where $\Delta E_{stab} = E_{stab}^{m,n} + E_{stab}^{j,k} - E_{stab}^{m',n'} - E_{stab}^{j',k'}$, i.e., the net change in stabilization energy on going from educts to products.

Now, noting by the application of eq ii that the coefficient of the term involving $E[PH_4]$ in eq iv is zero, and using eq 2 of the text to substitute for $E[F^aPH_3]$, we may derive after collection of like terms eq v. Here eq ii may again be applied, now elim-

$$\Delta E_{rxn} = \Delta E_{stab} + (m + j' - m - j + n' + k' - n - k)E[F^ePH_3] - (m' + j' - m - j)E_{ax} \quad \text{(v)}$$

inating the term involving $E[F^ePH_3]$, which delivers the desired eq 3, where $\Delta_{ax} = m' + j' - m - j$, i.e. the net change in the number of axial fluorine atoms on going from left to right.

$$\Delta E_{rxn} = \Delta E_{stab} - \Delta_{ax}E_{ax}$$

Although derived from the bimolecular case, eq 3 obviously holds for metatheses of termolecular and higher order as well. However, the likelihood of such reactions is minimal.

Note Added in Proof. Observation of axial–equatorial differences in anomeric stabilization has recently been made for closed-shell TBP systems as predicted here. See: Wang, P.; Zhang, Y.; Glaser, R.; Reed, A. E.; Schleyer, P. v. R.; Streitwieser, A. *J. Am. Chem. Soc.* **1991**, *113*, 55.

Supplementary Material Available: Table of absolute and relative projected UHF and PMPn energies for **1–5** (1 page). Ordering information is given on any current masthead page.

Correlation of Carbon-13 and Oxygen-17 Chemical Shifts and the Vibrational Frequency of Electrically Perturbed Carbon Monoxide: A Possible Model for Distal Ligand Effects in Carbonmonoxyheme Proteins

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Received June 21, 1990

Abstract: Ab initio calculations have been carried out that demonstrate an essentially linear correlation between the vibrational frequency of carbon monoxide and its carbon-13 and oxygen-17 chemical shifts, under a variety of external electrical influences. However, the correlations for carbon-13 and oxygen-17 shifts turn out be in opposite directions. Electronic structure calculations reveal that it is polarization of the electron charge density along the intermolecular axis that changes the chemical shielding oppositely for the carbon and oxygen nuclei. Recent experiments have pointed to just such a correlation in a wide range of carbonmonoxyheme proteins, and so electrical perturbation is a possible cause of distal ligand effects. Furthermore, the experimentally determined correlation of the vibrational frequency with oxygen-17 quadrupole coupling constants is also seen in the calculations.

Introduction

Chemical shifts, nuclear quadrupole coupling constants, and vibrational frequencies have long been useful measurements for ascertaining structure and bonding. This is particularly so for complex systems with embedded submolecules, e.g., ligands. For instance, the vibrational frequency of a carbonyl in a transition metal complex (an embedded CO) and/or its chemical shift are frequently taken to be a manifestation of the nature of the metal–carbonyl bonding, with stronger bonding associated qualitatively with a greater change in the CO characteristics. A composite picture of vibrational and chemical shifts, and perhaps other data, offers the possibility of quantitative relationships with structure and interaction energetics; however, this will require knowing the detailed nature of the interactions.

In recent NMR studies of ligand interactions in heme proteins, Park and co-workers[1] established a linear relationship between carbon-13 (^{13}C) and oxygen-17 (^{17}O) chemical shifts, and the ^{17}O nuclear quadrupole coupling constant, with the CO vibrational frequency, by surveying a number of different proteins containing distal ligands which might be expected to influence the heme protein's Fe–CO in different ways. The basis for that relationship lies in the nature of the interaction, and a model of the interaction must be able to reproduce it. As a first step toward a detailed, quantitative model, we report here a theoretical correlation of chemical shifts and coupling constants with vibrational frequencies of isolated CO upon varying an external electrical perturbation in a manner not dissimilar, we believe, to that of distal ligand species in heme proteins.[1]

External electrical perturbation is a simple means of influencing molecular vibration and other properties. In the hypothetical case of a nonrotating diatomic molecule with a dipole moment function that grows linearly with the bond distance, r, a uniform, axial electric field will generate a perturbation to the stretching potential that is also a linear function of r. As a result, the perturbed stretching potential has a different equilibrium point, and this corresponds to the molecule's net contraction or extension in response to the electric field. This change is the vibrational equivalent of the pure electronic structure response to an applied field, and it may be termed vibrational polarization.[2] If the original potential is anharmonic, there will also be a change in the vibrational level spacing,[2,3] and that is observed as a shift in the vibrational transition frequency. Or, if the dipole moment function has a quadratic or higher order dependence on r, this "electrical anharmonicity"[3] will give rise to a frequency shift as well.

Polarization of the electronic charge cloud by an applied field may lead to changes in molecular properties. An obvious example is the property change identified as an induced dipole moment. The polarization of the charge density can, in principle, alter the

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chemical shielding and the electric field gradient at a nucleus, since these develop from the electronic environment. Vibrational polarization will affect molecular properties, too, because properties usually vary with the bond distance, r. That is, if the equilibrium r value is changed by an external field, the equilibrium value of the property will change in a corresponding manner. Thus, to establish the effect of external electrical perturbations on properties such as chemical shifts and quadrupole coupling constants, it is necessary to consider not only the perturbation on the electronic structure but also the vibrational effects. We have carried out detailed ab initio calculations on the electromagnetic properties of CO as a function of the bond distance, r, and this provides the necessary information for rigorously evaluating the effect of external electrical potentials.

Theoretical Approach

A vibrational potential for unperturbed or isolated CO has been obtained from large basis set calculations using well-correlated, coupled cluster wave functions.[4] From numerous basis set tests,[4] we have developed a vibrational potential for CO that yields an equilibrium bond length, r_e, of 1.1306 Å versus the experimental value[5] of 1.1283 Å, an equilibrium vibrational frequency of 2175 cm^{-1} versus the experimental value[5] of 2170 cm^{-1}, and a fundamental transition frequency of 2153 cm^{-1} versus the experimental value[5] of 2143 cm^{-1}. We have explored the basis set and correlation effects on the vibrational potential of CO in some detail,[4] but for our purpose here, we are only concerned with using a realistic potential, not with how it was developed. The particular potential used here seems to offer a realistic representation of CO's true stretching potential, as judged by the r_e value and vibrational frequencies.[6]

Electrical and magnetic properties of CO were analytically calculated as a function of the bond distance, r, by the derivative Hartree–Fock (DHF) approach.[7,8] The basis set for these calculations was a 96-function set of contracted Gaussians. It consisted of the triple ζ core-valence basis of Huzinaga,[9] contracted according to Dunning,[10] but with the six p-functions only contracted into five, leaving four uncontracted p-functions. In other words, this was a (10s 6p/6s 5p) set for each atom. This basis was augmented with one diffuse s-function on each center (exponent of 0.05 for carbon and 0.06 for oxygen) and two diffuse p-functions (exponents of 0.03 and 0.005 for carbon and exponents of 0.05 and 0.007 for oxygen). To this, four sets of d-functions were added, and the exponents were the same for each center: 2.4, 0.6, 0.15, and 0.04. This is a particularly large and flexible basis for evaluating molecular properties.

The chemical shielding tensors at the oxygen and carbon centers were evaluated as the second derivative of the energy with respect to an applied magnetic field and the nuclear magnetic moment.[11] The quantum mechanical one-electron operators needed for the energy derivative evaluation were obtained using the general operator approach of Augspurger and Dykstra.[12] The gauge centers in these evaluations were the atomic centers, and test calculations revealed a sensitivity to the gauge center position of less than 1% over a range of ±0.5 Å along the molecular axis. A third derivative property, giving the change in the chemical shielding with respect to an applied electric field, was also obtained in the DHF calculations.

The permanent (electric) dipole and quadrupole moments of CO have been calculated[4] at the SCF level and at the well-correlated ACCDS level (approximate double substitution coupled clusters with singles)[13-15] using finite field methods for finding the derivative values. The correlated values are more accurate,[8] and these have been used in the electrical interaction calculations we report here. The electrical polarizabilities play a much smaller role in the electrical interaction analysis than do the permanent moments, and so the neglect of correlation effects, a 5-15% difference,[4,8] is relatively unimportant. All properties were obtained at five or more internuclear separation distances that spanned a range of at least ±0.07 Å from the equilibrium.

Vibrational wave functions were calculated by the Numerov–Cooley method[16] which provides an exact numerical determination of the vibrational energies and wave functions. Then, using the list of ab initio properties, the derivative Numerov–Cooley (DNC) method[17] was employed to find first, second, and third derivative properties for specific vibrational states of CO. It is important to realize that vibrational state properties are vibrational averages of the electronic wave function properties *only* for all first derivative properties,[2,8,17] e.g., permanent electrical moments. For second and higher order derivative properties, vibrational polarization, or similarly vibrational magnetization, may contribute; these are distinct from the averaging over vibrational motion.[2,8]

To examine the influence of an external electrical potential on the vibrational state-specific properties of carbon monoxide, we carried out further DNC calculations where the CO stretching potential was perturbed via an external electrical influence. The response properties of CO that we included in this analysis were the first two permanent moments, the dipole polarizability and hyperpolarizability, the quadrupole polarizability, and the dipole-quadrupole polarizability. This corresponds to the property list used to represent CO's electrical response in weak intermolecular interaction in the MMC (molecular mechanics for clusters) model of Dykstra.[18] In this way, we rigorously determine vibrational transition frequencies along with chemical shielding tensors for individual vibrational states, all as functions of the external electrical potential.

External perturbing electrical potentials of several types were considered. The first and simplest type was a uniform electric field. The second type was a field gradient (only). The third type was the potential due to a positive ($+e$) and a negative ($-e$) charge arranged as a dipole oriented either along or perpendicular to the CO axis. The charges were separated by 0.1 au and their center was at least 4 Å from the CO multipole center. These are four hypothetical electrical perturbations of the CO molecule that correspond in a rough way to the types of electrical perturbations that proximate molecules or ligand groups might generate. That is, through combining these perturbations, it should be possible to represent the primary long-range influence of perturbing molecules or ligands. Of course, the further step of realistically modelling the electrical potential of specific perturbing species still remains. Nevertheless, as we show elsewhere,[1] our calculations for the ^{13}C and ^{17}O isotropic chemical shifts and the chemical shielding anisotropies are in excellent agreement with experimental values for CO, and our observation of linear relations between the isotropic chemical shifts and the vibrational frequencies are in good semiquantitative accord with the trends found for CO in variously perturbed heme proteins.[1] In particular, the well-known opposite trends in ^{13}C and ^{17}O chemical shifts and ^{17}O nuclear quadrupole coupling constants with changes in CO vibrational frequency, usually described in terms of "back-bonding", appear to be well predicted solely on the basis of weak electrical polarization.

Results and Discussion

Figure 1 shows the effect of a uniform electric field on the vibrational transition frequency and on the ^{17}O and ^{13}C NMR isotropic chemical shifts (ground vibrational state) obtained from our calculations. The similar pattern of contours for these two properties, and for the carbon chemical shift, implies that they are definitely correlated under this particular influence. There is also a direct correspondence between the vibrational shift contours and the chemical shift contours when the influence is a field gradient instead of a uniform field (Figure 2). The angular dependence of the contours, though, is naturally different from that with a uniform field.

An interesting feature revealed in Figure 1 is that the carbon and oxygen chemical shifts change oppositely with an applied field. (The contours in Figure 1b are of opposite sign to the corresponding contours in Figure 1c.) So, if one nuclear shift increases, then the other decreases. As seen in Figure 2, this is not the case for an applied field gradient. The chemical shifts of carbon and oxygen either increase or decrease together with respect to the

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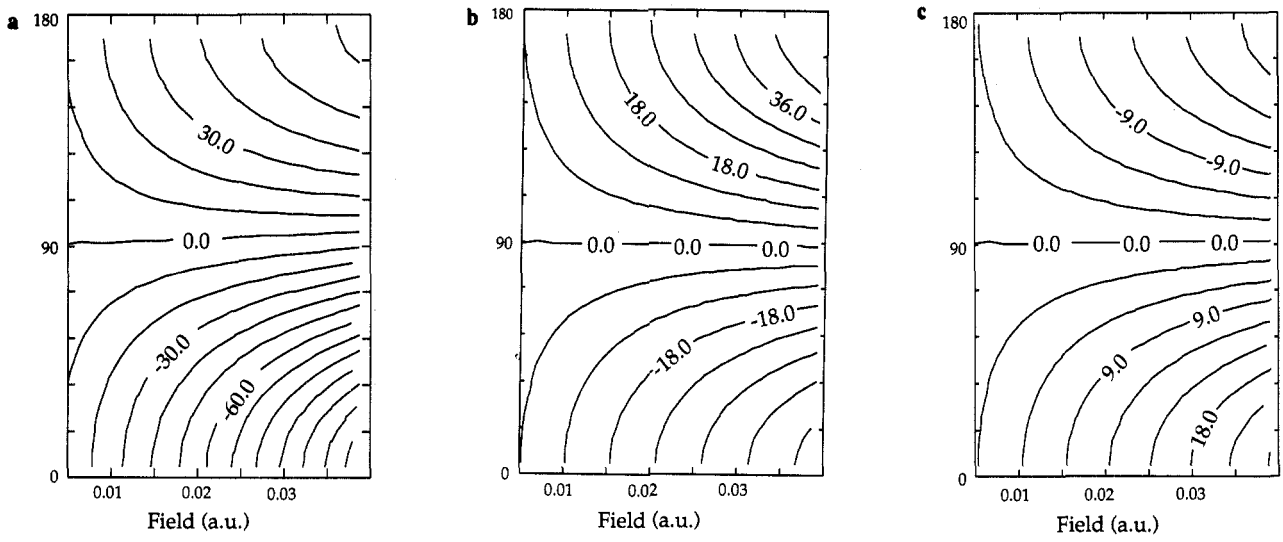

Figure 1. Contours of (a) the fundamental vibrational transition frequency of CO relative to the calculated unperturbed value of 2153 cm^{-1}, (b) the isotropic chemical shift at the oxygen nucleus of CO as a function of the strength of an applied field (horizontal axis) and the angle of orientation of the field with respect to the molecular axis (vertical axis), and (c) the isotropic chemical shift at the carbon nucleus of CO. The contour in (b) and (c) are from DNC calculations for the ground vibrational state of CO. The vibrational frequency contours are given in cm^{-1} and the chemical shifts are given in ppm relative to the unperturbed equilibrium value calculated. The field strengths are given in au (1.0 au = $5.142\,25 \times 10^9$ V/cm). An angle of 0° corresponds to a field orientation parallel to the molecule, and so 180° is the reverse orientation.

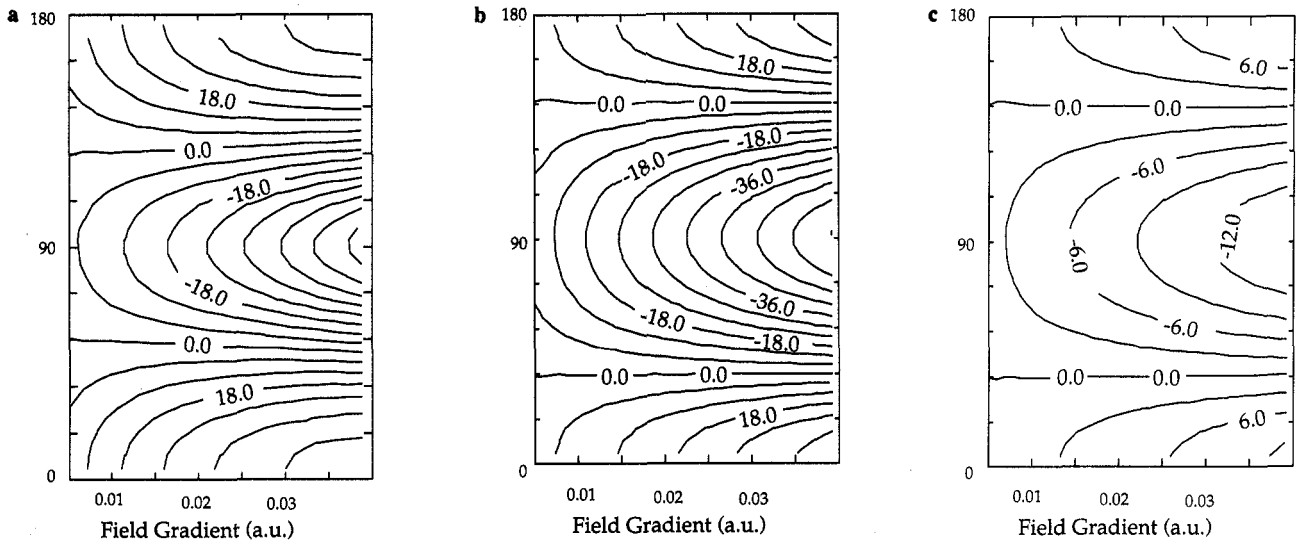

Figure 2. Contours of (a) the fundamental vibrational transition frequency relative to the calculated unperturbed value of 2153 cm^{-1}, (b) the isotropic chemical shift at the oxygen nucleus of CO as a function of the strength of an applied field gradient (horizontal axis) and the angle of orientation of the field gradient with respect to the molecular axis (vertical axis) for the ground state of CO, and (c) the isotropic chemical shift at the carbon nucleus. The vibrational frequency contours are given in cm^{-1} units and the chemical shifts are given in ppm relative to the unperturbed equilibrium value calculated. The field gradient strengths are given in au (1.0 au = $9.717\,45 \times 10^{17}$ V/cm^2). An angle of 0° corresponds to an orientation along the molecular axis, $E_{yy} = E_{xx} = -E_{zz}/2$.

applied field gradient. These features are the manifestations of the different types of electrical polarization arising from applying a field and from applying a field gradient. We may think of the effect of a field applied along the molecular axis by remembering that it induces a dipole, which means that charge is shifted along the axis. Charge density will be increased at one end of the molecule and decreased at the other end, and so it is natural to expect that polarization will lead to increased shielding at one nucleus and diminished shielding at the other. On the other hand, a field gradient induces a quadrupole moment, which means that it changes charge density in a like manner at both nuclei.

To quantify the effect of electrical polarization on chemical shielding, we may consider the first-order effect, as Buckingham has done.[19] We may term this property the shielding polarizability, A. Analogous to defining the dipole polarizability, α, as the first derivative of the dipole moment with respect to the strength of an applied field, the (dipole) shielding polarizability is a 3 × 3 × 3 array of elements, e.g.,

$$A_{yz,x} \equiv \left.\frac{\partial \sigma_{yz}}{\partial E_x}\right|_{E_x=0} \tag{1}$$

In a like manner, we may define the quadrupole shielding polarizability as a tensor of the derivatives of σ with respect to a field gradient component (e.g., E_{xx}). Being a derivative quantity, A is obtained analytically via the DHF approach. This property has already been obtained by other approaches, and calculations have been reported for H_2,[20-23] HF,[22,24,25] and CH_3F.[23] Also, the effect of the electric field on the internuclear separation vis-a-vis

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Table I. Calculated Shielding and Shielding Polarizabilities of CO[a]

	^{13}C		^{17}O	
	this work	ref 28	this work	ref 28
$\sigma_{\parallel}$	271.3	271.0	410.9	410.5
$\sigma_{\perp}$	−162.5	−171.3	−324.3	−331.5
$\bar{\sigma}$	−17.9	−23.8	−79.2	−84.1
$\Delta\sigma$	433.8	442.2	735.2	742.0
	Dipole Shielding Polarizabilities[b]			
$A_{yy,z}$	−548.2		2268	
$A_{zz,z}$	−27.2		44.5	
	Quadrupole Shielding Polarizabilities[b]			
$A_{zz,zz}$	−45.4		−29.7	
$A_{yy,zz}$	821.8		1581	
$A_{zz,yy}$	−3.8		−18.0	
$A_{yy,yy}$	368.9		263.6	
$A_{xx,yy}$	355.4		−1190	

[a] All properties calculated at the equilibrium separation distance, R = 1.128 Å. The absolute chemical shieldings are given in au (conversion factor for A: ppm/au [electric field] = 5.142 25 × 10^9 ppm·cm/V; ppm/au [electric field gradient] = 9.717 45 × 10^{17} ppm·cm^2/V). [b] Only unique, nonzero elements of the A tensors are listed. The symmetry properties of these tensors have been explained by Raynes and Ratcliffe.[27] z is the molecular axis. The subscript which follows the comma denotes the electric field component for a dipole shielding polarizability. The pair of subscripts following the comma are the electric field gradient component for the quadrupole shielding polarizability.

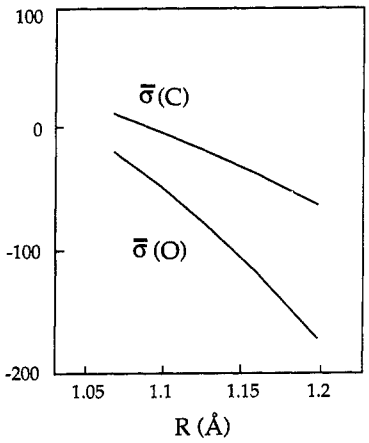

Figure 3. The calculated isotropic chemical shielding for ^{17}O and for ^{13}C, as a function of the CO separation distance, r. The units are ppm relative to the bare nuclei.

this property has been examined for the hydrogen halides.[26]

For a linear molecule, such as CO, a field oriented along the molecular axis (E_z) polarizes charge density, and it primarily changes the perpendicular elements of the shielding tensor. The chemical shieldings and shielding polarizabilities are collected in Table I and the shieldings compared with values from high level calculations by Schindler and Kutzelnigg.[28] In a homonuclear diatomic such as N_2, such a polarization gives rise to an equal but opposite change in σ_{yy} (and σ_{xx}) for the two nuclei; that is, $A_{yy,z}^{\text{N-left}} = -A_{yy,z}^{\text{N-right}}$. In CO, these properties are no longer equal in size, but they are still of opposite sign. Consequently, an electric field that dimishes the shielding on one nucleus will increase the shielding on the other. So, we expect a linear correlation of the chemical shieldings with the vibrational frequency on the basis of the detailed calculations represented in Figure 1, but that the carbon and oxygen shieldings correlate in an opposite way because of the respective shielding polarizabilities, A.

The electrical and magnetic properties of the ground electronic states of diatomic molecules tend to vary linearly with the separation distance, r, at least in the vicinity of the equilibrium separation. As shown in Figure 3, the isotropic chemical shieldings of the two nuclei of CO have a like dependence on r. To the extent that the electrical properties are linear functions of r, an external electrical influence of any sort will perturb the stretching potential with a function that is linear in r. If the unperturbed potential were strictly harmonic, the equilibrium separation will change by an amount that is proportional to the strength of the perturbation. That is, if the unperturbed potential is $V(r) = cr^2$ and the perturbing potential is $V'(r) = br$, then the minimum of $V''(r) = V'(r) + V(r)$ is shifted from $r = 0$ to $-b/2c$. Then, taking the chemical shielding to be linear in r, a shift of $-b/2c$ in the separation distance will change the shielding by an amount directly proportional to b. Since the carbon and oxygen shieldings change in the same direction with a change in r (Figure 3), then this effect will lead to a parallel, not opposed, change in shielding upon electrical perturbation. In our most complete analysis, however, we find the opposed correlation, and so, the change in shielding brought about by a change in r_{eq} is not the dominant effect. Rather, it is electrical polarization's effect on the shielding that is most sizable, and it happens to be opposite for the two nuclei.

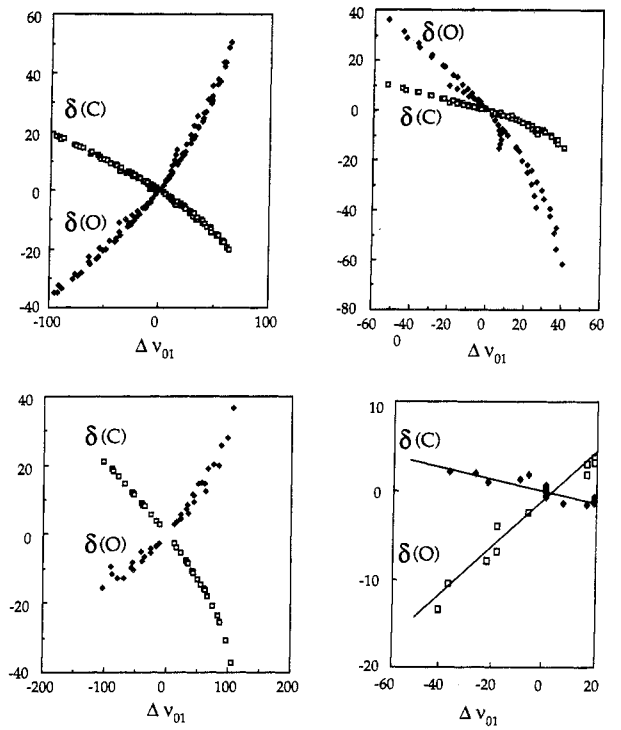

Figure 4. Plots of the isotropic chemical shifts for ^{17}O and for ^{13}C versus the change in the fundamental vibrational transition frequency calculated for (a) various uniform electric fields, (b) various field gradients, (c) various positions of an axial dipole consisting of two point charges, and (d) measured experimentally for a range of carbon monoxyheme proteins. For the experimental values, the carbonmonoxyheme proteins (from ref 1) were: *Glycera dibranchiata* hemoglobin, picket fence porphyrin, hemoglobin Zurich, *physete catadon* myoglobin (pH = 7.0, 7.2, and "low"), rabbit hemoglobin (α-chain), rabbit hemoglobin (β-chain), human adult hemoglobin (α-chain), human adult hemoglobin (β-chain), lactoperoxidase, horseradish peroxide *isoenzyme A* (pH = 9.5, 6.8, and 4.5), and horseradish peroxidase *isoenzyme B* (pH = 10.5, 7, and 6.4), and these are referenced to adult hemoglobin. The solid lines represent the straight-line, linear least-squares fit of the data. The slope of the line for ^{13}C is -0.07 ppm/cm^{-1}, and the corresponding slope from the calculations in (a) is -0.23 ppm/cm^{-1}. The slope of the line for ^{17}O is 0.26 ppm/cm^{-1}, and the corresponding slope from the calculations in (a) is 0.47 ppm/cm^{-1}.

A shift in the vibrational transition frequency upon electrical perturbation is a consequence of the intrinsic anharmonicity of the unperturbed potential. With only cubic anharmonicity, the perturbing potential $V'(r) = br$ will generate a change in the separation of adjacent levels that is directly proportional to b. In other words, the vibrational frequency shift will have a linear dependence on the field strength (via b) under the assumptions

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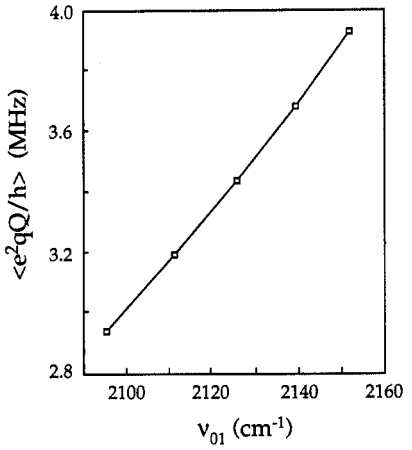

Figure 5. $\langle e^2qQ/h \rangle$ for the ground vibrational state of CO in MHz calculated for different axial electric fields, versus the vibrational frequency shifts that are calculated to arise due to the fields. The upper rightmost point is the field-free data point.

of linear electrical properties and only cubic anharmonicity in $V(r)$. Of course, the electric field's effect on the shielding via A is linear, and so the shielding and vibrational frequency shift vary together.

Figure 4 shows the net relation between the vibrational frequency and the chemical shifts for three different types of electrical environments that we examined, that of a uniform field, a field gradient, and an axial point-charge dipole together with experimental ^{13}C and ^{17}O isotropic chemical shieldings and vibrational frequencies for a range of carbonmonoxyheme proteins.[1] For each type of environment, the chemical shifts vary linearly with the vibrational frequency shift, at least for frequency shifts of up to ± 50 cm^{-1}. Beyond that, there is slight curvature. This shows that with a realistic treatment there is still a linear relationship, and importantly, a relationship that is opposite for ^{13}C and ^{17}O. Again, this is mainly because of the shielding polarizability property of CO. Since the electrical perturbation arising from almost any molecular charge distribution will have a uniform field component, and since this is the important and dominant influence on the chemical shieldings and vibrational frequencies, then this relationship should hold for most molecules or groups that are weakly perturbing CO.

The clear-cut result of these calculations is that weak electrical perturbation will affect CO in such a way that the vibrational frequency and the chemical shifts vary together as the strength of the electrical influence is varied. This would be expected even if CO were already perturbed by complexation to a metal center, since complexation is not likely to make a sharp change in the shielding polarizability or the variation of properties with r. In particular, we should not expect a qualitative change in there being opposite signs for the shielding polarizabilities of carbon and oxygen.

For now, the idea of weak electrical influence appears to offer an excellent explanation of the results of Park and co-workers.[1] These authors noted good correlations between the observed isotropic ^{13}C and ^{17}O chemical shifts and the CO vibrational frequency in a number of proteins, and gave a qualitative account of the observed trends in terms of the "back-bonding" model used previously by Li and Spiro.[29] The back-bonding and electrical polarization concepts are neither exclusive nor inconsistent, since there ought to be an interplay between the polarization of CO by a local electric field and the bonding/back-bonding to Fe. The polarization picture, though, is more suited to quantitative prediction provided that A is known.

Finally, an additional set of ab initio calculations was done to find the nuclear quadrupole coupling constant of ^{17}O, and its correlation with the vibrational frequency. Electronic structure calculations determined the electric field gradient at the nucleus as a function of the bond length, r, and of the strength of the external axial electric field. Using a value of -2.64 fm^2 for the nuclear quadrupole moment,[30] we obtained the quadrupole coupling constant, e^2qQ/h. Then, the vibrationally averaged value, $\langle e^2qQ/h \rangle$, for the ground vibrational state was found as a function of the external field. For the unperturbed molecule we obtained a quadrupole coupling constant of 3.9 MHz, compared to the experimental value of 4.52 MHz.[31] (The behavior of the electric field gradient at the nucleus as a function of the vibrational coordinate has already been considered in detail in ab initio studies of Cummins et al.[30] and Amos.[32]) From this, we obtain the result in Figure 5, which is the correlation of $\langle e^2qQ/h \rangle$ with vibrational frequency shift. This agrees nicely with the experimental data for heme-CO[1] and again supports the electrical polarization picture of distal ligand effects.

Acknowledgment. This work was supported, in part, by a grant to C.E.D. from the Physical Chemistry Program of the National Science Foundation (Grant No. CHE-8721467). The NMR measurements were supported by a grant to E.O. from the National Institutes of Health (Grant No. HL-19481).

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