The isotope shift in NMR

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The isotope shift observed in NMR is formulated in general for the diatomic molecule. The results are extended to polyatomic molecules and to a linear triatomic molecule in particular. General empirical observations which have been made on isotope shifts are explained in terms of the theoretical formulation given here.

Isotope shifts have long been observed in NMR in the gas phase, in liquids, and in solution. A review of NMR isotope shifts by Batiz-Hernandez and Bernheim summarizes the experimental data and notes some general patterns.[1] The interpretation of isotope shifts involves a consideration of the dynamic state of the molecule, since the vibrationally and rotationally averaged chemical shielding is in general different from the value at a fixed nuclear configuration. For this reason, the isotopic shift in NMR is intimately related to the temperature dependence of chemical shielding in an isolated molecule. In this work we will first consider isotope shifts in diatomic molecules since the calculation can be carried out explicitly in terms of the fractional change in mass upon isotopic substitution. Next we calculate the isotope shift in a linear triatomic molecule CO_2. Finally, we consider a general approximate expression for the isotope shift in terms of the fractional change in mass. With this theoretical framework, we can account for all of the five general empirical observations made by Batiz-Hernandez and Bernheim regarding the magnitudes of isotope shifts in NMR.

DIATOMIC MOLECULES

The general theory for the temperature dependence of NMR chemical shielding in isolated diatomic molecules has been derived in a previous paper.[2] For diatomic molecules the thermal average of the chemical shielding is given to second order as

$$\langle\sigma\rangle^T = \sigma_e + [f_{\mathrm{anh}}(T) + f_{\mathrm{rot}}(T)]\left(\frac{d\sigma}{dR}\right)_e + g(T)\left(\frac{d^2\sigma}{dR^2}\right)_e , \qquad (1)$$

where

$$f_{\mathrm{anh}}(T) = \frac{3h(1+\alpha\omega/6B_e^2)}{16\pi^2 c r_e \mu\omega}\coth\left(\frac{hc\omega}{2kT}\right),$$

$$f_{\mathrm{rot}}(T) = \frac{kT}{2\pi^2\mu r_e c^2\omega^2},$$

$$g(T) = \frac{h}{16\pi^2\mu c\omega}\coth\left(\frac{hc\omega}{2kT}\right).$$

This is essentially the same form which was given by Buckingham and Urland for a general property of a diatomic molecule.[3] The contributions to the temperature dependence of the chemical shielding come from the anharmonic vibration $f_{\mathrm{anh}}(T)$ and the centrifugal distortion $f_{\mathrm{rot}}(T)$, both appearing with the first derivative, and the contribution from harmonic vibration, $g(T)$, which is extremely small. In all the cases which have been studied, the coefficient of the second derivative is at least 1 order of magnitude smaller than the coefficient of the first derivative.[2] Thus, it will be sufficient to include only the linear term in discussions of the isotope shift in diatomic molecules.

In the context of the Born–Oppenheimer approximation, we may assume that $(d\sigma/dR)_e$ and σ_e are independent of nuclear masses. Then we can use the empirical $(d\sigma/dR)_e$ to determine the isotopic shift observed in NMR. For a diatomic molecule,

$$B_e^i = (\mu/\mu^i)B_e ,$$

$$\omega^i = (\mu/\mu^i)^{1/2}\omega ,$$

$$\alpha^i = (\mu/\mu^i)^{3/2}\alpha ,$$

where the superscript i refers to the isotopically substituted molecule. We see from Eq. (1) that to this order of approximation the rotational contribution is not affected by a change in masses. The major term which contributes to the isotope shift in the diatomic molecule is the anharmonic vibration term, since the term in the second derivative is considerably smaller. The isotope shift in a diatomic molecule is

$$\sigma^i - \sigma = \frac{3h(1+\alpha\omega/6B_e^2)}{16\pi^2 c r_e\mu\omega}\left(\frac{d\sigma}{dR}\right)_e \times\left\{-\left(\frac{\mu}{\mu^i}\right)^{1/2}\coth\left[\frac{hc\omega}{2kT}\left(\frac{\mu}{\mu^i}\right)^{1/2}\right] - \coth\left(\frac{hc\omega}{2kT}\right)\right\}. \qquad (2)$$

By neglecting terms of the order of $[(\mu^i-\mu)/\mu]^2$, we get

$$\sigma^i - \sigma = \frac{3h(1+\alpha\omega/6B_e^2)}{16\pi^2 c r_e\mu\omega}\left(\frac{d\sigma}{dR}\right)_e \times\left[-\frac{(\mu^i-\mu)}{2\mu}\coth\left(\frac{hc\omega}{2kT}\right) + \left(\frac{\mu^i-\mu}{\mu}\right)\frac{hc\omega}{kT}e^{-hc\omega/kT}\right]. \qquad (3)$$

For temperatures near room temperature (200–400 K), and for typical ω values, $(hc\omega/kT)$ is greater than ~3, so that the second term in Eq. (3) is much smaller than the first term. Nevertheless, the smaller second term is responsible for most of the temperature dependence of the isotope shift. In comparing magnitudes of shifts rather than their temperature dependence, the first term will be sufficient:

$$\sigma^i - \sigma = -\frac{(\mu^i-\mu)}{2\mu}f_{\mathrm{anh}}(T)\left(\frac{d\sigma}{dR}\right)_e . \qquad (4)$$

We can see from the formulation given here that although the centrifugal distortion may result in a somewhat more pronounced temperature dependence of σ than the anharmonic vibration,[2] the magnitude of the isotope shift is determined entirely by the anharmonic vibration in diatomic molecules. For a given $(\mu/\mu^i)^{1/2}$ we expect a larger isotope shift when the anharmonicity constant of the diatomic molecule is large. The isotope shift is in fact proportional to the mass-independent cubic force constant K_{111}. It should also be noted that Eqs. (2)–(4) apply to primary as well as secondary isotope shifts. However, in the case of the primary isotope shift, direct comparison with experiment is impossible owing to uncertainties in the nuclear moments of the bare nuclei. Comparison may be made, however, by using two different molecules A and B. The primary isotope shift may be cast in the form

$$\frac{\gamma^i}{\gamma}\left(\frac{1-\sigma_A^i}{1-\sigma_A}-\frac{1-\sigma_B^i}{1-\sigma_B}\right)\simeq\frac{\gamma^i}{\gamma}\left[(\sigma_B^i-\sigma_B)-(\sigma_A^i-\sigma_A)\right]$$

and the chemical shifts between molecules A and B measured using the two isotopic resonant nuclei.

We now calculate the isotope shift which may be observed between ^{35}ClF and ^{37}ClF. The results obtained using Eq. (2) are given in Table I. The values for $\sigma(^{35}ClF)-\sigma(^{37}ClF)$ are negative; ^{35}ClF is downfield of ^{37}ClF. At the observation frequency of 84.6 MHz, this is an isotope shift of about 7 Hz, with only a slight temperature dependence, going from 6.92 Hz at 350 K to 7.64 Hz at 280 K. Since nearly all the temperature dependence is in the term left out of Eq. (4), the approximate equation (4) gives values close to that obtained by Eq. (2) but with a temperature dependence in the opposite direction.

Let us see how Eq. (2) or (4) can account for some of the general observations which have been made about isotope shifts. In the review of NMR isotope shifts by Batiz-Hernandez and Bernheim, the following were noted[1]:

(1) Heavy isotopic substitution shifts the NMR signal of a nearby nucleus toward a higher magnetic field.

(2) The magnitude of the isotope shift is dependent on how remote the isotopic substitution is from the nucleus under observation.

(3) The magnitude of the shift is a function of the resonant nucleus reflecting the differences in the range of chemical shifts observed for the nuclei.

(4) The magnitude of the shift is largest where the fractional change in mass upon isotopic substitution is largest.

(5) The magnitude of the shift is approximately proportional to the number of atoms in the molecule that have been substituted by isotopes.

TABLE I. Isotope shift between ^{35}ClF and ^{37}ClF in ppm and in Hz at 84.651 MHz.

T	$10^2 f_{anh}(T)$ ^{37}ClF	$10^2 f_{anh}(T)$ ^{35}ClF	$\sigma(^{37}ClF)-\sigma(^{35}ClF)$ (ppm)	(Hz)
280	0.5176	0.5219	+0.0902	7.64
290	0.5204	0.5247	+0.0891	7.54
300	0.5234	0.5277	+0.0878	7.43
310	0.5266	0.5308	+0.0866	7.33
320	0.5300	0.5342	+0.0854	7.23
330	0.5336	0.5377	+0.0842	7.13
340	0.5374	0.5414	+0.0830	7.03
350	0.5414	0.5453	+0.0818	6.92

The observation that heavier atoms lead to upfield shifts is easily borne out by Eq. (4). If $(d\sigma/dR)_e$ is negative, as have been observed in F_2, ClF, and CO, then for $\mu^i > \mu$, $(\sigma^i - \sigma)$ is positive. This shows that the resonant nucleus in the heavier molecule is more shielded than (appears upfield of) the lighter molecule. For polyatomic molecules the situation is somewhat more complicated, but a trend parallel to that predicted by Eq. (4) might be expected.

For a given molecule, the quantities $\langle q_s\rangle^T$ and $\langle q_s^2\rangle^T$, which are properties of the dynamic state of the molecule, are fixed. Thus, given a molecule and its isotopically substituted counterpart, the quantities L_{is} and $\langle q_s\rangle^T$ and $\langle q_s^2\rangle^T$ are fully determined at a given temperature. If we now observe different resonant nuclei on this same pair of isotopically related species, then the isotope shift is different for each resonant nucleus only due to differences in $(d\sigma/dR_i)_e$ for the observed nuclei. In a diatomic molecule, the magnitude of the isotope shift is proportional to $(d\sigma/dR)_e$. In a polyatomic molecule, it is related to a particular linear combination of $(d\sigma/dR_i)_e$ at a given temperature. Let us first consider observing resonant nuclei of the *same* kind of atom. It is perfectly reasonable to expect that the shielding of a resonant nucleus depends to a greater extent on an angle displacement or bond stretch in its vicinity in the molecule, and that it depends to a lesser extent on an internal coordinate further removed from it. That is, $(d\sigma/dR_i)_e$ is expected to be smaller for an internal coordinate R_i which is further away from the resonant nucleus, thus leading to a smaller isotope shift for the resonant nucleus more remote from the substitution site, as is observed by Batiz-Hernandez and Bernheim.

Let us now consider observing resonant nuclei of different kinds of atoms, e.g., ^1H and ^{19}F, in the same pair of isotopically related molecules. As in the above discussion, the properties of the dynamic state and L_{is} are fully determined, and the isotope shift is different for each resonant nucleus only due to differences in $(d\sigma/dR_i)_e$. The range of chemical shifts of some nuclei are much greater than others. Such general trends have been discussed by Jameson and Gutowsky in terms of both the molecular orbital treatment and the valence bond treatment of chemical shielding. In an approximate theory of chemical shielding in which only the electrons in orbitals centered on the nucleus in question were considered, Jameson and Gutowsky were able to explain the dependence on atomic number of the magnitudes of the range of chemical shifts for a multitude of nuclei observed in NMR.[4] Their discussion was based on the extent of deviations from spherical symmetry with increasing atomic number and the periodic changes in $\langle 1/r^3\rangle$ for atoms across the periodic table. This approximate theory was successful in explaining the range of chemical shifts of nuclei reported at that time and additional data have continued to bear out their conclusions. The nuclear species with a larger range of chemical shifts is expected to have larger derivatives of chemical shielding. The $(d\sigma/dR_i)_e$ are measures of the change in σ with relatively minor changes in molecular configuration around the equilibrium configuration, whereas the range of chemical shifts is a measure of the change in σ accompanying changes in nuclear environment in going from one molecule to another. The generally larger derivatives for σ of a resonant nucleus whose range of chemical shifts is large leads to a larger isotope shift.

For a given resonant nucleus in a diatomic molecule $(d\sigma/dR)_e$ is fixed so that from Eq. (4) we see that the isotope shift is proportional to $(\mu^i-\mu)/\mu$. Thus, the ^1H isotope shift between $^1H^3T$ and $^1H_2$ is greater than that between $^1H^2D$ and $^1H_2$. In polyatomic molecules the situation is more complicated but it is to be expected that the mass dependent terms also lead to magnitudes of isotope shifts which are related to $(\mu^i-\mu)/\mu$. Thus, we should expect that the largest isotope shifts occur where the fractional change in mass upon isotopic substitution is largest.

The fifth general observation by Batiz-Hernandez and Bernheim of approximate proportionality of isotope shifts to number of atoms which have been isotopically substituted cannot be discussed in terms of Eq. (2) or (4) because in a diatomic molecule there is only one other nucleus. However, we can explore this aspect of isotope shifts in terms of the triatomic molecule.

POLYATOMIC MOLECULES

For polyatomic molecules with three or more atoms, unlike diatomic molecules, the rotational contribution to the isotope shift is not necessarily zero. The formulation of the isotope shift is more complicated since several masses are involved. For a polyatomic molecule, the thermal average of chemical shielding is[2]

$$\begin{aligned}\langle\sigma\rangle^T = \sigma_e &+ \sum_j\left(\frac{\partial\sigma}{\partial R_j}\right)_e \sum_s \frac{-\bar{L}_{js}}{2\omega_s}\left[3k_{sss}\coth\left(\frac{hc\omega_s}{2kT}\right) + {\sum_{s'}}' g_{s'}k_{ss's'}\coth\left(\frac{hc\omega_{s'}}{2kT}\right)\right] \\ &- \frac{kT}{2\pi c}\left(\frac{1}{hc\omega_s}\right)^{1/2}\sum_\alpha \frac{a_s^{\alpha\alpha}}{I_{\alpha\alpha}(e)} + \frac{1}{4}\sum_j\sum_k\left(\frac{\partial^2\sigma}{\partial R_j\partial R_k}\right)_e \sum_s \coth\left(\frac{hc\omega_s}{2kT}\right)\bar{L}_{js}\bar{L}_{ks}\ . \end{aligned} \qquad (5)$$

In the notation introduced by Nielsen, k_{sss} is a cubic force constant in terms of the dimensionless normal coordinates, g_s is the degeneracy of the sth vibrational mode, and $a^{\alpha\alpha}$ are the coefficients in the expression of the moments of inertia in terms of the normal coordinates.[5] All the other symbols have their usual meaning. Then, the isotope shift is given by

$$\begin{aligned}\sigma^i - \sigma = &\sum_j\left(\frac{\partial\sigma}{\partial R_j}\right)_e \sum_s\left\{\frac{-\bar{L}^i_{js}}{2\omega^i_s}\left[3k^i_{sss}\coth\left(\frac{hc\omega^i_s}{2kT}\right)+\cdots\right] + \frac{\bar{L}_{js}}{2\omega_s}\left[3k_{sss}\coth\left(\frac{hc\omega_s}{2kT}\right)+\cdots\right]\right\} \\ &+ \frac{1}{4}\sum_j\sum_k\left(\frac{\partial^2\sigma}{\partial R_j\partial R_k}\right)_e\sum_s\left[\coth\left(\frac{hc\omega^i_s}{2kT}\right)\bar{L}^i_{js}\bar{L}^i_{ks} - \coth\left(\frac{hc\omega_s}{2kT}\right)\bar{L}_{js}\bar{L}_{ks}\right]. \end{aligned} \qquad (6)$$

The cubic force constants for dimensionless normal coordinates k_{rst} are expressible in terms of the force constants in the internal displacement coordinates K_{ijk} by

$$k_{rst} = \sum_{i,j,k} K_{ijk}\bar{L}_{ir}\bar{L}_{js}\bar{L}_{kt} \qquad (7)$$

[see, for example, Ref. 6, Eqs. (4)–(6)]. $\bar{L}$ is the transformation matrix which converts the dimensionless normal coordinates to internal displacement coordinates,

$$R_i = \sum_r \bar{L}_{ir}q_r\ .$$

In the context of the Born–Oppenheimer approximation, the force constants K_{ijk} are essentially mass independent. As we have already seen, for x values of interest here, the $\coth(x)$ function changes much more slowly than x, so that for a small mass change, $\coth(hc\omega/2kT)$ remains essentially the same. Therefore, nearly the entire mass dependence of σ rests in the mass dependence of $\bar{L}_{js}$. For example, the explicit mass dependence of $\bar{L}$ for $^{12}C^{16}O_2$ is given by Buckingham and Urland as follows[3]:

$$\bar{L} = \begin{bmatrix} \sqrt{\dfrac{h(m_O)^{-1}}{8\pi^2\omega_1 c}} & 0 & \sqrt{\dfrac{h[(m_O)^{-1}+2(m_C)^{-1}]}{8\pi^2\omega_3 c}} \\ 0 & \sqrt{\dfrac{h[(m_O)^{-1}+2(m_C)^{-1}]}{2\pi^2 r_e^2\omega_2 c}} & 0 \\ \sqrt{\dfrac{h(m_O)^{-1}}{8\pi^2\omega_1 c}} & 0 & -\sqrt{\dfrac{h[(m_O)^{-1}+2(m_C)^{-1}]}{8\pi^2\omega_3 c}} \end{bmatrix}.$$

The form of $\overline{L}_{js}$ is different for each molecular type, so that a general expression for the isotope shift which is simpler than Eq. (6), and which explicitly accounts for some of the observed trends in polyatomic molecules, is not easily obtained. While there are product rules which relate the ratio of the products of vibrational frequencies to products of masses, and sum rules which relate sums of the squares of frequencies of isotopic molecules, a completely general treatment of the isotope effect in polyatomic molecules which is explicit in terms of mass ratios is not possible. The details of the isotope shift in σ vary with each molecular type, e.g., planar XY_3.

However, a few general observations can be made:

(a) For molecules with a high degree of symmetry, the rotational contribution is independent of the masses of the atoms, if substitution is made symmetrically. In these cases the rotational contribution to the isotope shift is zero. This is based on the mass-independent centrifugal distortion in these molecules.[7] Examples are

$$CO_2 \text{ type: } (\sigma-\sigma_e)_{\mathrm{rot}} = \frac{kT}{r(F_{11}+F_{12})}\left(\frac{\partial\sigma}{\partial R}\right)_e ,$$

$$CH_4 \text{ type: } (\sigma-\sigma_e)_{\mathrm{rot}} = \frac{3kT}{4rF_{11}}\left(\frac{\partial\sigma}{\partial R}\right)_e ,$$

$$BF_3 \text{ type: } (\sigma-\sigma_e)_{\mathrm{rot}} = \frac{3kT}{nrF_{11}}\left(\frac{\partial\sigma}{\partial R}\right)_e \text{ for planar } AX_n ,$$

$$SF_6 \text{ type: } (\sigma-\sigma_e)_{\mathrm{rot}} = \frac{3kT}{6rF_{11}}\left(\frac{\partial\sigma}{\partial R}\right)_e .$$

Since the force constants F_{ij} and the derivatives $(\partial\sigma/\partial R)_e$ are independent of isotopic substitution in the context of the Born–Oppenheimer approximation, so are the rotational contributions to σ, if isotopic substitution is made symmetrically. Thus, in these cases there is no rotational contribution to the isotope shift. Any isotopic shift observed comes from anharmonic vibration or the second order harmonic terms. Substitution of peripheral atoms can lead to a substantial anharmonic vibrational contribution to the isotope shift. The disappearance of the centrifugal distortion contribution to the isotope shift upon symmetrical substitution indicates that the centrifugal distortion cannot be the dominant contribution to isotope shifts in polyatomic molecules. If the centrifugal distortion dominated isotope shifts then the empirically observed approximate proportionality of the shift to the number of atoms substituted would not be observed. For example, the ^{13}C shift in CH_3D, CH_2D_2, CHD_3, and CD_4 relative to CH_4 would increase with each additional deuterium and then go to zero for CD_4. That behavior of this type has not been observed implies that the centrifugal distortion contribution probably does not dominate isotope shifts.

(b) The thermal average of only the totally symmetric normal coordinates appear in the linear term. Isotopic substitution of an atom which is located at more than one principal axis (the central atom), such as C in CO_2 or Si in SiF_4, will have no effect on $\overline{L}_{is}$. Here s refers to the totally symmetric normal coordinate. In such cases, the ω_s as well as k_{sss} are independent of the isotopic substitution. In Eq. (5) we still have the terms $\sum_{s'}' g_{s'} k_{ss's'} \coth(hc\omega_{s'}/2kT)$, where s' refers to non-totally-symmetric normal coordinates. These will be affected by isotopic substitution. The centrifugal distortion contribution will not have an isotope shift, as seen above in (a). As a consequence of some of the contributions being zero, it is to be expected that the isotope shifts are somewhat smaller in cases where the central atom rather than a peripheral atom is substituted.

In polyatomic molecules the number of distinct second derivatives of σ with respect to internal coordinates can be rather large; for example, in BF_3 and NH_3, there are six second derivatives, in CF_4-type molecules there are seven, in SF_6-type molecules there are 11, and in CF_3Cl-type molecules there are 16. The fact that the isotope shift in polyatomic molecules has been found to be in the same direction in nearly all the observations listed by Batiz-Hernandez and Bernheim, and in those shifts which were reported after their review article appeared, implies two very general conditions:

(a) The linear terms nearly always dominate over the quadratic terms.

(b) The first derivatives are always the same sign. Any other conditions would require a highly unusual combination of coincidences in each of hundreds of examples of isotope shifts.

Let us consider CO_2 as an example and derive the anharmonicity contribution to the ^{13}C isotope shift between $^{16}O^{13}C^{16}O$ and $^{18}O^{13}C^{16}O$ or $^{18}O^{13}C^{18}O$. For a triatomic molecule,

$$(\sigma^i-\sigma)_{\mathrm{anh}} = \sum_{j=1}^{3}\left(\frac{\partial\sigma}{\partial R_j}\right)_e\left(\sum_s \overline{L}{}^i_{js}\langle q^i_s\rangle^T_{\mathrm{anh}} - \sum_s \overline{L}_{js}\langle q_s\rangle^T_{\mathrm{anh}}\right) .$$

In the Born–Oppenheimer approximation for ^{13}C shielding, $(\partial\sigma/\partial R_1)_e = (\partial\sigma/\partial R_2)_e$, regardless of symmetric or asymmetric ^{18}O substitution. Thus, there are only two first derivatives to consider, and they are equal to each other. The remaining first derivative, that with respect to the angle displacement, does not appear. The only normal coordinate in which it can be expressed is non-totally-symmetric, for which $\langle q\rangle^T = 0$. Thus, for ^{13}C shielding in CO_2,

$$\begin{aligned}(\sigma^i-\sigma)_{\mathrm{anh}} = \left(\frac{\partial\sigma}{\partial R_1}\right)_e [(\overline{L}{}^i_{11}+\overline{L}{}^i_{31})\langle q^i_1\rangle^T_{\mathrm{anh}} - (\overline{L}_{11}+\overline{L}_{31})\langle q_1\rangle^T_{\mathrm{anh}} \\ + (\overline{L}{}^i_{13}+\overline{L}{}^i_{33})\langle q^i_3\rangle^T_{\mathrm{anh}} - (\overline{L}_{13}+\overline{L}_{33})\langle q_3\rangle^T_{\mathrm{anh}}] ,\end{aligned} \qquad (8)$$

where

$$\langle q_s\rangle^T_{\mathrm{anh}} = -\frac{1}{2\omega s}\left[3k_{sss}\coth\left(\frac{hc\omega_s}{2kT}\right) + \sum_{s'}{}' g_{s'}k_{ss's'}\coth\left(\frac{hc\omega_{s'}}{2kT}\right)\right] .$$

The spectroscopic constants and $\overline{L}_{is}$ for CO_2 molecules are given in Table II. The $\overline{L}_{is}$ are obtained from Wilson's L matrix elements as follows:

$$\overline{L}_{is} = \left(\frac{h}{4\pi^2 c\omega_s}\right)^{1/2} L_{is} .$$

TABLE II. Molecular constants of isotopic carbon dioxide.

	$^{13}C^{16}O_2$ [a]	$^{13}C^{16}O^{18}O$ [a]	$^{13}C^{18}O_2$
ω_1	1353.96 cm^{-1}	1315.13	1276.5 [b]
ω_2	653.96	648.42	643.38 [b]
ω_3	2328.09	2309.85	2290.4 [b]
k_{111}	−45.56 cm^{-1}	−43.86	−42.16 [c]
k_{122}	72.36	70.88	69.4 [c]
k_{133}	−241.84	−236.24	−230.64 [c]
k_{311}	0	−4.78	0
k_{322}	0	−6.67	0
k_{333}	0	8.21	0
$\bar{L}_{11}$ [d]	0.2788×10^{-9} cm	0.2684×10^{-9}	0.2708×10^{-9}
$\bar{L}_{13}$	0.3957×10^{-9}	0.4029×10^{-9}	0.3924×10^{-9}
$\bar{L}_{31}$	0.2788×10^{-9}	0.2803×10^{-9}	0.2708×10^{-9}
$\bar{L}_{33}$	-0.3957×10^{-9}	-0.3483×10^{-9}	-0.3924×10^{-9}
$\bar{L}_{22}$	0.1287	0.1282	0.1277

[a] ω_s and k_{rst} are from I. Suzuki, J. Mol. Spectrosc. 25, 479 (1968).

[b] Calculated from $^{13}C^{16}O_2$ data using

$$\left(\frac{\omega_1^i}{\omega_1}\right)^2=\frac{m_O}{m_O^i}\quad\left(\frac{\omega_2^i}{\omega_2}\right)^2=\left(\frac{\omega_3^i}{\omega_3}\right)^2=\frac{m_O(1+2m_O^i/m_C^i)}{m_O^i(1+2m_O/m_C)}\,.$$

[c] The isotopic relationships for anharmonic force constants, unlike the fundamental frequencies, are not trivial. However, the isotopic k_{111}, etc., can be obtained from relationships such as

$$k_{111}=\frac{K_{111}}{2hc}(\bar{L}_{11}^3+\bar{L}_{31}^3)+\frac{K_{133}}{2hc}(\bar{L}_{11}^2\bar{L}_{31}+\bar{L}_{11}\bar{L}_{31}^2),$$

where K_{111} and K_{133} are mass-independent force constants available from I. Suzuki (see Footnote a above).

[d] L_{ts} values are calculated according to the method described in the text.

L_{ts} are the normalized eigenvectors of the secular equation[8]

$$|\mathbf{F}-\mathbf{G}^{-1}\lambda_s|=0$$

in Wilson's notation. We use the relationship

$$\coth(y+\Delta y)\simeq[1-4(\Delta y)e^{-2y}]\coth(y) \qquad (9)$$

for coth(y) very close to 1.00, and the constants given in Table II to get the following isotope shifts:

$$\sigma(^{13}C^{18}O_2)-\sigma(^{13}C^{16}O_2)$$
$$=\left(\frac{\partial\sigma}{\partial R_1}\right)_e\left(-0.000183-\frac{0.1709}{T}\exp(-1793.68/T)\right) \qquad (10)$$

and

$$\sigma(^{13}C^{16}O^{18}O)-\sigma(^{13}C^{16}O_2)$$
$$=\left(\frac{\partial\sigma}{\partial R_1}\right)_e\left(-0.000101-\frac{0.08974}{T}\exp(-1793.68/T)\right)\,. \qquad (11)$$

Using a value of − 1000 ppm/Å for $(\partial\sigma/\partial R_1)_e$, the ^{13}C isotope shift between $^{16}O^{13}C^{16}O$ and $^{16}O^{13}C^{18}O$ and that between $^{16}O^{13}C^{16}O$ and $^{18}O^{13}C^{18}O$ are calculated. The results are shown in Table III. Note that the isotopic shift for the doubly ^{18}O-labeled CO_2 is about twice that of the singly labeled. This is consistent with the fifth empirical observation made by Batiz-Hernandez and Bernheim, that the magnitude of the isotope shift is approximately proportional to the number of isotopically substituted atoms.[1] It appears that the anharmonic vibration contribution to the linear term is primarily responsible for this trend. Note that the rotational contribution to the $C^{18}O_2$–$C^{16}O_2$ shift is zero owing to symmetrical substitution, whereas the $^{16}OC^{18}O$–$C^{16}O_2$ shift should have a small rotational contribution which we have not included here.

We can get an approximate proportionality of the isotope shift to the number of isotopically substituted atoms for a general type of polyatomic molecule. The typical element of Wilson's G matrix is of the form $[(1/m_1)+(1/m_2)]$ or $\cos\phi/m_1$. General formulas for G matrix elements are given in Ref. 8. The L matrix elements are normalized such that

$$\mathbf{L}\mathbf{L}^T=\mathbf{G}.$$

Thus, the L matrix elements involve one or two atomic masses and typically have the form

$$l=\left(\frac{1}{m_1}+\frac{1}{m_2}\right)^{1/2}.$$

For example, for the CO_2 molecule

$$L_{11}=\left(\frac{1}{2m_O}\right)^{1/2}, \quad L_{13}=\left(\frac{1}{2m_O}+\frac{1}{m_C}\right)^{1/2}.$$

Let us consider $[(1/m_1)+(1/m_2)]^{1/2}$ as a typical form of L_{ts}. For an isotope molecule, $m_1+\Delta m_1$ replaces m_1, so that

$$l^i=\left(\frac{1}{m_1+\Delta m_1}+\frac{1}{m_2}\right)^{1/2}$$

when Δm_1 is small compared to m_1,

$$\frac{1}{m_1+\Delta m_1}\simeq\frac{1}{m_1}\left(1-\frac{\Delta m_1}{m_1}+\cdots\right),$$

so that if we neglect second order terms,

$$l^i\simeq\left(1+\frac{\Delta m_1}{m_1+m_2}-\frac{\Delta m_1}{m_1}\right)^{1/2}l\,.$$

Using the approximation $(1-x)^{1/2}\simeq1-x/2$ for small x, we get

$$l^i\simeq l\,\frac{1}{2}\left(\frac{\Delta m_1}{m_1}-\frac{\Delta m_1}{m_1+m_2}\right).$$

There are two parts to the linear term in σ_1, the anharmonic vibration and the centrifugal distortion. The L_{ts} appear in the rotational part in a linear combination. On the other hand, the L_{ts} appear in the anharmonic vi-

TABLE III. ^{13}C isotope shift in isotopic carbon dioxide, relative to $^{13}C^{16}O_2$ [a] using $(\partial\sigma/\partial R_1)_e=-1000.$ ppm/Å.

T(K)	$\sigma(^{13}C^{18}O_2)-\sigma(^{13}C^{16}O_2)$ (ppm)	$\sigma(^{13}C^{16}O^{18}O)-\sigma(^{13}C^{16}O_2)$ (ppm)
200	0.1830	0.1010
250	0.1835	0.1013
300	0.1844	0.1017
350	0.1859	0.1025
400	0.1878	0.1035

[a] At 22.6 MHz, the shifts at 300 K correspond to 4.2 Hz and 2.3 Hz, respectively.

bration part of σ in the fourth power. [See Eqs. (5) and (7).] For example, one term in the anharmonic part of σ for CO_2 appears with the factor $(L_{11}+L_{31})(L_{11}^3+L_{31}^3)$. As each L_{is} is replaced by

$$\left[1-\frac{1}{2}\left(\frac{\Delta m_j}{m_j}-\frac{\Delta m_j}{m_j+m_k}\right)\right]L_{is}\ ,$$

then the anharmonic term for the isotopically substituted case becomes

$$\sigma_{\mathrm{anh}}^{i}\simeq\left[1-\frac{1}{2}\sum_j\left(\frac{\Delta m_j}{m_j}-\frac{\Delta m_j}{m_j+m_k}\right)\right]\sigma_{\mathrm{anh}}\ .$$

Only the leading terms are included in the above approximate equation. The terms which have been dropped vary from one molecule to another and are less easily generalized. If we ignore the smaller rotational contribution, the isotope shift for polyatomic molecules is approximately given by

$$(\sigma^i-\sigma)\simeq-\frac{1}{2}\sum_j\left(\frac{\Delta m_j}{m_j}-\frac{\Delta m_j}{m_j+m_k}\right)\sigma_{\mathrm{anh}}\ . \qquad (12)$$

This general form for the approximate isotope shift is consistent with Eq. (4) for diatomic molecules. It is, of course, only a crude approximation since we used a form $[(1/m_j)+(1/m_k)]^{1/2}$ for all L_{is} whereas they do not all have this form. We have already discussed the smaller terms which have been left out of Eq. (4) for diatomics. Comparable small terms have been left out of Eq. (12). For example, in CO_2, we calculate isotope shifts at 300 K of 0.134 and 0.268 ppm using Eq. (12) while the full calculation gave 0.1017 and 0.1844 ppm, respectively.

Several points can be noted about Eq. (12). First, the isotope shift will be usually positive, that is, the heavier isotopic molecule appears upfield. This will result if σ_{anh} is usually negative. For the diatomic molecules ClF, F_2, CO, H_2, HBr, and HCl, the values of $(\partial\sigma/\partial R_1)_e$ are negative.[2] Thus, σ_{anh} is negative for these molecules. Moreover, the empirical values for $(\langle\sigma\rangle^{300}-\sigma_e)$ for these molecules are negative, ranging from − 0.8 to − 39 ppm.[2] If we neglect the quadratic term, $(\langle\sigma\rangle^{300}-\sigma_e)$ is a measure of the linear term in σ at 300 K, again negative. Secondly, the sum rule for the number of isotopic substitutions is clearly seen in Eq. (12), where there will be a term $\Delta m_j/m_j$ for every isotopically substituted atom. Thus, the magnitude of the isotope shift will be approximately proportional to the number of isotopically substituted atoms, as was found by Batiz-Hernandez and Bernheim. Thirdly, the isotope shift is large for a large linear term in σ. Although both the temperature dependence of σ and the isotope shift depend on the electronic property $(\partial\sigma/\partial R_1)_e$, these two observables are not necessarily related in magnitude. The first comes from the temperature dependence of the dynamic state of the molecule, the second comes from the mass dependence.

We have shown that the general empirical observations regarding isotope shifts in NMR can be explained by the approximate theoretical treatment given here. In some cases the temperature dependence of chemical shielding is so small as to be within the precision of the measurements at different temperatures. In these instances, the isotope shift may be a more reliable method of obtaining an empirical $(\partial\sigma/\partial R_1)_e$ since the observed frequency difference at a given temperature can be measured with great precision provided the observed peaks are sufficiently narrow.

Although the molecular property considered here has been the NMR chemical shielding, the theoretical treatment holds for any molecular electronic property such as dipole moment, hyperfine coupling constant, quadrupole coupling constant, diamagnetic susceptibility, etc. Each molecular property will have characteristic derivatives with respect to internal displacement coordinates. However, all the molecular constants which have to do with the dynamic state of the molecule remain the same. In fact, since the isotope shifts in the other molecular electronic properties are determined by relationships similar to Eq. (12), we can predict the following general observations: (a) The magnitude of the isotope shift in any such property is largest where the fractional change in mass upon isotopic substitution is largest, and (b) the magnitude of the shifts in these properties is approximately proportional to the number of atoms in the molecule that have been substituted by isotopes.

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