The additivity of NMR isotope shifts

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One of the most interesting and useful aspects of the isotope effect on nuclear magnetic shielding is the proportionality of the shift to the number of substituted atoms in equivalent positions. In this paper we show the quantitative basis for the additivity of isotope shifts in NMR, using the $CX_{4-n}Y_n$ (X,Y = H,D,T) system and the linear triatomic systems CO_2, NNO, and OCS as examples. We also predict small deviations from additivity and find that these deviations are consistent with those observed for ^{14}N shifts in the $NH_{4-n}D_n^+$ homologous series. Furthermore, we determine the mass dependence of the one-bond isotope shift.

INTRODUCTION

Isotope shifts have been observed since the very early days of high-resolution NMR. The review by Batiz–Hernandez and Bernheim in 1967[1] summarized experimental data and recognized some of the patterns which provide the basis for many of the applications of intrinsic isotope shifts. Briefly, these are (1) the sign of the isotope shift is nearly always negative, that is, with heavy isotope substitution, the resonance frequency decreases (shielding increases). (2) The magnitude of the shift is a function of the resonant nucleus, greater for nuclei with large chemical shifts. (3) The magnitude depends on the remoteness of the isotopic substitution site from the observed nucleus, and (4) the fractional change in mass. (5) The magnitude of the isotope shift is proportional to the number of atoms that have been substituted by isotopes.

We interpreted these general observations in terms of the same theoretical framework as the temperature dependent nuclear shielding in a previous paper (paper I).[2] Briefly, this interpretation is as follows:

$$\sigma_0 = \sigma_e + \sum_i (\partial\sigma/\partial\Delta r_i)_e \langle \Delta r_i \rangle + \cdots . \tag{1}$$

If the Born–Oppenheimer separation is valid, then all isotopomers have the same shielding surface and also the same potential energy surface. Thus σ_e and its derivatives are characteristic of all isotopomers at the equilibrium nuclear configuration. The shielding difference between two isotopically related molecules is then given by

$$\sigma_0^* - \sigma_0 = \sum_i (\partial\sigma/\partial\Delta r_i)_e [\langle \Delta r_i \rangle^* - \langle \Delta r_i \rangle] + \cdots, \tag{2}$$

where the derivatives of nuclear shielding with respect to bond extension $(\partial\sigma/\partial\Delta r_i)_e$ are mass independent, large and usually negative for Δr_i corresponding to extension of the bond in which the observed nucleus is directly involved. The sign of $(\partial\sigma/\partial\Delta r_i)_e$ for Δr_i one or more bonds away is probably also negative, but has not been investigated. The mean bond displacement $\langle \Delta r_i \rangle$ is usually greater when one of the atoms involved in it is replaced by a lighter isotope. The effect of a remote isotopic substitution on the mean bond displacement has not been explored. There may be important terms involving second derivatives with respect to bond extension and bond angle deformation. However, the general trends can be explained using only the linear terms.[2] Our recent calculations on CO_2, NNO, and COF_2 support this conclusion.[3,4] In paper I, we explained the general trends in isotope shifts using formulas and numerical results derived for a diatomic molecule and for CO_2. A more complete theory is now in order.

One of the theoretically interesting and practically useful aspects of the isotope effect on NMR chemical shifts is the proportionality of the shift to the number of substituted atoms in equivalent positions. The practical consequences of this is a spectrum with equally spaced peaks, the intensities giving an indication of the relative amounts of each isotopomer in the sample. For example, the one-bond $^{2/1}H$-induced isotope shift in the ^{13}C spectrum of the CH_nD_{4-n} isotopomers result in incremental isotope shifts as n goes from 0 to 4.[5] There are similar observations in other systems, such as in PO_4^{-3},[6] NO_2^-,[7] NO_3^-,[8] $NH_{4-n}D_n^+$,[9] $BH_{4-n}D_n^-$,[10] $NH_{3-n}D_n$,[11] $PH_{3-n}D_n$,[12] $SeH_{2-n}D_n$.[13] Nor is this observation limited to one-bond isotope shifts. For example, the ^{59}Co spectrum of $Co(en)_3Cl_3$ in H_2O/D_2O solution shows 13 equally spaced peaks separated by 5.2 ppm, the peaks corresponding to all the members of the isotopic homologous series in which the 12 exchangable hydrogen atoms per molecule of the cobalt complex are replaced by deuterium atoms.[14] This additivity of the isotope effect on the chemical shift upon substitution in equivalent locations appears to be without exception, and the deviations from additivity usually appear to be small and have been noticed outside of experimental error only in isolated cases.

There are some indications of additivity of mass effects in other molecular spectroscopy. The sum of the squares of the vibrational frequencies of members of an isotopic homologous series is linearly related to the number of isotopes substituted, and this relation is valid for symmetry types which are common to all members of the series. This was derived rigorously by Decius and Wilson.[15] The sum of vibrational frequencies in $CH_{4-n}D_n$ was found empirically to depend on the number (n) of the substitutions by the heavy isotope, that is, the zero-point energies of these molecules are linearly related to n.[16] This was found to be generally true for members of isotopic homologous series, but with second or-

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der corrections.[17] This additivity of mass effects on zero-point vibrational energies was cited by Batiz–Hernandez and Bernheim as a parallel case to and as a possible reason for NMR isotope shift additivity, although the connection is not at all clear.

There is some indication of additivity of mass effects on average nuclear positions as well. Kuchitsu and Oyanagi[18] determined the isotopic differences in the average nuclear positions in the principal inertial axes for linear triatomic molecules. They calculated $r_z = r_e + \langle \Delta z \rangle_0$, where Δz denotes an instantaneous displacement of r projected on the equilibrium bond direction (taken as a temporary z axis) and 0 denotes an average over the ground vibrational state. Their results can be summarized as follows: (1) $(r_z^* - r_z)$ caused by multiple isotopic substitutions are additive. For example, $r_z(^{18}O^{13}C^{34}S) - r_z(^{16}O^{12}C^{32}S) = [r_z(^{18}O^{12}C^{32}S) - r_z(^{16}O^{12}C^{32}S)] + [r_z(^{16}O^{13}C^{32}S) - r_z(^{16}O^{12}C^{32}S)] + [r_z(^{16}O^{12}C^{34}S) - r_z(^{16}O^{12}C^{32}S)]$. The additive increments are of the order of $(1-10) \times 10^{-5}$ Å for OCS, HCN. (2) When a nucleus is substituted by its heavier isotope, the change in r_z may not necessarily be negative. (3) When a nucleus, say O, is substituted, the change in r_z for a bond, say CS, which is not directly associated with O can be comparable, even larger than that directly associated with O. Results (1) do not include the isotopic differences in the perpendicular displacements, therefore they are insufficient for the explanation of the isotope shift in NMR. Nevertheless, the additivity in Δz changes due to isotopic substitution indicate that isotopic effects on the thermal average internuclear distances $\langle \Delta r \rangle$ may be additive as well. With respect to our application, results (2) and (3) of Kuchitsu and Oyanagi are somewhat disturbing in that they do not seem to be parallel to observed NMR isotope shifts in their sign and attenuation with remoteness of substitution.

In this paper, we consider the factors which are involved in the observation that the magnitude of the isotope shift is proportional to the number of atoms in equivalent positions which have been substituted. We also examine the mass dependence of the shift and its attenuation with remoteness of substitution from the observed nucleus. The first two are strictly consequences of dynamic factors; the observed nucleus may be viewed merely as a sensor of the bond displacements. We examine the origin of the observed additivity, determine if any systematic deviations from additivity can be expected, and how large they may be. We consider the dynamic aspects of the attenuation of the isotope shift with remoteness of substitution. Finally, we explore the explicit dependence of the isotope shift on fractional mass change.

THE BASIS FOR ADDITIVITY OF ISOTOPE SHIFTS

The methanes

We calculated mean bond displacements in the methane family $CX_{4-n}Y_n$ (X,Y = H,D,T) with the method described in the accompanying paper,[19] based on the anharmonic force field of Gray and Robiette.[20]

We find that the substitution effects on the vibrational contribution to mean bond displacements are strictly additive. This is shown in Fig. 1 for $\langle \Delta r_{CH} \rangle$ and $\langle \Delta r_{CD} \rangle$ in $^{12}CH_{4-n}D_n$. The mean bond displacements in $^{12}CH_{4-n}T_n$ and $^{12}CD_{4-n}T_n$ exhibit the same strictly linear dependence on n.

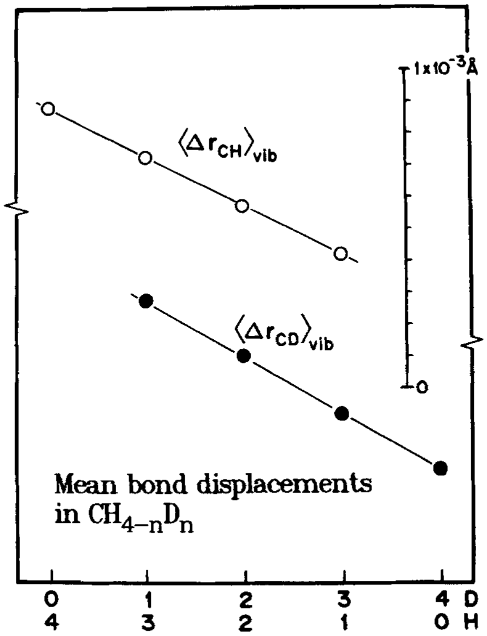

FIG. 1. The vibrational contribution to the mean bond displacements in the methanes, showing strict additivity. $\langle \Delta r_{CD} \rangle = 2.0881 \times 10^{-2} - \Delta + (4-n)\delta_D$; $\langle \Delta r_{CH} \rangle = 2.0881 \times 10^{-2} - n\delta_H$. These were calculated at 300 K using the anharmonic force field of Gray and Robiette (Ref. 20), details are given in Ref. 19.

We can express $\langle \Delta r_{CH} \rangle$ and $\langle \Delta r_{CD} \rangle$ in $^{12}CH_{4-n}D_n$ as follows: Let

$$d = \langle \Delta r_{CH} \rangle \text{ in } CH_4 \text{ at 300 K},$$

$$d - \Delta = \langle \Delta r_{CD} \rangle \text{ in } CD_4 \text{ at 300 K},$$

where $d = 2.0881 \times 10^{-2}$ Å and $\Delta = 5.5345 \times 10^{-3}$ Å. We find

$$\langle \Delta r_{CD} \rangle = d - \Delta + (4-n)\delta_D, \tag{3a}$$

$$\langle \Delta r_{CH} \rangle = d - n\delta_H, \tag{3b}$$

where $\delta_D = 1.75 \times 10^{-4}$ Å and $\delta_H = 1.55 \times 10^{-4}$ Å. Similarly for $^{12}CH_{4-n}T_n$:

$$\langle \Delta r_{CH} \rangle = d - n\delta'_H, \tag{4a}$$

$$\langle \Delta r_{CT} \rangle = d - \Delta' + (4-n)\delta'_T, \tag{4b}$$

where $d - \Delta' = \langle \Delta r_{CT} \rangle$ in CT_4 at 300 K, $\Delta' = 7.893 \times 10^{-3}$ Å, $\delta'_H = 2.13 \times 10^{-4}$, and $\delta'_T = 2.56 \times 10^{-4}$ Å. That is, for a given bond, substitution of an isotope involved in this bond has an effect Δ on its own mean bond length, each substitution of an isotope at some other bonds has a smaller effect δ. The latter is a secondary isotope effect on the mean bond displacement. While $\delta_D > \delta_H$ for the methanes, the order may be reversed in other molecules.

The rotational contribution (centrifugal stretching) to the mean bond displacement is shown in Fig. 2. In CH_4 and CD_4, $\langle \Delta r_{CH} \rangle_{CH_4} = \langle \Delta r_{CD} \rangle_{CD_4} = d_{rot} = 5.24 \times 10^{-4}$ Å. For the mixed isotopomers, the C–D bond gets longer and the C–H bond gets shorter in $CH_{4-n}D_n$ but the sum is invariant to n:

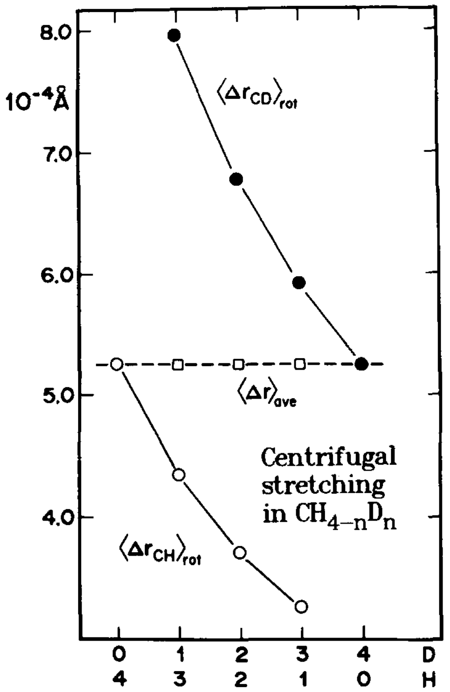

FIG. 2. The rotational contribution to mean bond displacements in the methanes.

$$(4-n)\langle \Delta r_{CH} \rangle_{rot} + n\langle \Delta r_{CD} \rangle_{rot} = 4d_{rot}. \tag{5}$$

A fairly good description of the centrifugal stretching is given by

$$\langle \Delta r_{CH} \rangle_{rot} = d_{rot}(1 + c_H)^{-1};$$
$$\langle \Delta r_{CD} \rangle_{rot} = d_{rot}\,[1 - c_D(4-\mathrm{n})]^{-1}, \tag{6}$$

where $c_H = 0.205$, $c_D = 0.113$. The invariance of the centrifugal distortion to isotopic substitution which preserves T_d symmetry has been pointed out previously.[1] Here we find that the sum is invariant. Equation (6) may depend on having neglected $\Sigma\langle \Delta\alpha_{ij} \rangle$ in our calculations.

Following Eq. (2), the isotope shift of the central nucleus, ^{13}C in $CH_{4-n}D_n$, is given by $(\partial\sigma^C/\partial\Delta r)_e \Sigma_i [\langle \Delta r_i \rangle^* - \langle \Delta r_i \rangle]$ or $(\partial\sigma^C/\partial\Delta r)_e [\Sigma_i \langle \Delta r_i \rangle^* - \Sigma_i \langle \Delta r_i \rangle]$. The centrifugal distortion does not contribute to the isotope shift of the central nucleus because $\Sigma_i \langle \Delta r_i \rangle_{rot}$ is invariant to isotopic substitution. The vibrational contribution to the isotope shift depends on

$$\sum_i \langle \Delta r_i \rangle_{vib} = (4-n)\langle \Delta r_{CH} \rangle_{vib} + n\langle \Delta r_{CD} \rangle_{vib}$$
$$= 4d - n\Delta + (4-n)n(\delta_D - \delta_H), \tag{7}$$

which is very nearly linear with n, since $\delta_D - \delta_H \lessdot \Delta$.

The $^{2/1}$H-induced ^{13}C NMR isotope shift between any two isotopomers of $CH_{4-n}D_n$ can then be expressed, following Eq. (2), as

$$[\sigma^C(CH_{4-n}D_n) - \sigma^C(CH_{4-n'}D_{n'})]$$
$$= (\partial\sigma^C/\partial\Delta r)_e (n'-n)[\Delta - (\delta_D - \delta_H)(4-n-n')] + \dots$$
$$\simeq (\partial\sigma^C/\partial\Delta r)_e (n'-n)\Delta. \tag{8}$$

Equation (8) is the basis for the near additivity of isotope shifts due to substitution at equivalent sites. If we leave out the term in $(\delta_D - \delta_H)$ which is two orders of magnitude smaller than Δ, then we have strict additivity: The magnitude of the shift is proportional to the number $(n'-n)$ of atoms which have been substituted by isotopes.

Thus, we have established quantitatively the additivity of one-bond isotope shifts. Let us now consider additivity of two-bond isotope shifts. For substitution at a bond not involving the observed nucleus, there will always be two important contributions to the isotope shift which have to be considered. The first is the secondary isotope effect on the bond at the nuclear site sensed by the derivative associated with this bond (a primary change of the shielding). The second is the primary isotope effect on the bond at the substitution site sensed by the derivative of the shielding with respect to the extension of that bond, which is remote from the observed nucleus (a secondary change of the shielding).

We can examine the effects of remote isotopic substitution on shielding, using the ^{1}H shielding in the methane homologous series as an example. We need to include at least two derivatives: $\mathrm{P} = (\partial\sigma^{H_i}/\partial\Delta r_{CH_i})_e$ describing the change in σ^{H_i} due to the CH_i bond extension, and $\mathrm{S} = (\partial\sigma^{H_i}/\partial\Delta r_{CH_j})_e$ describing the change in σ^{H_i} due to a remote bond CH_j extension. Using the mean bond displacements in Eq. (3) (vibrational contribution) and Eq. (6) (rotational contribution) we can write the isotope shifts in ^{1}H resonance as

$$\sigma^H(CH_{4-n}D_n) - \sigma^H(CH_{4-n'}D_{n'})$$
$$= (n'-n)\left\{\begin{matrix} \mathrm{P}\delta_H + \mathrm{S}[\Delta - \delta_D - (\delta_D - \delta_H)(3-n-n')] \\ + (\mathrm{P{-}S})d_{rot}c_H\,[(1+nc_H)(1+n'c_H)]^{-1} \end{matrix}\right\}. \tag{9}$$

In Table I we see that additivity will be observed if the small terms nearly cancel out, so that

$$\sigma^H(CH_{4-n}D_n) - \sigma^H(CH_{4-n'}D_{n'})$$
$$\simeq (n'-n)[P(\delta_H + \delta_{rot}) + S(\Delta - \delta_D)], \tag{10}$$

in which $\delta_{rot} \simeq d_{rot}c_H\,[(1+c_H)(1+2c_H)]^{-1}$. All published $^{2/1}$H-induced ^{1}H isotope shifts in tetrahedral molecules (CH_4,[21] NH_4^+,[22] BH_4^-[23]) show strict additivity within experimental errors. At the present time it is not possible to make a general statement as to which of the P or S terms is more important; they are found to be of the same order of magnitude in two cases.[3,19]

The ^{13}C shielding in the $Sn(CH_3)_{4-n}(CD_3)_n$ system[24] shows the additivity of the secondary isotope effects on the mean bond displacement. Here the $^{2/1}$H-induced shifts for the ^{13}C in the CH_3 groups form a straight line with n and changes by 0.088 ppm per CD_3 group added, due entirely to secondary isotope effects on mean bond displacements. The isotope shift of the CD_3 group is also linear with n, with the same slope, that is, this also changes by 0.088 ppm per CD_3 group added. The CD_3 and CH_3 signals in the same molecule differ by 0.700 ppm. Following Eq. (3) we can write

$$\begin{aligned} \langle \Delta r_{CH} \rangle &= d - n\epsilon_H, \\ \langle \Delta r_{CD} \rangle &= d - \Delta + (4-n)\epsilon_D, \\ \langle \Delta r_{SnCH_3} \rangle &= b - n\gamma_H, \\ \langle \Delta r_{SnCD_3} \rangle &= b - \beta + (4-n)\gamma_D, \end{aligned} \tag{11}$$

TABLE I. Near cancellation of n dependence of the small terms in Eq. (9), the secondary vibration and the centrifugal stretching contributions to the two-bond isotope shift in $CH_{4-n}D_n$.

n	n'		Typical values, 10^{-4} ppm[a]		
			rot	vib	tot
0	1	$-2S(\delta_D-\delta_H)+(P-S)d_{rot}c_H(1+c_H)^{-1}$	0.54	-3.32	-2.78
1	2	$(P-S)d_{rot}c_H[(1+c_H)(1+2c_H)]^{-1}$	0	-2.36	-2.36
2	3	$2S(\delta_D-\delta_H)+(P-S)d_{rot}c_H[(1+2c_H)(1+3c_H)]^{-1}$	-0.54	-1.78	-2.32
3	4	$4S(\delta_D-\delta_H)+(P-S)d_{rot}c_H[(1+3c_H)(1+4c_H)]^{-1}$	-1.04	-1.38	-2.42

[a] Using values calculated in Ref. 19.

where ϵ and γ are the secondary effects on the C–H/D and Sn–C mean bond lengths due to substitution of three deuteriums at a remote carbon, Δ and β are the differences in carbon–hydrogen and Sn–C bond length, respectively, between $Sn(CH_3)_4$ and $Sn(CD_3)_4$. Then, following Eq. (2),

$$-0.700 \text{ ppm} = 3(\partial\sigma^C/\partial r_{CH})_e\Delta + (\partial\sigma^C/\partial\Delta r_{SnC})_e\beta + \cdots . \tag{12a}$$

Also, in the same way that we derived Eq. (10) we can write,

$$\begin{aligned}\{\sigma^C[Sn(CH_3)_{4-n}(CD_3)_n] &- \sigma^C[Sn(CH_3)_{4-n'}(CD_3)_{n'}]\}\\ &= (n'-n)(-0.088) \text{ ppm}\\ &= (n'-n)\{3(\partial\sigma^C/\partial\Delta r_{CH})_e\epsilon + (\partial\sigma^C/\partial\Delta r_{SnC})_e\gamma\\ &\quad + (\partial\sigma^C/\partial\Delta r_{SnC'})_e\beta\}. \end{aligned}\tag{12b}$$

Equations (10) and (12b) are the bases for the observed near additivity of two-bond (or more) isotope shifts due to substitution at equivalent sites. The magnitude of the shift is proportional to the number $(n'-n)$ of atoms or groups which have been substituted by isotopes.

Linear triatomic molecules

To test the more general validity of the findings in the methanes, we calculated the mean bond displacements for different isotopomers of a symmetric (CO_2) and nonsymmetric (OCS,NNO) linear triatomic molecules. The results that we present here on various isotopic species are based on calculations[4] using anharmonic force fields in curvilinear coordinates derived by variational calculations.[25-27] The details of the calculations of shielding in the triatomic molecules are given elsewhere.[4] We present the results for single substitution in CO_2 and OCS in Fig. 3, but the conclusions which follow are based on calculations for all possible isotopomers using $^{18/17/16}O$, $^{15/14}N$, $^{13/12}C$, and $^{34/33/32}S$. As shown in Fig. 3, we found exactly the same effect as for the methanes: substitution of a heavier isotope provides a drastic shortening of the average length of the bond directly attached to this isotope by a constant Δ and as a secondary effect it shortens the other bond by a constant δ, where $\delta \ll \Delta$. We also found an empirical general additivity rule which is valid for all triatomics,

$$\begin{aligned}\langle\Delta r(^{M'}YA^{N'}X)\rangle_{av} &- \langle\Delta r(^{M}YA^{N}X)\rangle_{av}\\ &= [\langle\Delta r(^{M'}YA^{N}X)\rangle_{av} - \langle\Delta r(^{M}YA^{N}X)\rangle_{av}]\\ &\quad + [\langle\Delta r(^{M}YA^{N'}X)\rangle_{av} - \langle\Delta r(^{M}YA^{N}X)\rangle_{av}],\end{aligned}\tag{13a}$$

where

$$\langle\Delta r\rangle_{av} = (1/2)[\langle\Delta r_{AY}\rangle + \langle\Delta r_{AX}\rangle]. \tag{13b}$$

Thus, if we include only linear terms, as in Eq. (2), for the shielding of the central atom in the linear triatomic,

$$\sigma_0 = \sigma_e + (\partial\sigma/\partial\Delta r_{av})_e 2\langle\Delta r\rangle_{av}. \tag{14}$$

The additivity of the isotope shifts for the central atom which follows from Eqs. (13) and (14) may be written in Gombler's notation,[28] for ^{13}C in OCS, for example:

$$^1\Delta\ ^{13}C(^{18/16}O,^{34/32}S) = {}^1\Delta\ ^{13}C(^{18/16}O) + {}^1\Delta\ ^{13}C(^{34/32}S). \tag{15}$$

Once again, additivity of isotope shifts are predicted on the basis of additivity of mass effects on $\langle\Delta r\rangle$.

The two-bond isotope shifts of the end nuclei in YAX are analogous to the isotope shifts of ^1H in the methanes. Here again there will be two terms.

$$^2\Delta\ X(^{M'/M}Y) = P\delta_{AX} + S\Delta_{AY}, \tag{16}$$

where $\delta_{AX} \ll \Delta_{AY}$ as can be seen clearly in Fig. 3. For example, the isotope shift of ^{17}O in OCS is

$$^2\Delta\ ^{17}O(^{34/32}S) = (\partial\sigma^O/\partial\Delta r_{CO})_e\delta_{CO} + (\partial\sigma^O/\partial\Delta r_{CS})_e\Delta_{CS}. \tag{17}$$

The additivity in isotope shifts, for example, for the end N in NNO follows from Eq. (13):

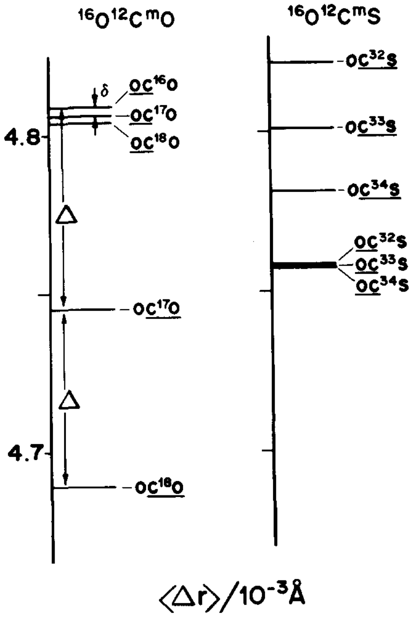

FIG. 3. Mean bond displacements in CO_2 and OCS calculated at 300 K using the method described previously (Ref. 4), from the anharmonic force fields of Lacy (Ref. 25) and Whiffen (Ref. 27), drawn to scale, illustrating the primary effect Δ, the secondary effect δ, and the additivity of the effects.

$$^{1,2}\Delta\ ^{15}\mathrm{N}(^{15/14}\mathrm{N},^{18/16}\mathrm{O}) = {}^{1}\Delta\ ^{15}\mathrm{N}(^{15/14}\mathrm{N}) + {}^{2}\Delta\ ^{15}\mathrm{N}(^{18/16}\mathrm{O}). \tag{18}$$

Unfortunately, there have been no systematic experimental investigation of these shifts. With the empirical $(\partial\sigma^{\mathrm{N}}/\partial\Delta r)_e$ and $(\partial\sigma^{\mathrm{C}}/\partial\Delta r)_e$ which we have obtained by fitting NNO and $\mathrm{CO_2}$ $\sigma_0(\mathrm{T})$ data,[4] we can estimate some isotope shifts in these molecules:

for NNO:
$^{1}\Delta\ ^{15}\bar{\mathrm{N}}(^{15/14}\mathrm{N}) = -0.089$ ppm
$^{1}\Delta\ ^{15}\mathrm{N}(^{18/16}\mathrm{O}) = -0.164$ ppm
$^{1}\Delta\ ^{15}\mathrm{N}(^{15/14}\mathrm{N},^{18/16}\mathrm{O}) = -0.254$ ppm

and for $\mathrm{CO_2}$:
$^{1}\Delta\ ^{13}\mathrm{C}(^{18/16}\mathrm{O}) = -0.0276$ ppm
$^{1}\Delta\ ^{13}\mathrm{C}(^{18/16}\mathrm{O_2}) = -0.0554$ ppm.

DEVIATIONS FROM ADDITIVITY

Although the secondary isotope effects on the mean bond displacements are small, the term in $(\delta_{\mathrm{D}} - \delta_{\mathrm{H}})$ in Eq. (8) provides a theoretical basis for deviations from strict additivity of isotope shifts. Since all four bonds contribute to the shielding of the central atom, we can observe the nature of the deviations from additivity by using an average $\langle\Delta r\rangle_{\mathrm{av}}$. We write the shielding in $\mathrm{CH}_{4-n}\mathrm{D}_n$ as:

$$\sigma_0^{\mathrm{C}} = \sigma_e + (\partial\sigma^{\mathrm{C}}/\partial\Delta r)_e 4\langle\Delta r\rangle_{\mathrm{av}} + \cdots, \tag{19a}$$

where

$$\langle\Delta r\rangle_{\mathrm{av}} = [(4-n)\langle\Delta r_{\mathrm{CH}}\rangle + n\langle\Delta r_{\mathrm{CD}}\rangle]/4. \tag{19b}$$

The $\langle\Delta r\rangle_{\mathrm{av}}$ in the series $\mathrm{CH}_{4-n}\mathrm{D}_n$ are then given by

$$\begin{aligned}
n&=0 \quad d_{\mathrm{rot}} + d,\\
n&=1 \quad d_{\mathrm{rot}} + d - (1/4)\Delta + (3/4)(\delta_{\mathrm{D}} - \delta_{\mathrm{H}}),\\
n&=2 \quad d_{\mathrm{rot}} + d - (1/2)\Delta + (\delta_{\mathrm{D}} - \delta_{\mathrm{H}}),\\
n&=3 \quad d_{\mathrm{rot}} + d - (3/4)\Delta + (3/4)(\delta_{\mathrm{D}} - \delta_{\mathrm{H}}),\\
n&=4 \quad d_{\mathrm{rot}} + d - \Delta.
\end{aligned} \tag{20}$$

[We noted in Fig. 2 and in Eq. (5) that the centrifugal stretching contribution to this average is constant.] The deviations from additivity are in the ratio 0:3:4:3:0 for $n = 0$ to 4. Equation (20) is an algebraic consequence of Eq. (3) which was based on the results of calculations of mean bond displacements[19] using the best available anharmonic force field for methane.[20]

It should be noted that Eq. (20) is strictly parallel to the results obtained by Bigeleisen and Goldstein[17] for zero-point energies in the methanes. They treated the four bonds in $\mathrm{CH}_{4-n}\mathrm{D}_n$ as four coupled oscillators. The deviation from linear behavior of the zero-point energy vs n comes from the term in the energy which corresponds to the mutual motion of two atoms in different oscillators from their equilibrium position. With this model, they derived deviations from linear behavior of the zero-point energies as follows:

$$E_n - (1/4)[(4-n)E_0 + nE_4] = 3(n - n^2/4)A, \tag{21}$$

where $A = (\mu_{\mathrm{H}} - \mu_{\mathrm{D}})\mu_{\mathrm{H}} a_{\mathrm{HH}}^2/(48\pi^2\omega_0^3)$ in which a_{HH} is the force constant which couples two C–H oscillators and ω_0 a characteristic frequency. μ_{H} and μ_{D} are reciprocal masses. The deviations for $n = 0$ to 4 are then in the ratios 0:3:4:3:0, in units of A, exactly the same as we have found above for mean bond displacements due to vibration.

The isotope effects on the $^{13}\mathrm{C}$ shifts in $\mathrm{CH}_{4-n}\mathrm{D}_n$ have been measured,[5] but the associated errors are not small enough to be able to see these systematic deviations from additivity. On the other hand, excellent measurements have been carried out by Wasylishen and Friedrich for the $^{14}\mathrm{N}$ shifts in the ammonium ion, $^{14}\mathrm{NH}_{4-n}\mathrm{D}_n^+$, with precision ± 0.001 ppm.[9] In Table II, we compare the actual experimental results with the strictly additive parts. From the latter we obtain $(\partial\sigma^{\mathrm{N}}/\partial\Delta r)_e\Delta = -0.293$ ppm. Since Δ is positive, then $(\partial\sigma^{\mathrm{N}}/\partial\Delta r)_e$ is negative (the usual sign). The experimental deviations from additivity shown in the last column are in exactly the same ratio as those calculated in Eq. (20). Thus, we can attribute the observed deviations from additivity in ammonium ion to small vibrational terms related to $(\delta_{\mathrm{D}} - \delta_{\mathrm{H}})$.

The isotope shifts of the $^{119}\mathrm{Sn}$ nucleus in the $\mathrm{Sn(CH_3)}_{4-n}\mathrm{(CD_3)}_n$ system[24] show deviations from additivity in the same direction as those in Table II, although the ratios are not 0:3:4:3:0 exactly. If we consider the $\mathrm{CD_3}$ and $\mathrm{CH_3}$ groups as point masses, then the centrifugal stretching contribution to $\langle\Delta r_{\mathrm{SnC}}\rangle_{\mathrm{av}}$ can be neglected, if our findings in $\mathrm{CH}_{4-n}\mathrm{D}_n$ can be extended to $\mathrm{Sn(CH_3)}_{4-n}\mathrm{(CD_3)}_n$. The nonvanishing mean CSnC angle deformations may be important to centrifugal stretching in the less symmetric ($n = 1$–3) isotopomers, exaggerating the deviations from additivity due to vibrations.

There may also be deviations from additivity which arise from the second derivative terms which we have not included in our treatment.

THE MASS DEPENDENCE OF THE ISOTOPE SHIFT

The primary effect of isotopic substitution on the mean bond displacement Δ depends on the masses. We find $\langle\Delta r_{\mathrm{CH}}\rangle_{\mathrm{CH_4}} - \langle\Delta r_{\mathrm{CD}}\rangle_{\mathrm{CD_4}} = 5.533\times 10^{-3}$ Å, whereas $\langle\Delta r_{\mathrm{CH}}\rangle_{\mathrm{CH_4}} - \langle\Delta r_{\mathrm{CT}}\rangle_{\mathrm{CT_4}} = 7.893\times 10^{-3}$ Å. It appears that Δ is proportional to $(m_{\mathrm{D}} - m_{\mathrm{H}})/m_{\mathrm{D}}$ since

$$(5.533/7.893) \simeq \frac{(m_{\mathrm{D}} - m_{\mathrm{H}})/m_{\mathrm{D}}}{(m_{\mathrm{T}} - m_{\mathrm{H}})/m_{\mathrm{T}}}.$$

From our results with the methanes and the triatomic molecules,[4] as well as $\mathrm{O{=}CF_2}$,[3] we find in general (for any molecular type and any substitution site) that the change in the mean bond displacement upon isotopic substitution can be expressed as follows:

TABLE II. $^{2/1}$H-induced ^{14}N isotope shifts in the ammonium ion and their deviations from additivity from Wasylishen and Friedrich (experimental precision: ± 0.001 ppm) (Ref. 9).

	Expt	Strictly additive	Observed difference	Predicted from Eq. (20)
$\mathrm{NH_4^+}$	0	0	0	0
$\mathrm{NH_3D^+}$	-0.307	-0.293	-0.014	$-3(\delta_{\mathrm{D}} - \delta_{\mathrm{H}})(\partial\sigma^{N}/\partial\Delta r)_e$
$\mathrm{NH_2D_2^+}$	-0.607	-0.585	-0.020	$-4(\delta_{\mathrm{D}} - \delta_{\mathrm{H}})(\partial\sigma^{N}/\partial\Delta r)_e$
$\mathrm{NHD_3^+}$	-0.892	-0.878	-0.014	$-3(\delta_{\mathrm{D}} - \delta_{\mathrm{H}})(\partial\sigma^{N}/\partial\Delta r)_e$
$\mathrm{ND_4^+}$	-1.171	-1.171	0	0

$$\Delta = \langle \Delta r\rangle - \langle \Delta r\rangle' = \langle \Delta r\rangle [(m'-m)/m']\, f(m,m_A,\ldots). \quad (22)$$

The consequences of Eq. (22) for one-bond-isotope shifts in NMR are clear if Eq. (2) holds (including only linear terms in the expansion of nuclear shielding in bond displacements). Comparing several isotopic species which differ only in one mass m', to the parent species with mass m, we should get a constant value for the ratio

$$\frac{\langle \Delta r\rangle - \langle \Delta r\rangle'}{\langle \Delta r\rangle [(m'-m)/m']} = f. \quad (23)$$

That is, we should find

$$\frac{\sigma - \sigma'}{[(m'-m)/m']} = \text{constant}. \quad (24)$$

An excellent test for Eq. (24) is provided by the $^{m'/m}$Se-induced ^{77}Se isotope shifts in diselenides. We have plotted in Fig. 4 for $m = 74$, $m' = 76, 77, 78, 80, 82$, the isotope shifts in $CF_3\underline{Se}SeCF_3$, $CH_3\underline{Se}SeCH_3$, $CH_3\underline{Se}SeCF_3$ and $CF_3\underline{Se}SeCH_3$ which had been measured by Gombler.[29] The strictly linear behavior of the isotope shifts $^1\Delta\ ^{77}\text{Se}(^{m'/74}\text{Se})$ vs $(m'-m)/m'$ (for $m = 74$) for all four cases shows that Eq. (24) holds for this system. This seems to indicate that either the interpretation of isotope shifts entirely by Eq. (2) (i.e., neglecting second derivatives) is sufficient, or else all the dynamic variables $(\langle \Delta r_i\rangle, \langle (\Delta r_j)^2\rangle, \langle (\Delta\alpha)^2\rangle, \langle \Delta r\Delta\alpha\rangle$, etc.) on which the shielding depends are scaled by $(m'-m)/m'$ upon isotopic substitution. The slopes of the lines in Fig. 4 give

$$\frac{\sigma - \sigma'}{[(m'-m)/m']} \simeq \{(\partial\sigma/\partial\Delta r_{\text{SeSe}})_e \langle \Delta r\rangle f\}. \quad (25)$$

These values are -2.09, -1.83, -1.56, -1.30 ppm for $CH_3\underline{Se}SeCF_3$, $CH_3\underline{Se}SeCH_3$, $CF_3\underline{Se}SeCF_3$, and $CF_3\underline{Se}SeCH_3$, respectively.

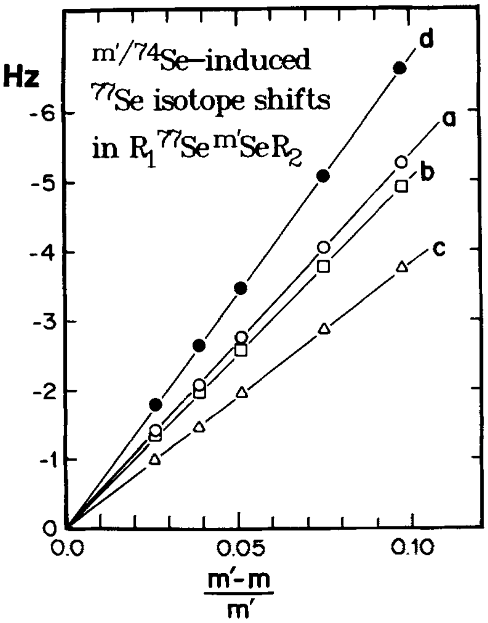

FIG. 4. Effect of selenium isotopes on the ^{77}Se nuclear shielding in the diselenides $R_1{}^{77}Se^{m'}SeR_2$. (a) $R_1 = R_2 = CH_3$ (b) $R_1 = R_2 = CF_3$ (c) $R_1 = CF_3$, $R_2 = CH_3$ (d) $R_1 = CH_3$, $R_2 = CF_3$ from the experimental results by Gombler (Ref. 29). This plot of $^1\Delta\ ^{77}\text{Se}(^{m'/74}\text{Se}) = \sigma(R_1{}^{77}Se^{74}SeR_2) - \sigma(R_1{}^{77}Se^{m'}SeR_2)$ vs $(m'-74)/m'$ illustrates the validity of Eq. (24).

Now we need to examine the functional form of $f(m,m_A,\ldots)$. We have not been able to find a universal functional form for f in case of substitution at other than an end atom. By comparing the mean bond lengths of various isotopomers of several molecular types, we have found a functional form that can reproduce the primary effect of isotopic substitution on the mean bond displacements for substitution at an end atom. Examples of these isotopomers are AX_4 and AX'_4 or AX_2 and AX'_2, or YAX and YAX', even XAY_2 and $X'AY_2$. For these molecular types,

$$f \simeq (1/2)[m_A/(m_A+m)]. \quad (26)$$

Equation (22) then becomes

$$\Delta \simeq \langle \Delta r\rangle - \langle \Delta r\rangle' = \langle \Delta r\rangle [(m'-m)/m'](1/2)[m_A/(m_A+m)]. \quad (27)$$

In diatomic molecules this reduces to the same form as we had previously derived[2]:

$$\langle \Delta r\rangle - \langle \Delta r\rangle' = \langle \Delta r\rangle (\mu'-\mu)/\mu'(1/2). \quad (28)$$

We tested Eq. (27) in several molecules, as shown in Table III. Although the agreement is not perfect, we find that for substitution at an end atom the change in the mean bond length is largely reproduced by Eq. (27). For the purposes of estimating such effects, this formula is probably good enough. It is good to the extent that in so far as isotopic substitution at an atom is concerned, a bond responds like a diatomic molecule. Equation (27) should provide estimates for one-bond isotope shifts if we have an estimate for the derivative $(\partial\sigma/\partial\Delta r)_e$. Following Eq. (8), the one-bond isotope shift of nucleus A for a single replacement of m by m', where m is an end atom, is given by

$$\sigma - \sigma' \simeq (\partial\sigma^A/\partial\Delta r_{Am})_e \langle \Delta r_{Am}\rangle \times [(m'-m)/m'](1/2)[m_A/(m_A+m)]. \quad (29)$$

Since all of the above correlations with experiment have been obtained by using only terms in the first derivatives of shielding, it may be concluded that the terms in the second derivative do not play a dominant role in the interpretation of isotope shifts in NMR.

CONCLUSIONS

In summary, we have derived the basis for the widely observed additivity in the isotope shift for replacement of equivalent atoms, both for isotopic substitution at a bond involving the observed nucleus and for substitution at a remote site. Thus, we have shown why one-bond and two-or-more-bond isotope shifts are found to be proportional to the number of substituted atoms in equivalent positions [Eqs. (8), (10), and (12)]. The predicted slight deviation from additivity has been confirmed by a classic example (Table II). The attenuation of isotope shift with remoteness of substitution has been shown to be due to the secondary nature of the effect when the bond involved is not at the nuclear site. The terms that contribute to two-or-more-bond isotope shifts involve either a secondary effect on the bond length or a secondary effect on the shielding.

We have also shown that the direct effect of substitution on a bond is to change its mean length by an amount Δ, and Δ has been shown to be directly proportional to the fractional mass change $(m'-m)/m'$, [Eq. (22)] and confirmed by ex-

TABLE III. Mass dependence of f, compared with an assumed form, $(1/2)[m_A/(m_A+m)]$ for a variety of molecular types.

r	r'	molecule	$f=\left[\frac{\langle\Delta r\rangle-\langle\Delta r\rangle'}{\langle\Delta r\rangle}\frac{m'}{m'-m}\right]$	$\frac{1}{2}\frac{m_A}{m_A+m}$
CH	CD	$CH_{4-n}D_n$	0.48	0.46
CH	CT	$CH_{4-n}T_n$	0.51	0.46
CD	CT	$CD_{4-n}T_n$	0.42	0.43
^{14}NN	^{15}NN	$^{15/14}N^{14}NO$	0.24	0.25
$N^{16}O$	$N^{18}O$	$N^{14}N^{18/16}O$	0.24	0.23
$C^{16}O$	$C^{18}O$	$O^{12}C^{18/16}O$	0.22	0.21
$C^{32}S$	$C^{34}S$	$O^{12}C^{34/32}S$	0.14	0.14
$C^{16}O$	$C^{18}O$	$^{18/16}O^{12}CF_2$	0.27	0.23
SeH	SeD	$^{2/1}H_2Se$	0.50	0.49
SH	SD	$^{2/1}H_2S$	0.48	0.48
OH	OD	$^{2/1}H_2O$	0.49	0.47

periment (Fig. 4). For substitution at an end atom, we have shown that an approximate form for Δ [Eq. (27)] holds quite well, and from this we propose an expression for a one-bond isotope shift [Eq. (29)].

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