Theory of Linear Electric Field Shifts in Carbon-13 Nuclear Magnetic Resonance

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Abstract: The description of electric field shifts may be considerably improved by the addition of an extra linear term, the "field gradient" contribution, to the "uniform field" term in current use. A semiempirical method is given for the calculation of both these linear contributions to ^{13}C shielding. Symmetry properties are used to simplify the calculation of the linear electric field shift (LEFS) coefficients for various saturated and unsaturated carbons. The orientation dependences of both linear electric field shift contributions are investigated, a simple dependence being obtained for the uniform field LEFS of a carbon possessing a symmetry axis. The uniform field LEFS of a saturated carbon may be extracted from the total electric field shift by subtracting from this the electric field shift of a corresponding quaternary carbon. In a stringent test, the shifts derived for the α carbons of a series of primary amines were found to agree with theoretical predictions within a margin of 30%. It is now possible to interpret the electric field shifts of carbons close to a field source.

It has recently been demonstrated that linear electric field shifts (LEFS) of ^{13}C resonances are many times larger than those observed for proton resonances.[2] Since electric field shift contributions in ^{13}C nuclear magnetic resonance (NMR) are so large, they may be expected to dominate ^{13}C shifts caused by the introduction of molecular charges or dipoles. One area in which such shifts have recently received much attention is the protonation of amino acids.[3-6] The interpretation of the ^{13}C protonation shifts of amino acids would undoubtedly benefit considerably from an understanding of electric field shifts of ^{13}C resonances. I therefore present here a theoretical basis for the analysis of ^{13}C LEFS. In subsequent papers, this theory will be used to rationalize the protonation shifts of amino acids and peptides and to show that conformational information may be obtained from these protonation shifts.

Division of Total Electric Field Shifts into First- and Second-Order Contributions

It has been shown that the changes in chemical shift, δ_{el}, of the resonance of any nucleus caused by electric fields may be expressed as a power series in the electric field at the nucleus:[2,7]

$$\delta_{el} = \boldsymbol{E}_i\mathbf{A}_{ij}r_j + \boldsymbol{E}_i\boldsymbol{E}_j\mathbf{B}_{ijk}r_k + \ldots \qquad (1)$$

where $\boldsymbol{E}_i$ are components of the field vector, $\boldsymbol{r}_j$ are unit vectors of a coordinate system fixed in the molecular framework, $\mathbf{A}_{ij}$ are components of a second rank tensor, and $\mathbf{B}_{ijk}$ are components of a third rank tensor.

Only the first two terms of this series have been shown to be significant, namely the linear and second-order electric field effects.[7] The first-order term is due to polarization of charge along the bonds on the atom leading to a change in charge density at its nucleus. The second-order term is due to the mixing of excited states into the molecular wave function raising the ground-state energy by causing orbital distortion. This second term has been further analyzed into two components: one due to steady electric fields (which also contribute to the first-order term); and one due to fluctuating fields (with zero mean) of the kind giving rise to van der Waals forces.[8]

Since linear shifts are directly proportional to changes in local electric fields, they may be directly related to changes in field and vice versa. However, second-order effects depend on the square of the field, and therefore changes in second-order shifts depend not only on the change in local electric field but also on the original electric field strength because $d(\mathbf{E})^2 = 2d\boldsymbol{E}\cdot\boldsymbol{E}$. Thus second-order effects will be very difficult to interpret, and the discussion in this paper will be concerned only with linear electric field effects.

Division of Total LEFS into Uniform Field and Field Gradient Contributions

Buckingham proposed that the total electric field shifts of a nucleus could be expressed in terms of a power series in the electric field *at the nucleus,* as indicated in eq 1.[7] However, this formulation applies only when the electric field is uniform. In most applications of electric field effects, the field source is a molecular point charge or dipole, and hence the field falls off with distance. Thus the change in charge density on a nucleus due to polarization of an adjoining bond by the electric field will depend not on the field at the nucleus but on the field averaged by integration along the bond. The resultant field will be approximately equal to the field observed at the midpoint of the bond. Just as the total electric field shift can be expressed as a power series in the field, so the total LEFS can be expressed as an expansion in terms of the field and its derivatives. In eq 2, $\mathbf{A}'_{ij}$ is a second

$$\delta_{el}(\text{linear}) = \mathbf{A}_{ij}\boldsymbol{E}_i r_j + \mathbf{A}_{ij}'\frac{\partial \boldsymbol{E}_i}{\partial r_j} + \ldots \qquad (2)$$

rank tensor, $\boldsymbol{r}_j$ are vectors along the coordinate axes fixed in the molecular framework, and both the field and the field gradient components are evaluated at the observed nucleus. Once again only the first two terms will be of significance. The first term represents the linear electric field shift calculated from the electric field at the nucleus and will be referred to as the "uniform field" term since it is the total shift which would be observed in a uniform field. The second term is the "field gradient LEFS". Together these two terms should describe accurately the change in shielding due to a change in charge density at any carbon caused by protonation of a titratable group.

The field gradient term has not been discussed in studies of ^{1}H and ^{19}F electric field effects because, for monovalent nuclei, there is no simple way of distinguishing field gradient effects from uniform field effects. However, it will be shown below that it is possible, to obtain some estimate of the uniform field contribution experimentally for ^{13}C nuclei. For a multivalent nucleus, such as ^{13}C, the field gradient LEFS will have a large magnitude relative to the uniform field LEFS and a different directional dependence. It is therefore necessary to investigate the magnitudes and orientational dependences of both terms.

Uniform Field Linear Electric Field Shifts

In any axially symmetric situation, e.g., for ^1H, A_{ij} may be reduced to a single nonzero term if the coordinate system is chosen with an axis parallel to the symmetry axis since electron polarization perpendicular to the symmetry axis cannot produce any linear shift contribution.[7] Thus, the first term in eq 2, the uniform field LEFS, can be reduced to vector form as follows:

$$\delta_{\mathrm{UFLEFS}} = \boldsymbol{A}_i\boldsymbol{E}_i \tag{3}$$

where $A_x = A_y = 0$ if z is parallel to the axis of cylindrical symmetry.

It has been suggested previously[2,9,10] that the magnitudes of linear electric field shifts can be estimated by a simple consideration of polarization of electrons along molecular bonds and the resulting changes in nuclear charge density. This approach, which will be used here, involves a number of assumptions, and their limitations are discussed in the Appendix. Future refinement of the method could involve the replacement of empirical parameters with calculated values or the direct calculation of the coefficients, $\boldsymbol{A}_z$, by MO methods. However, although the absolute magnitudes of the currently predicted $\boldsymbol{A}_z$ values may involve errors[2] up to a factor of ~2, their relative magnitudes for similar carbons, e.g., CH_3 and CH_2, should be fairly reliable.

Following Horsley and Sternlicht,[9] the predicted uniform field shift of a univalent nucleus, e.g., ^1H, is given by

$$\delta_{\mathrm{UFLEFS}} = \frac{b_l}{el}\boldsymbol{E}_z(\delta/e) \tag{4}$$

where b_l is the longitudinal polarizability of the X-H bond,[11] z is the direction of the X-H bond, e is the electronic charge, and δ/e is an empirically determined coefficient relating changes in charge density to resulting chemical shift changes for a given nucleus.[12,13]

Thus by analogy with eq 3

$$\delta_{\mathrm{UFLEFS}} = \boldsymbol{A}_z\boldsymbol{E}_z \tag{5}$$

and

$$\boldsymbol{A}_z = \frac{b_l}{el}(\delta/e) \tag{6}$$

Only the longitudinal polarizations of bonds will give rise to linear electric field effects,[7] and it will therefore be possible to avoid confusion later in the discussion by referring to the quantity $\boldsymbol{A}_z$ defined in eq 6 as $\boldsymbol{A}_{\mathrm{bond}}$. The subscript "bond" indicates that this quantity is the contribution from a single bond to the uniform field LEFS coefficient of a multivalent nucleus.

Upon application to ^{13}C nuclei, eq 5 must be extended to a sum over all the bonds attached to the carbon atom:

$$\delta_{\mathrm{UFLEFS}} = \sum_{\mathrm{bonds}} \boldsymbol{A}_{\mathrm{bond}}\boldsymbol{E}_{\mathrm{bond}} \tag{7}$$

where $\boldsymbol{E}_{\mathrm{bond}}$ is the electric field component parallel to the direction from the observed nucleus along each bond. At this point, it becomes necessary to draw a distinction between the coordinate systems appropriate for describing the electric field shifts of monovalent and multivalent nuclei. When considering LEFS of monovalent nuclei or the contributions to the LEFS of a multivalent nucleus due to electron polarization along a single bond, it is most convenient to place the z axis along the bond direction, this being a symmetry axis. However, to determine the total LEFS of a multivalent nucleus, it is more convenient to choose a single orthogonal coordinate system for the observed nucleus. It is then necessary to derive the vector of coefficients, $\boldsymbol{A}_i$, which relates the shift contributions due to charge polarization to the field components along the principal axes, as indicated by eq 3. The uniform field LEFS of a multivalent nucleus may now be written as:

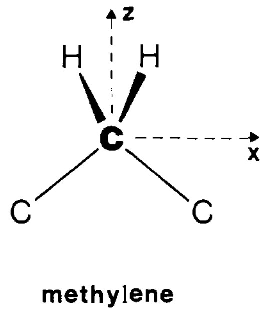


Figure 1. Coordinate system used for the description of LEFS of methylene carbons.

$$\delta_{\mathrm{UFLEFS}} = \sum_{\mathrm{bonds}} \boldsymbol{A}_{\mathrm{bond}}(\cos\theta_i)\boldsymbol{E}_i \tag{8}$$

where θ_i is the angle between a bond and the coordinate direction, i. From eq 3 and 8, it follows that

$$\boldsymbol{A}_i(\mathrm{C}) = \sum_{\mathrm{bonds}} \boldsymbol{A}_{\mathrm{bond}}\cos\theta_i \tag{9}$$

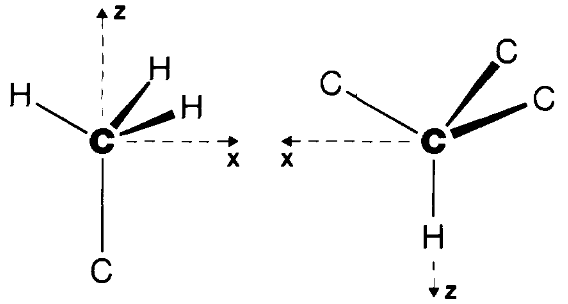
where $\boldsymbol{A}_i(\mathrm{C})$ is a three component vector. However, for any carbon with a rotational symmetry axis, the vector $\boldsymbol{A}(\mathrm{C})$ may be simplified to a single nonzero term by choosing the z coordinate axis along the symmetry axis. Full axial symmetry will be shown below to be unnecessary.

Uniform field LEFS coefficients are derived here for a range of sp^3, sp^2, and sp hybridized carbons. All these carbons possess rotational symmetry axes, and therefore their vectors, $\boldsymbol{A}(\mathrm{C})$, can be represented solely by $\boldsymbol{A}_z(\mathrm{C})$. Related carbons such as amino acid α carbons, amide carbons, and those substituted by oxygen or sulfur may be treated similarly but their vectors, $\boldsymbol{A}(\mathrm{C})$, will consist of more than one nonzero term.

A. Values of $\boldsymbol{A}_z$(C) for Saturated Carbons. The methylene carbon will be discussed first (Figure 1). The z axis has been chosen along the diad axis which bisects the HCH angle with direction such that a positive field parallel to the positive z direction will produce an upfield uniform field LEFS, i.e., the value of $\boldsymbol{A}_z(-CH_2-)$ is positive. The x and y axes are perpendicular to z and, for simplicity, lie in the two mirror planes. However, they could lie anywhere in the plane perpendicular to z without changing the form of the vector, $\boldsymbol{A}(-CH_2-)$. Two methods can be used to demonstrate that $\boldsymbol{A}_x(-CH_2-) = \boldsymbol{A}_y(-CH_2-) = 0$. The first approach is to consider the polarization along each of the bonds. The x axis is perpendicular to the C-C bonds and makes supplementary angles with the two C-H bonds. Similarly the y axis is perpendicular to the C-H bonds and makes supplementary angles with the C-C bonds. Thus a field component along the x axis produces no polarization along the C-C bonds and equal and opposite polarizations along the C-H bonds with respect to the methylene carbon. Therefore, field components along the x and y axes will produce no net change in charge density on the methylene carbon. Only a field component along the z axis will produce such a change since the C-H and C-C bonds have slightly different polarizabilities.[14] Thus the LEFS coefficient for a methylene carbon will be given by

$$\boldsymbol{A}_z(-CH_2-) = \frac{2}{(3)^{1/2}}[\boldsymbol{A}_{\mathrm{C\text{-}H}} - \boldsymbol{A}_{\mathrm{C\text{-}C}}] \tag{10}$$

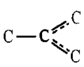
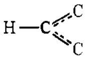
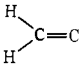
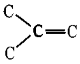
since the angles between the z axis and C-H and C-C bonds are plus and minus 54° 44 min, respectively, and cos 54° 44 min = $1/(3)^{1/2}$.



a. methyl **b. methine**

Figure 2. Coordinate systems used for the description of LEFS of (a) methyl and (b) methine carbons.

Table I. Calculated Carbon-13 Uniform Field LEFS Coefficients

Carbon	A_z(C), 10^{-11} esu	Carbon	A_z(C), 10^{-11} esu
$-CH_3$	2.0		3.6
$-CH_2-$	2.4		1.6
$-\overset{\mid}{C}H-$	2.0		3.4
$-\overset{\mid}{\underset{\mid}{C}}-$	0.0		5.5
$N-CH_3$	1.4	$C-C\equiv C$	5.8
$N-\overset{\displaystyle C}{\underset{\displaystyle C}{\overset{\mid}{\underset{\mid}{C}}}}-C$	0.6	$H-C\equiv C$	4.4

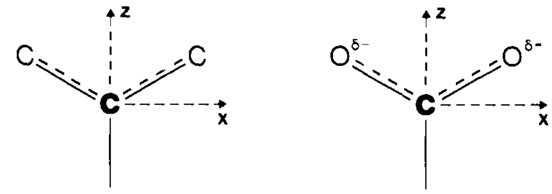
The second approach is to consider the symmetry properties of the bond environment. If the diad symmetry element operates on the coordinate system, x will be transformed into $-x$ and y into $-y$. However, the bonds will appear unchanged in these new coordinates. Therefore a field along $-x$ must produce the same LEFS as a field along $+x$. This LEFS must then be zero. The same applies to the y axis. Thus the presence of a diad axis is a sufficient condition for $A_x(C) = A_y(C) = 0$, full axial symmetry is not necessary. Furthermore, if there is more than one symmetry axis, as in the tetrahedrally symmetric case, all $A_i = 0$.

Since methyl and methine carbons both possess a triad axis, Figure 2, A_z is again the only nonzero term. Its magnitude is given by

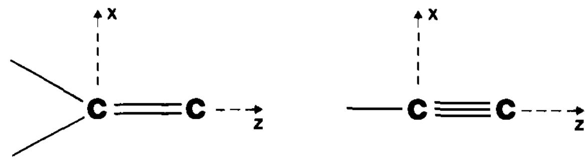
$$A_z(\text{—CH}_3) = A_z(\text{—}\overset{\mid}{\text{C}}\text{H—}) = A_{\text{C-H}} - A_{\text{C-C}} \qquad (11)$$

The z axis of a methyl carbon is along its C-C bond, and that of a methine carbon is along its C-H bond.

Values of A_z for all the above carbons calculated using eq 9 are given in Table I. The longitudinal bond polarizabilities used were 0.99×10^{-24} cm^3, 1.18×10^{-24} cm^3, and 1.30×10^{-24} cm^3 for C-C, C-N, and C-H bonds, respectively.[15] The shift/electron coefficient used here, 182 ppm/electron, is a value derived from aromatic carbon shifts.[13] The validity of this figure is discussed in the Appendix. As the polarizabilities of C-H, C-C, and C-N bonds are very similar,[14] the electric field shift coefficients calculated for the above carbons are quite small; e.g., the value obtained for A_z(-CH$_3$) is only ca. five times larger than that obtained for A_z(-H) by the same method, although the shift/electron coefficient of ^{13}C nuclei is ca. ten times larger than that of protons.[9]



a. aromatic b. carboxylate



c. olefinic d. acetylenic

Figure 3. Coordinate systems used for the description of LEFS of (a) aromatic, (b) carboxylate, (c) olefinic, and (d) acetylenic carbons.

B. Values of A_z(C) for Unsaturated Carbons. Since unsaturated bonds have much higher polarizabilities than saturated bonds,[14] sp^2 and sp hybridized carbons will give rise to the largest ^{13}C electric field shift coefficients. Aromatic ring carbons, carboxylate carbons, and symmetric olefinic carbons all have diad axes, and z is chosen along these axes (Figure 3). A_z values for aromatic and olefinic carbons, estimated using the longitudinal polarizabilities of unsaturated bonds given in ref 11, are shown in Table I. Bond polarizability measurements are not available for the bonds of carboxylate anions but, for C=O and C—O bonds, the longitudinal polarizabilities are ~90% of those for C=C and C—C bonds, respectively.[11] Thus $A_z(\text{-COO}^-)$ may be expected to be $\sim 3 \times 10^{-11}$ esu.

For acetylenic carbons, the z axis is chosen along the triple bond (Figure 3). The values of A_z(C) given in Table I were calculated on the assumption that the shift/electron coefficient for acetylenic carbons is $\frac{2}{3}$ the value for other carbons because of the linear bonding.[16]

Field Gradient Linear Electric Field Shifts

Field gradient LEFS will be caused by changes in electron charge density on a nucleus because of the presence of field gradients. Thus, for example, tetrahedrally symmetric quaternary carbons will show field gradient LEFS if there is a field gradient, even though they will never show uniform field LEFS. Any nucleus may show a field gradient LEFS if there is a field gradient at the nucleus, even if the electric field at the nucleus is zero.

Three derivatives of each electric field component ($\boldsymbol{E}_x$, $\boldsymbol{E}_y$, and $\boldsymbol{E}_z$) may contribute to the total field gradient shift which will be related to the field gradient components by a second rank tensor, A′(C), with nine components. Field gradient shifts will therefore be more complicated and harder to predict than the uniform field LEFS contributions.

The contribution of a single bond to the field gradient shift will be due to the electron polarization along that bond caused by the difference between the electric field at the midpoint of the bond and the field at the observed nucleus. For any given bond with a unit gradient in the i direction, of the electric field in the j direction, $d\boldsymbol{E}_j/dr_i$, this electric field difference will be the product of the component of half the bond length in the direction i ($\frac{1}{2}l \cos \theta_i$) and the cosine of the angle between the bond and the field direction j ($\cos \theta_j$). Thus A′(C) is given by

$$\mathbf{A}'_{ij}(\mathrm{C}) = \tfrac{1}{2} \sum_{\text{bonds}} A_{\text{bond}} l \cos \theta_i \cos \theta_j \qquad (12)$$

For carbons with symmetry axes, all the off diagonal ele-

Table II. Calculated Field Gradient LEFS Coefficients of Saturated Carbons

Carbon	$A'_{xx}(C)$, 10^{-19} esu	$A'_{yy}(C)$, 10^{-19} esu	$A'_{zz}(C)$, 10^{-19} esu	Orientational variation as % of maximum	Rotationally averaged shift coefficient $\frac{1}{3}(A'_{xx} + A'_{yy} + A'_{zz})$, 10^{-19} esu
$-CH_3$	3.3	3.3	2.7	18	3.1
$-CH_2-$	3.3	2.5	2.9	23	2.9
$-\overset{\vert}{C}H-$	2.5	2.5	3.1	19	2.7
$-\overset{\vert}{\underset{\vert}{C}}-$	2.5	2.5	2.5	0	2.5
$N-CH_3$	3.3	3.3	3.1	7	3.2
$N-\overset{C}{\underset{C}{C}}-C$	2.5	2.5	2.9	13	2.6

ments become zero if the z axis is chosen along the symmetry axis. The diagonal elements are given by

$$A'_{ii}(C) = \tfrac{1}{2} \sum_{\text{bonds}} A_{\text{bond}} l \cos^2 \theta_i > 0 \qquad (13)$$

and are always positive for all nuclei. The directions of field gradient shifts are thus determined solely by the sign of the field gradient and not by the bond environment of the nucleus; i.e., a positive charge will produce a negative field gradient and hence downfield field gradient LEFS, whereas a negative charge will produce a positive field gradient and hence upfield field gradient LEFS. Thus field gradient LEFS contributions due to protonation will, in most cases, oppose the uniform field LEFS experienced by ^{13}C nuclei (generally upfield).

The minimum number of significant terms in the field gradient LEFS tensor, $A'(C)$, of a given carbon is the number of dimensions of the bond environment. Thus one term is sufficient for a linear, sp hybridized carbon, two terms for a planar, sp^2 hybridized carbon, and three terms for an sp^3 hybridized carbon.

For saturated carbons, the simplest case is that of a quaternary carbon with perfect tetrahedral symmetry for which $A'(C)$ becomes a multiple of the unit tensor, all three diagonal elements being equal.

$$A'_{zz}(-\overset{|}{\underset{|}{C}}-) = A'_{xx}(-\overset{|}{\underset{|}{C}}-) = A'_{yy}(-\overset{|}{\underset{|}{C}}-) = \frac{2}{3}A_{C\text{-}C}l_{C\text{-}C} \qquad (14)$$

For methyl carbons

$$A'_{zz}(-CH_3) = \frac{1}{2}A_{C\text{-}C}l_{C\text{-}C} + \frac{1}{6}A_{C\text{-}H}l_{C\text{-}H} \qquad (15)$$

$$A'_{xx}(-CH_3) = A'_{yy}(-CH_3) = \frac{2}{3}A_{C\text{-}H}\, l_{C\text{-}H} \qquad (16)$$

For methylenes

$$A'_{zz}(-CH_2-) = \frac{1}{3}[A_{C\text{-}C}l_{C\text{-}C} + A_{C\text{-}H}l_{C\text{-}H}] \qquad (17)$$

$$A'_{xx}(-CH_2-) = \frac{2}{3}A_{C\text{-}C}l_{C\text{-}C} \qquad (18)$$

$$A'_{yy}(-CH_2-) = \frac{2}{3}A_{C\text{-}H}l_{C\text{-}H} \qquad (19)$$

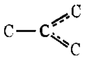
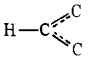
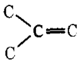
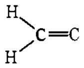
For methine carbons

$$A'_{zz}(-\overset{|}{C}H-) = \frac{1}{2}A_{C\text{-}H}\, l_{C\text{-}H} + \frac{1}{6}A_{C\text{-}C}l_{C\text{-}C} \qquad (20)$$

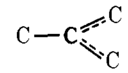
$$A'_{xx}(-\overset{|}{C}H-) = A'_{yy}(-\overset{|}{C}H-) = \frac{2}{3}A_{C\text{-}C}l_{C\text{-}C} \qquad (21)$$

The diagonal elements of the field gradient LEFS coefficient tensors, $A'_{ii}(C)$, of these saturated carbons have been estimated using A_{bond}(C–H), A_{bond}(C–C), and A_{bond}(C–N) equal to 4.5×10^{-11}, 2.4×10^{-11}, and 3.0×10^{-11} esu, respectively, and are given in Table II. Also shown are the rotational variations of the field gradient LEFS for each carbon, expressed as a percentage of the maximum shift in each case, and the rotationally averaged field gradient LEFS coefficient of each carbon (one-third of the trace of each tensor).

Table III. Calculated Field Gradient LEFS Coefficients of Unsaturated Carbons

Carbon	A'_{xx} (C), 10^{-19} esu	A'_{yy} (C), 10^{-19} esu	A'_{zz} (C), 10^{-19} esu
	6.4	0.0	4.0
	6.4	0.0	4.6
	2.8	0.0	6.3
	3.7	0.0	6.5
$C-C\equiv C$	0.0	0.0	5.7
$H-C\equiv C$	0.0	0.0	6.1

The diagonal elements, $A'_{ii}(C)$, of representative unsaturated carbons are given below. For an aromatic carbon, e.g.:



$$A'_{zz}(C_{ar}) = \frac{1}{4}A_{C_{ar}\text{-}C_{ar}}l_{C_{ar}\text{-}C_{ar}} + \frac{1}{2}A_{C\text{-}C}l_{C\text{-}C} \qquad (22)$$

$$A'_{xx}(C_{ar}) = \frac{3}{4}A_{C_{ar}\text{-}C_{ar}}l_{C_{ar}\text{-}C_{ar}} \qquad (23)$$

$$A'_{yy}(C_{ar}) = 0 \qquad (24)$$

and for an acetylenic carbon, *e.g.*, $C-C\equiv C$

$$A'_{zz}(-C\equiv C-) = \frac{1}{2}A_{C\equiv C}l_{C\equiv C} + \frac{1}{2}A_{C\text{-}C}l_{C\text{-}C} \qquad (25)$$

$$A'_{xx}(-C\equiv C-) = A'_{yy}(-C\equiv C-) = 0 \qquad (26)$$

Estimates of $A'_{ii}(C)$ for these and other unsaturated carbons are shown in Table III. The maximum field gradient shift coefficients for unsaturated carbons are larger than those of saturated carbons as are the maximum uniform field shift coefficients.

Orientation Dependence of LEFS

The first step toward understanding the orientation dependence of linear electric field shifts is the separation of the total LEFS into uniform field and field gradient contributions. The uniform field and field gradient terms have simple but quite different orientational dependence.

A. Uniform Field Term. The orientational dependence of uniform field LEFS is complex for carbons not possessing a symmetry axis. It involves the cosines of the angles, α, between each bond and the electric field, E.

$$\delta_{\text{UFLEFS}} = \sum_{\text{bonds}} A_{\text{bond}} E \cos \alpha \tag{27}$$

However, for carbons possessing a symmetry axis, all the bonds on the carbon atom may be represented by a single virtual bond along the z axis so that the shift coefficient, $A_z(\mathrm{C})$, is equal to A_{bond} of the virtual bond. Then the uniform field LEFS depends only on the angle θ between the electric field and the z axis.

$$\delta_{\text{UFLEFS}} = A_z(\mathrm{C}) E \cos \theta \tag{28}$$

Thus δ_{UFLEFS} can have values between $+A_z(\mathrm{C})E$ and $-A_z(\mathrm{C})E$ (a 200% variation).

Since the distance dependence of electric fields within molecules may not be simple, the distance dependence of the uniform field LEFS will probably be less useful in conformational analysis than their orientation dependence.

If a carbon has a symmetry axis, z, the x–y plane is a null shift plane; *i.e.*, a charge placed in this plane would produce no uniform field LEFS. The direction of any uniform field LEFS induced at this carbon will depend on whether the field source lies above or below the x–y plane. An upfield uniform field LEFS is caused by a positive charge on the negative side of the x–y plane. The positive side of this plane is defined as that on which the more polarizable bond(s) to the carbon are situated. Thus a positive field parallel to the positive z direction produces an upfield shift. Therefore, it might be expected that considerable conformational information could be obtained from a study of uniform field LEFS.

B. Field Gradient Term. The orientation dependence of the field gradient LEFS of a saturated carbon will be much less than that of its uniform field LEFS, because the three diagonal elements, $A'_{ii}(\mathrm{C})$, are very similar. Table II shows that rotational variations of the field gradient LEFS are expected to be only 20%.

For an unsaturated carbon, the orientation dependence of the field gradient LEFS will be much greater than that of a saturated carbon since, in this case, the shift can vary between its maximum value and zero. This 100% variation is due to the fact that A'_{yy} is zero.

Isolation of Uniform Field LEFS

Since uniform field LEFS, field gradient LEFS, and second-order electric field shifts all have quite different orientation dependences, it is necesssary to be able to analyse observed electric field shifts into their component parts. As the orientation dependence of the uniform field LEFS is the largest and simplest, the uniform field LEFS is the most interesting component. Fortunately it has proved possible to derive a method to separate the uniform field LEFS to a great extent from the other electric field shift contributions.

This method is based on the fact, noted earlier, that any carbon with perfect tetrahedral bond symmetry will have a null tensor, $A(\mathrm{C})$, and will show no uniform field LEFS. Whatever the field orientation, no net charge density will be induced on such a carbon because of polarization of the attached bonds by a uniform electric field; the flow of electrons onto the carbon will exactly equal the flow from it. Thus a quaternary carbon will show no uniform field LEFS. If the field gradient LEFS and second-order electric field shifts of a quaternary carbon were identical with those of a similar carbon with attached hydrogens, the difference between the electric field shifts of the two carbons would be exactly equal to the uniform field LEFS of the carbon with attached hydrogens. Thus a separation could be effected between the uniform field LEFS and the other electric field shift contributions.

It has been shown above that the differences between the field gradient shifts of methyl, methylene, methine, and quaternary carbons are small, and a method has been given to estimate and correct for these differences. As yet, however, it is not known whether the second-order electric field shift coefficients of carbons are dependent on the degree of methyl substitution. The value of B for a methyl carbon has been given as 6.5×10^{-18} esu.[8] Thus, for a methyl situated 4 Å from a point electronic charge in vacuo, the uniform field shift would be +6.0 ppm (upfield), the field gradient shift −4.1 ppm, and the second-order shift −0.6 ppm. However, static molecular electric fields may be accompanied by much larger fluctuating fields so that total second-order electric field shifts, and hence the dependence of B on methyl substitution, may be significant.

Ideally, in order to determine the magnitude of the errors involved in the proposed method for extracting uniform field LEFS, the residual electric field shifts of corresponding methyl, methylene, methine, and quaternary carbons should be obtained; unfortunately, there is no direct way of measuring residual shifts. However, a related test would be to compare the relative magnitudes of derived uniform field LEFS of corresponding methyl, methylene, and methine carbons with those predicted by the theory presented in this paper. For such a test, one must choose molecules with well-defined conformations in which the angle between the electric field and the z axis is accurately known. The simplest system, therefore, is one with the observed carbons in the α position to a titratable group. Such a system provides a rigorous test since field gradient and second-order shifts will be largest at α carbons. Therefore the series of primary amines, methylamine, ethylamine, isopropylamine, and *tert*-butylamine was chosen. For these compounds, the electric field due to protonation will be parallel to the N–C$_\alpha$ bond making equal angles with each of the α–β bonds. In this case, the basic assumption that the residual shifts of all the α carbons in these compounds are identical becomes equivalent to the assumption that the ratios of the uniform field LEFS[17] of the methyl, methylene, and methine carbons are 1.0:0.67:0.33.

The protonation shifts of this series of amines and the uniform field LEFS contributions derived from them are presented in Table IV. As predicted, the protonation shifts become more negative (downfield) as the α carbon becomes more highly substituted. The ratios of the derived uniform field LEFS given in Table IV conform quite well to the predicted ratios, the greatest discrepancy being 0.10.

This test of the method for extracting uniform field LEFS has been performed under most demanding conditions where the residual shifts are very large. Thus for more remote carbons, the accuracy of the technique will be greater since second-order and field gradient effects are smaller. However, for α carbons, where the uniform field LEFS and residual shifts are both large and are almost equal and opposite, the success of the method is most striking. Using the protonation shift of the α carbon of ethylamine (0.28 ppm) as an estimate of its uniform field LEFS would lead to an error of a factor more than 20. However, it is now possible to obtain values of uniform field LEFS accurate to within 30%. As our understanding of ^{13}C electric field shifts improves, it should be possible to make corrections to increase the accuracy of the derived uniform field LEFS.

Already it is possible to obtain some understanding of aspects of ^{13}C protonation shift data which previously ap-

Table IV. Protonation Shifts[a] of Amine α Carbons

Compd	Protonation shift, ppm	Derived uniform field LEFS,[b] ppm	Predicted ratio of uniform field LEFS	Observed ratio of uniform field LEFS
Methylamine	2.04	7.50	1.00	(1.00)
Ethylamine	0.28	5.75	0.67	0.77
Isopropylamine	−2.36	3.15	0.33	0.42
tert-Butylamine	−5.50	(0.00)	0.00	(0.00)

[a] Positive shifts upfield, measured on a Varian XL-100-15 FT spectrometer at 25.2 MHz using a 2000-Hz spectral width. [b] Taking the residual shift to be the protonation shift of *tert*-butylamine.

peared inexplicable. For example, the total protonation shifts of the ^{13}C resonances of pentylamine (Figure 4) exhibit unusual behavior, increasing from C_α to C_β and decreasing from C_β to C_ϵ. However, the derived uniform field LEFS contributions show the expected behavior (Figure 4); i.e., they decrease monotonically with the number of bonds separating the observed carbon from the field source. This example demonstrates that the protonation shifts of carbons close to a field source can only be understood when the total shifts are analysed into their component contributions.

The method proposed here for the extraction of uniform field linear components of electric field shifts by subtraction of the electric field shifts of corresponding quaternary carbons is a considerable step forward in the study of electric field shifts. In a following paper, it will be shown how the derivation of uniform field LEFS by this technique enables one to understand many aspects of the protonation shifts of amino acids which previously appeared anomalous.

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Appendix

Although the concept of a linear electric field effect is independent of any assumptions concerning the relationship between shielding and charge density, it has been necessary here, for the purpose of calculating values of A_z and A'_{ii}, to assume that (a) charge density changes on a nucleus (Δq) caused by polarization of electrons along neighboring bonds by an electric field, E, and (b) the shielding (δ_q) caused by such charge density changes can both be expressed in power series

$$\Delta q = a_1E + b_1E^2 + c_1E^3 \ldots \quad (29)$$

$$\delta_q = a_2\Delta q + b_2(\Delta q)^2 + c_2(\Delta q)^3 \ldots \quad (30)$$

where the coefficients a_1 etc. are constants. (Second and higher order terms in eq 29 and 30 can only contribute to high-order electric field shift terms.) In a number of studies,[12,13] a proportional relationship has been found between shielding and charge density; i.e., eq 30 is valid with only the first term significant. However, in many situations, the influence of shielding mechanisms which are independent of nuclear charge density e.g., second-order electric field and magnetic anisotropy effects, will obscure the relationship between charge density and shielding, and therefore the extent of the validity of eq 30 is unknown. For eq 30 to be incorrect, an electric field must produce a shielding contribution which is itself independent of nuclear charge density. If that were the case, the analysis presented in this paper would be incomplete, the calculated shift coefficients, A_z and A'_{ii} only being components of the total LEFS coefficients. Even so, an important generalization would remain true; because of the antisymmetry of LEFS, A_x and A_y would still be zero for a nucleus with a bond environment possessing an axial symmetry element, thus the orientation dependence of the uniform field LEFS would not be altered, only their magnitudes.

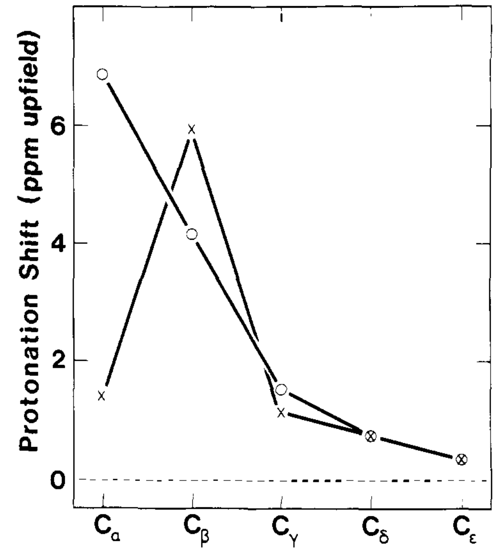

Figure 4. ^{13}C protonation shifts of pentylamine: (X) total protonation shifts; and (O) derived uniform field shift contributions.

Inaccuracies in the calculated values of A_z and A'_{ii} might also arise from the values used for δ/e. Numerous values of δ/e' have been obtained by different authors ranging from less than 100 to more than 300 because of, at least partly, the use of different procedures for calculating charge densities and the presence of shielding from mechanisms independent of charge density but also, quite possibly, because of genuine differences between the values of δ/e for carbons with different electronic structures. However, in the absence of values of δ/e for saturated carbons, other than those obtained from shifts due to directly bonded substituents, a typical value derived from aromatic carbon shifts, 182 ppm/electron,[13] was used here for nuclei in all environments. Despite possible uncertinities in the absolute magnitudes of the A_z and A'_{ii} values in Tables I–III, the *relative* magnitudes for different carbons in a series, e.g., CH_3, CH_2, and CH, the *relative* magnitudes of uniform field and field gradient shifts, and the orientation dependences of both uniform field and field gradient shifts should be unaffected by this source of error.

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