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Electric Field Effects on ^{13}C and ^{17}O Chemical Shifts and CO Stretching Frequency of Carbon Monoxide Bound to Fe^{2+}

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Using a model consisting of Fe^{2+} octahedrally coordinated to five negative point charges and a CO molecule, the effects of a uniform external electric field applied along the Fe−C−O axis on the chemical shifts of ^{13}C and ^{17}O and the CO stretching frequency are investigated. Both the vibrational frequency and the ^{17}O chemical shift are observed to increase as the electric field applied parallel to the Fe−C−O axis is increased. On the other hand, the ^{13}C chemical shift changes in the opposite direction. The influence of a nonuniform field is also studied by introducing an additional variable point charge along the Fe−C−O axis. Results of the calculations agree well with observed correlations of ^{13}C and ^{17}O chemical shifts and CO vibrational frequencies in carbonmonoxy heme proteins.

Introduction

There is considerable interest in measuring and interpreting the influence of electric fields on nuclear magnetic resonance (NMR) chemical shifts.[1] In real systems, the presence of nearby molecules or charged groups can be regarded as the source of the perturbing electric field. A sound interpretation of how and why chemical shifts change with environment can lead to a better understanding of the intermolecular interactions that give rise to such perturbations. Evaluation of intermolecular effects on the NMR chemical shift via a full *ab initio* calculation is still an extremely difficult task. Several simplified strategies addressing effects of long-range interactions on the NMR chemical shift are now available. One solution begins with expanding the NMR chemical shift in the presence of a nonuniform electric field into a Taylor series in terms of field and field gradients[2]

$$\delta_{\alpha\beta} = (\delta_{\alpha\beta})_0 + A_{\alpha\beta,\gamma}V_\gamma + B_{\alpha\beta,\gamma,\epsilon}V_\gamma V_\epsilon + C_{\alpha\beta,\gamma\epsilon}V_{\gamma\epsilon} + ...,$$

where $\delta_{\alpha\beta}$ is one of the chemical shift tensor elements, $(\delta_{\alpha\beta})_0$ is the field-free value, $A_{\alpha\beta,\gamma}$ is the first derivative of the chemical shift tensor element $\delta_{\alpha\beta}$ with respect to a uniform electric field V along the γ direction, $\mathrm{B}_{\alpha\beta,\gamma,\epsilon}$ is the second derivative of the chemical shift with respect to uniform fields V_γ and V_ϵ, and $C_{\alpha\beta,\gamma\epsilon}$ is the first-order response of the chemical shift to a field gradient $V_{\gamma\epsilon}$. A second approach that does not rely on how quickly a Taylor expansion converges involves the use of a point charge to represent the source of perturbation.[3]

Although sufficient data are available for intermolecular contributions to the chemical shift in the gas phase,[4] the measured numbers normally involve a significant averaging over a wide range of distances and orientations. As a result, data from these experiments are dominated by second-order contributions, and it becomes difficult to extract information regarding the first-order response of the NMR chemical shift to an external electrical field. Fortunately, NMR chemical shift inequivalences in proteins where semirigid segments are present can serve as excellent testing ground for theories regarding intermolecular effects on the NMR chemical shift.[5]

Park et al. first noted interesting correlations between various electronic properties such as vibrational frequencies, chemical shifts, and quadrupole coupling constants in various carbonmonoxy heme proteins.[6] In this series of proteins, they established a linear relationship between the ^{13}C and ^{17}O chemical shifts with the CO vibrational frequencies. Augspurger et al. later proposed a model for these observed correlations.[7] In their model, the dependence of the vibrational and magnetic properties on an external uniform field, field gradients, and dipole for an isolated CO molecule were calculated at the Hartree−Fock level. With these *ab initio* calculations, they found that the ^{13}C and ^{17}O chemical shifts indeed correlate with the CO stretching frequency when a uniform field is applied. Changes in both chemical shifts were direct consequences of the imposed electrical perturbation, while changes in the vibrational frequency were due to changes in the bond length brought about by the external field. The computed relationships bear the same sign as the experiment although the magnitudes seem overestimated. Using field gradients, however, the trend found for the ^{17}O chemical shift was opposite to that of the experiment. Their model was simple enough, yet it was able to demonstrate that the reason such properties correlate with each other is electrical perturbation.

This paper aims to improve the isolated CO model. Chemical shifts are sensitive to other factors such as local geometry. In the case of CO bound to Fe^{2+} in a heme protein, questions arise regarding bending or tilting of the CO ligand as well as distortion of the porphyrin ring. These factors can likewise affect the observed NMR chemical shifts. To pinpoint convincingly that perturbation from weak electrical interactions is the source of both ^{13}C and ^{17}O chemical shift inequivalencies in carbonmonoxy heme proteins, a closer agreement between theory and experiment is warranted.

At present, it is still cumbersome to perform *ab initio* calculations on a system containing a porphyrin ring, a histidine side chain, Fe, and a CO ligand. An isolated CO molecule contains a triple bond and a permanent dipole. These characteristics play an important role in deciding how susceptible the vibrational frequency would be to electrical perturbations. In addition, the permanent dipole contributes significantly to the sensitivity of the NMR chemical shift to electrostatic interactions. Both charge distribution on the CO molecule and its bond length change upon coordination to Fe^{2+}. The CO bond is now relatively weaker due to π-back bonding, and the CO bond dipole should also change upon coordination with an Fe^{2+} ion.

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TABLE 1: Correlation of ^{13}C and ^{17}O NMR Chemical Shifts and the CO Vibrational Frequency ($\Delta\delta/\Delta\nu$, ppm/cm^{-1}) in the Presence of an Electrical Perturbation

	this work			
nucleus	uniform field	point charge	isolated CO[a]	exptl[b]
^{13}C	−0.14	−0.16	−0.23	−0.07
^{17}O	0.36	0.26	0.47	0.26

[a] From ref 7. [b] From ref 6.

Thus, the first step in improving the model should involve the incorporation of an Fe^{2+} ion.

Computational Details

The proposed model consists of an Fe^{2+} ion placed at the origin of a Cartesian frame with a CO molecule lying along the z-axis with the C coordinated to the Fe. In addition, five point charges are added. Four of these point charges lie on the xy-plane, forming a square arrangement around the Fe^{2+} ion. A fifth point charge is placed along the z-axis, *trans* to the CO ligand. All point charges lie 2 Å from the Fe nucleus. These point charges have been included to guarantee that only one pair of the d orbitals (d_{xz} and d_{yz}) on Fe is degenerate and, thus, ensuring a diamagnetic electronic ground state as opposed to an isolated Fe^{2+}−CO system where in addition to d_{xz} and d_{yz}, d_{xy} and $d_{x_2-y_2}$ also form a degenerate pair. The distance of 2 Å is chosen since it mimics the Fe−N distances in heme. The magnitude of charge at each of these points is $-0.4e$ so that the whole model is neutral.

The basis sets for the calculations are (14s9p5d/8s5p5d) for Fe and IGLO-III for C and O. Geometry optimization with Fe fixed at the origin and vibrational frequency calculations were obtained using the density functional program deMon-KS.[8−10] The sum over states density functional perturbation theory (SOS-DFPT) shielding calculations were performed with the additional deMon-NMR code.[11−13] This particular program uses the IGLO[14] method for the chemical shift computations. The exchange correlation functional employed was taken from Perdew and Wang[15] (PW91), the one recommended by the authors of the deMon-NMR program.[13]

Two types of electrical perturbation were studied. First, a uniform electrical field is applied parallel to the Fe−C−O axis with the following strengths: −0.02 to 0.02 au (1 au = 5.142 25 × 10^9 V/cm). A positive field is equivalent in sign to a field experienced by the CO molecule when a negative point charge is placed near the oxygen end. Second, a sixth point charge of variable magnitude ($-e$ to $+e$) is placed along the z-axis, 6 Å from the Fe (on the CO side), which places it at about 3.5 Å from the O nucleus. This distance is chosen because it produces a range of values for the chemical shifts and vibrational frequencies similar to those of the uniform field calculations. All calculations were performed on an IBM RS/6000 model 390 computer.

Results and Discussion

A summary of the results is shown in Table 1. These are compared with previous calculations of Augspurger et al.[7] and experimental values obtained by Park et al.[8] from a series of carbonmonoxy heme proteins. The CO vibrational frequency changes at a rate of about 4700 cm^{-1}/au as a uniform electric field is applied. This is higher than the value obtained by Augspurger et al.[7] for the isolated CO molecule, 3200 cm^{-1}/au. This is expected since the CO bond is now relatively weaker when attached to an Fe^{2+}. The first derivative of the ^{13}C chemical shift with respect to a uniform field, or dipole shielding polarizability, is about −690 ppm/au, which is slightly more negative than the isolated molecule's value, −610 ppm/au. For ^{17}O, this work yields 1800 ppm/au, which is significantly larger than that of the isolated molecule, 1100 ppm/au. The dramatic increase in sensitivity of the ^{17}O chemical shift that does not occur with ^{13}C is due to the fact that with Fe^{2+}, only the O atom sits on the periphery of the molecule and C has become a central atom. When the two chemical shifts are plotted against the CO vibrational frequencies (see Figure 1), the following slopes are obtained: for ^{13}C, −0.14 ppm/cm^{-1}; for ^{17}O, 0.36 ppm/cm^{-1}. These values are still higher than the experimental values:[6] ^{13}C, −0.07 ppm/cm^{-1} and ^{17}O, 0.26 ppm/cm^{-1}; nevertheless, they represent a significant improvement over the values obtained by Augspurger et al.: ^{13}C, −0.23 ppm/cm^{-1} and ^{17}O, 0.47 ppm/cm^{-1}.

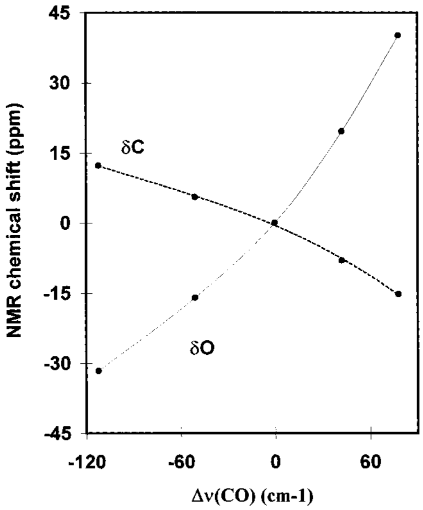

Figure 1. Changes in the ^{13}C and ^{17}O NMR chemical shifts plotted against the change in CO stretching frequency calculated at various uniform electric fields.

There are two factors that may contribute to the changes in the chemical shift. One is the electric field, and the other is the change in equilibrium bond length as the field is applied. As the external electrical field becomes more positive, the CO bond contracts, leading to a decrease in both ^{13}C and ^{17}O chemical shifts. On the other hand, the direct dependences of the ^{13}C and ^{17}O chemical shifts on the external field are of opposing signs. The applied field induces a dipole causing a change in the charge distribution within the CO ligand. One atom becomes more positive while the other becomes more negative resulting in opposite signs in changes of the shielding at the two sites. As in the previous work of Augspurger et al., the electrical polarization is the more dominant factor, explaining why the ^{17}O dipole shielding polarizability is opposite in sign and higher in absolute terms than that of ^{13}C.

The linear relationship holds true only at weak electric field strengths. There is a significant curvature as seen in Figure 1. As the field becomes more positive (the reader is reminded here that a positive field is equivalent in sign to that of a field generated by placing a negative charge near the O end of the CO molecule), the rate of decrease in the optimized CO bond length becomes slower. Consequently, the change in vibrational frequency with increasingly positive field becomes less. Moreover, the second derivative of the chemical shift with respect to increasing bond length is normally positive,[16] which means that both ^{13}C and ^{17}O chemical shifts are becoming more positive at a faster rate at longer bond lengths. The effect of the bond length to the ^{17}O chemical shift is opposite in sign compared to the electrical polarization effect. As a result, the ^{17}O chemical shift changes more rapidly at higher vibrational frequencies

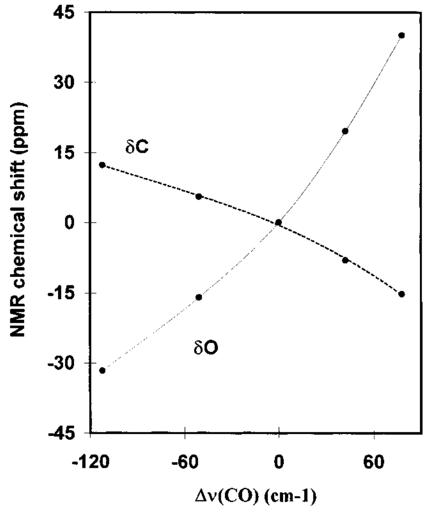

Figure 2. Changes in the ^{13}C and ^{17}O NMR chemical shifts plotted against the change in CO stretching frequency calculated in the presence of a point charge of various magnitudes.

where the bond length is shorter and the applied field is positive. More importantly, the second derivative of the ^{17}O chemical shift with respect to a uniform electric field is positive, adding to the rate of increase in chemical shift at positive field values. In real systems such as heme proteins, it is more likely that the perturbing electrical field is negative since the O end of the CO ligand bears the partial negative charge, thus tending to attract positive groups. Thus, for a better comparison between calculated and experimental values, points obtained at negative field values (longer CO bond lengths and lower CO stretching frequencies) should be given more weight. If one considers only the points obtained with negative electric fields, the slopes obtained are as follows: ^{13}C, -0.11 ppm/cm^{-1} and ^{17}O, 0.28 ppm/cm^{-1}. These values are already within the error margin of the experiment.

An additional drawback of using a uniform electric field is the fact that in real systems, electrostatic fields are not uniform. The use of a uniform electric field hinges on the adequacy of truncating the Taylor series expansion of the chemical shift with respect to a nonuniform electric field at the first term. Previous work has shown that terms arising from the field gradient and the hypergradient are also significant.[17] It should also be noted that the contribution from the field gradient is opposite in sign to that of the uniform field. Thus, working with a uniform field is likely to overestimate the change in chemical shift. To represent the nonuniform environment felt by a CO molecule, instead of imposing an external electrical field, an additional point charge is added to the model, at 6 Å from the Fe, along the Fe$-$C$-$O axis, near the oxygen end. The value of this point charge is varied from $+e$ to $-e$. The calculated ^{13}C and ^{17}O chemical shifts are plotted against the calculated CO stretching frequencies as shown in Figure 2. First, compared to the uniform field results, the correlations between the chemical shifts and the stretching frequency are evidently more linear when a point charge is used. The slopes obtained from this plot are: ^{13}C, -0.16 ppm/cm^{-1} and ^{17}O, 0.26 ppm/cm^{-1}. If the points obtained with a negative point charge placed near the O are disregarded, the slopes obtained are: ^{13}C, -0.14 ppm/cm^{-1} and ^{17}O, 0.25 ppm/cm^{-1}. The slope for ^{17}O compares favorably with experiment, 0.26 ppm/cm^{-1}. There is still, however, a significant discrepancy for ^{13}C. The C nucleus lies closer to the heme ring; thus, it may be more susceptible to the inadequacy of the model employed in this work.

Conclusion

The very close agreement between calculated and experimental values provides a very strong support to the explanation first proposed by Park et al.[6] after observing good correlations between the isotropic ^{13}C and ^{17}O chemical shifts and the CO vibrational frequency. This work strongly supports the idea that the observed correlations between the ^{13}C and ^{17}O chemical shifts with the CO stretching frequencies can be explained by weak electrical perturbations. Moreover, since the data of Park et al.[6] included those of a picket fence porphyrin in which the Fe$-$C$-$O group is neither tilted nor bent, our results also strongly support a linear geometry for Fe$-$C$-$O in carbonmonoxyheme proteins. It is unlikely that such good correlations between the chemical shifts and stretching frequency will exist if some of the systems Park et al. studied had tilted or bent geometries. ^{13}C and ^{17}O chemical shifts as well as the CO vibrational frequency will have an additional dependence on the geometry of the Fe$-$C$-$O group. Weak electrical perturbation acting as the main factor appears to be responsible for the observed inverse relationship between ^{13}C and ^{17}O chemical shifts. The presence of factors other than weak electrical perturbations may not lead to such a relationship. Lastly, the success of the model used in this work illustrates the adequacy of present shielding computational methodologies in extracting intermolecular effects on the NMR chemical shift.

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