paramagnetic Haem Proteins, Dr. T. Drakenberg covers the NMR of Less Common Quadrupolar Nuclei which was last treated in Volume 9 and Prof. P. Pregosin reviews Platinum NMR.

I am very grateful to all of the contributors for their diligence and kind cooperation in the production of this volume.

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G. A. WEBB
November 1985

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Theoretical Aspects of Isotope Effects on Nuclear Shielding

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I. INTRODUCTION

Isotope shifts have long been observed in high resolution NMR in the gas phase, in liquids and in solutions. There are large shifts associated with the mass dependence of rate constants for chemical reactions or changes in

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conformational structure. We do not consider these equilibrium or kinetic isotope effects, only intrinsic isotope effects. The review by Batiz-Hernandez and Bernheim[1] and the more recent one by Hansen[2a] in this series include most of the published data up to 1982. There is also a recent discussion of ^{13}C isotope shifts by Forsyth.[2b] Here we review the theory underlying the interpretation of isotope shifts in NMR. The interpretation of isotope shifts involves a consideration of the vibrational and rotational averaging of nuclear shielding. For this reason the isotope shift is intimately related to the observed temperature dependence of nuclear shielding in the gas phase in the zero-pressure limit. These two measurable properties share the same electronic factors - the change in shielding with bond extension or bond angle deformation.

We follow the notation introduced by Gombler[3] for the isotope shift observed for nucleus A upon substitution of the neighbouring ^{m}X isotope in the molecule with the heavier $^{m'}X$ isotope:

$$ {}^{n}\Delta A({}^{m'/m}X) = \frac{\nu_A(A\,{}^{m'}X\cdots) - \nu_A(A\,{}^{m}X\cdots)}{\nu_A(A\,{}^{m}X\cdots)} \qquad (m' > m) \qquad (1a) $$

where $\nu_A(A\,{}^{m'}X\cdots)$ is the resonance frequency of the A nucleus in the molecule having the heavier $^{m'}X$ isotope which is n bonds away from the observed nucleus. The molecules $(A\,{}^{m'}X\cdots)$ and $(A\,{}^{m}X\cdots)$ are isotopomers. The isotope shift can also be written in terms of the nuclear shielding difference:

$$ \begin{aligned} {}^{n}\Delta A({}^{m'/m}X) &= \sigma^{A}(A\,{}^{m}X\cdots) - \sigma^{A}(A\,{}^{m'}X\cdots) \qquad (1b) \\ &= \sigma - \sigma^{*} \end{aligned} $$

where the asterisk applies to the heavy isotopomer. Just as for spin–spin couplings, this notation becomes ambiguous when A and X are atoms in cyclic compounds in which there are at least two paths connecting the observed nucleus and substituted atom. In this case the observed quantity is an isotope shift corresponding to two or more bond paths.

There are several general observations which have been made about magnitudes and signs of isotope shifts:[1]

(i) Upon substitution with a heavier isotope the NMR signal of the nearby nucleus usually shifts towards lower frequencies (higher shielding). Thus, as defined in equation (1), isotope shifts are generally negative in sign.

(ii) The magnitude of the isotope shift is dependent on how remote the isotopic substitution is from the observed nucleus. Although there are exceptions, one-bond isotope shifts are larger than two-bond or three-bond isotope shifts.

(iii) The magnitude of the shift is a function of the observed nucleus and reflects its chemical shift range.

(iv) The magnitude of the shift is related to the fractional change in mass upon isotopic substitution.

(v) The magnitude of the shift is approximately proportional to the number of equivalent atoms which have been substituted by isotopes. In other words, isotope shifts exhibit additivity.

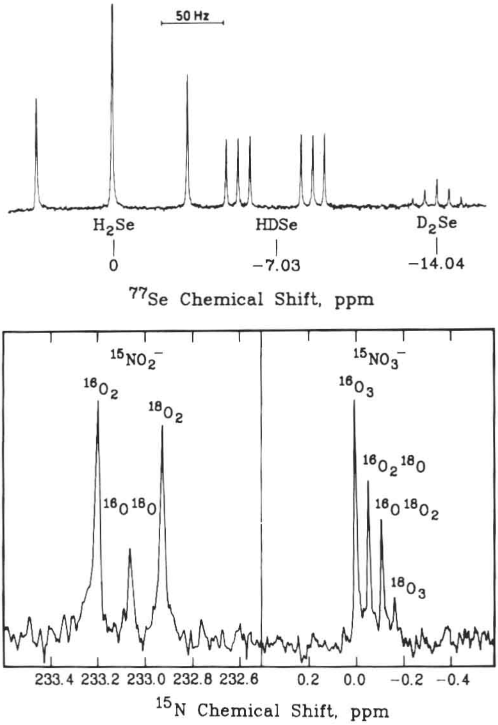

FIG. 1. ^{77}Se FT NMR spectrum of a mixture of H_2Se, HDSe and D_2Se, and ^{15}N spectra of $^{18/16}$O derivatives of NO_2^- and NO_3^-. From references 4 and 5, respectively, with permission.

Examples of isotope shifts in Fig. 1 illustrate these trends. The ^{77}Se shifts on D substitution in H_2Se are proportionately large (−7.02 ppm per D) compared to ^{17}O shifts on D substitution in H_2O (−1.54 ppm per D), reflecting the large chemical shift range of ^{77}Se compared to ^{17}O. ^{15}N shifts in NH_3 on D substitution (−0.65 ppm per D) are large compared to that for ^{15}N on ^{18}O substitution in NO_2^- (−0.138 ppm) showing the more favourable fractional mass changes in D substitution compared to O substitution. Figure 1 also clearly shows the additivity of isotope shifts; the isotope shift is proportional to the number of substituted atoms, giving rise to spectra exhibiting equal spacing of characteristic peaks for each isotopomer. We shall discuss the theory underlying these general observations.

There are some less general trends which have been observed, correlating isotope shift with molecular structure.

(a) One-bond isotope shifts tend to increase with increasing bond order[6-8] and decreasing bond length[3] between the observed nucleus and the substituted atom.

(b) The magnitudes of isotope shifts in similar bonds increase with the magnitude of the spin–spin coupling between the observed nucleus and the substituted atom.[9-11]

(c) The magnitudes of one-bond isotope shifts correlate with the chemical shift of the observed nucleus, i.e. the less shielded nuclei have larger isotope shifts.[11-13]

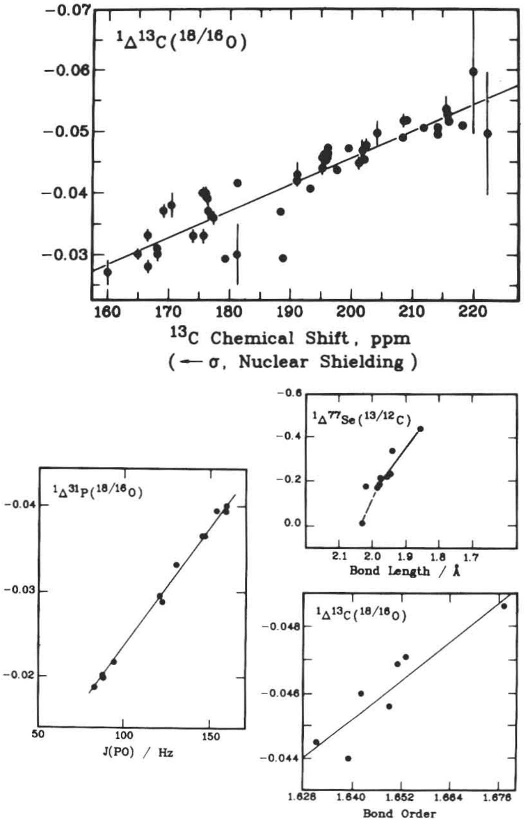

FIG. 2. Correlations between one-bond isotope shifts and various indices of the chemical bond: bond order, bond length, spin–spin coupling, nuclear shielding. From references 12, 10, 3 and 6, with permission.

(d) There is a lone pair effect on the isotope shifts. A nucleus with a σ lone pair tends to have a larger isotope shift in comparison with a related bond in which there is no lone pair on the observed nucleus; for example, the isotope shift for ^{15}N in NH_3 (−0.65 ppm per D) with one lone pair may be compared to that in NH_4^+ (−0.307 ppm per D) with zero lone pairs, or ^{15}N in NO_2^- can be compared with ^{15}N in NO_3^- (see Fig. 1).[14]

(e) The isotope shift tends to be larger when electronegative substituents are introduced at the nuclear site.[8]

Trends (a)–(c) are demonstrated in Fig. 2. These trends are interesting and require interpretation with a suitable theory. It is important to know which aspects of isotope shifts are due to dynamical factors (to rovibrational averaging) and which aspects can be attributed to electronic factors (changes in nuclear shielding with bond extension or bond angle deformation). If the theory can sort out the former, isotope shifts can be used to extract the latter, thus providing chemically interesting information which would make the isotope shift an easily measurable index of the chemical bond.

II. ROVIBRATIONAL EFFECTS ON NUCLEAR SHIELDING

The effects of intramolecular dynamics (vibration and rotation) on nuclear shielding were theoretically predicted by Ramsey[15] and have been observed in two ways. First, there is an observable temperature dependence of the resonance frequency even for the "isolated" molecule (apart from the temperature dependence due to intermolecular interactions).[16] Second, there is an observable shift upon isotopic substitution of neighbouring nuclei. Both are effects of differences in averaging over nuclear configuration as the molecule undergoes vibration and rotation. The temperature dependence of nuclear shielding is observed in the dilute gas phase, where the average shielding can be written as a virial expansion in the gas density ρ,

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

The intermolecular effects are contained in the density dependent terms.

The nuclear shielding in an "isolated" molecule, $\sigma_0(T)$, is actually observed as the nuclear shielding in the limit of pressure approaching zero. Yet, the pressure must be high enough so that collisional interactions cause a given molecule to pass through a representative number of thermally accessible vibrational and rotational states in a time that is short compared to the reciprocal of the NMR frequency difference between nuclei in different rovibrational states. Thus, mathematically speaking, one does not extrapolate the results to a true zero pressure, but to a pressure so low that collisional deformation of the molecule no longer contributes to σ, while there are still enough collisions to provide the required rate of transition between vibrational and rotational states.

The observed isotropic nuclear shielding of a nucleus in an isolated molecule, $\sigma_0(T)$, is a statistical average of the nuclear magnetic shielding tensor over all possible orientations of the molecule in the magnetic field. It is also an average over all possible rovibrational states of the molecule weighted according to the fraction of molecules occupying that state at that temperature. Thus, the value of the shielding of a nucleus in a gas sample extrapolated to zero density at a given temperature is a weighted average of the values characteristic of each occupied state.

The average shielding for a given rovibrational state is different for each of several isotopically related species because the masses enter into the solution of the vibrational-rotational hamiltonian. Thus, the thermal average shielding $\sigma_0(T)$ is different for the isotopomers. These differences are measured as isotope shifts. It has been found that mass effects on intermolecular interactions (except in hydrogen-bonding or complex-formation) are not significant, i.e. the mass dependence of $\sigma_1(T)$ in equation (2) is small.[17] Therefore, even isotope shifts measured in condensed phase can sometimes be interpreted as the differences between $\sigma_0(T)$ values of the isotopically related species.

A. Basic principles

The Born–Oppenheimer approximation allows us to consider the nuclear motion in rotation and vibration separately from the electronic motion. Within the Born–Oppenheimer approximation, we can consider a shielding surface which gives the values of nuclear shielding at rigidly fixed nuclear configurations. The interpretation of the experimentally observed nuclear magnetic shielding then involves the two surfaces, the potential energy surface and the nuclear shielding surface, with simultaneous averaging on both surfaces. Figure 3 shows the proton shielding surface[18] and the potential energy surface of the H_2^+ molecule.[19] The shielding surface gives the ^1H nuclear shielding calculated with the relativistic theory for fixed nuclear configurations. For a given rovibrational state, there will be a characteristic average shielding which can be evaluated from the vibrational and rotational wavefunctions and the nuclear shielding function such as the one shown in the figure. The vibrational levels of the HD^+ and D_2^+ isotopomers (which have lower vibrational frequencies than H_2^+) sit lower in the potential well and thus will give different average values of proton shielding. In this case the shielding surface is known for a wide range of nuclear configurations. For most systems, however, there is very limited information, the shielding surface being calculated for just a few points in the vicinity of r_e. For semirigid molecules that we often observe in NMR (excluding molecules

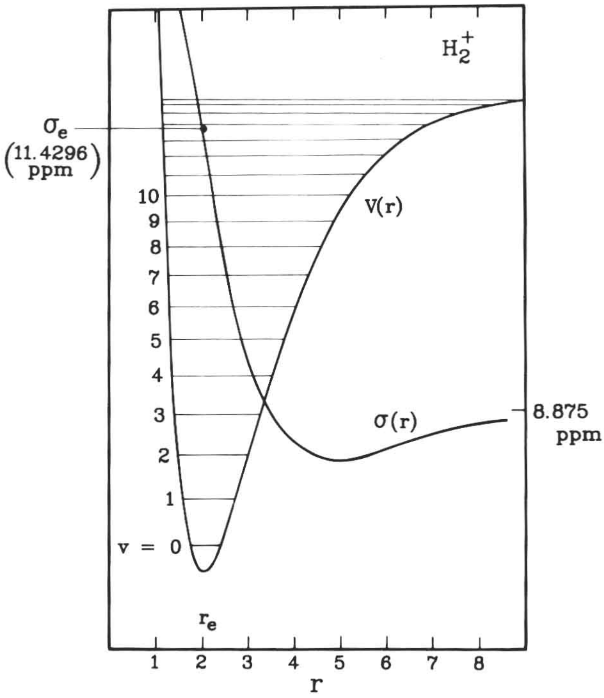

FIG. 3. The ^{1}H shielding surface and the potential energy surface for $^1H_2^+$. From references 18 and 19, with permission.

which are fluxional or which undergo low frequency torsion), the motions involved in the averaging take place in a small pocket of the potential energy surface close to the equilibrium configuration. Therefore this corresponds to averaging over small displacements on the shielding surface. Then it makes physical sense to expand the nuclear shielding in terms of the normal coordinates Q_s (a concept of significance only for small displacements):

$$\sigma = \sigma_e + \sum_s \left(\frac{\partial \sigma}{\partial Q_s}\right)_e Q_s + \frac{1}{2} \sum_{s,r} \left(\frac{\partial^2 \sigma}{\partial Q_r \, \partial Q_s}\right)_e Q_r \, Q_s + \cdots \tag{3}$$

where the shielding derivatives are taken at the equilibrium configuration. The application of this equation to a general molecular electronic property (not just nuclear shielding) for a general molecular type (an asymmetric rotor) as well as for specific types (spherical tops and symmetric tops) has been formulated.[20–22] Normal coordinates are a logical choice for this expansion since methods of evaluating the average values $\langle Q_s \rangle$, $\langle Q_r \, Q_s \rangle$ are well known in vibrational spectroscopy. However, the derivatives of the nuclear shielding with respect to the normal coordinates are not invariant under isotopic substitution. For the purpose of discussing the isotope shift it is more convenient to expand the shielding in terms of internal displacement coordinates:

$$\sigma = \sigma_e + \sum_i \left(\frac{\partial\sigma}{\partial\mathcal{R}_i}\right)_e \mathcal{R}_i + \frac{1}{2}\sum_{i,j}\left(\frac{\partial^2\sigma}{\partial\mathcal{R}_i\,\partial\mathcal{R}_j}\right)_e \mathcal{R}_i\,\mathcal{R}_j + \cdots \tag{4}$$

where $\mathcal{R}_i$ stands for the bond displacements (Δr_i) and the bond angle deformations $(\Delta\alpha_{ij})$.

The theoretical interpretation of isotope shifts in NMR therefore involves the mass-independent electronic quantities such as

$$(\partial\sigma/\partial\mathcal{R})_e = (\partial\sigma/\partial\Delta r)_e, (\partial\sigma/\partial\Delta\alpha)_e, \ldots$$

which describe the change in nuclear shielding with bond extension or angle deformation, and the mass-dependent thermal averages $\langle\mathcal{R}_i\rangle^T$ which are $\langle\Delta r\rangle^T$, $\langle\Delta\alpha\rangle^T$, ... and $\langle\mathcal{R}_i\,\mathcal{R}_j\rangle^T$ which are $\langle(\Delta r)^2\rangle^T$, $\langle(\Delta\alpha)^2\rangle^T$, $\langle\Delta r\,\Delta\alpha\rangle^T$, ... The isotope shift is given by

$$\begin{aligned}\sigma - \sigma^* = {} & \sum_i \left(\frac{\partial\sigma}{\partial\mathcal{R}_i}\right)_e [\langle\mathcal{R}_i\rangle^T - \langle\mathcal{R}_i\rangle^{T*}] \\ & + \frac{1}{2}\sum_{i,j}\left(\frac{\partial^2\sigma}{\partial\mathcal{R}_i\,\partial\mathcal{R}_j}\right)_e [\langle\mathcal{R}_i\,\mathcal{R}_j\rangle^T - \langle\mathcal{R}_i\,\mathcal{R}_j\rangle^{T*}] + \cdots\end{aligned} \tag{5}$$

B. Effect of vibration and rotation on the internuclear distance

1. The vibrational average bond extension

In order to be able to evaluate $\langle\mathcal{R}_i\rangle^T$, $\langle\mathcal{R}_i\,\mathcal{R}_j\rangle^T$, ... etc. we need a potential surface in which the vibrational motion of the molecule takes place. The known derivatives of this surface are the quadratic, cubic, etc. force constants. Normal coordinate analysis with the quadratic force constants gives the solutions to the harmonic problem whch are the harmonic frequencies (ω), the normal coordinates (Q), and the L matrix.[23] The internal displacement coordinates $\mathcal{R}_i = \Delta r_i, \Delta\alpha_{ij}$, etc. can be expressed in terms of these normal coordinates as follows:

$$\boldsymbol{\mathcal{R}} = \mathbf{LQ} \tag{6}$$

where **L** is a tensor which contains the transformation coefficients between the curvilinear internal coordinates and various powers of Q. The vibrational part of Δr_i is then

$$\Delta r_i = \sum_r L_i^r\, Q_r + \frac{1}{2}\sum_{r,s} L_i^{rs} Q_r\, Q_s + \frac{1}{6}\sum_{r,s,t} L_i^{rst}\, Q_r\, Q_s\, Q_t + \cdots \tag{7}$$

Thus the vibrational average $\langle\Delta r\rangle_{vib}$ can be expressed in terms of $\langle Q_r\rangle$,