

An NMR shielding model for protons above the plane of a carbonyl group

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Abstract

Covalently bonded hydrogen nuclei located over the plane of a carbonyl group in a strong magnetic field experience magnetic shielding (or deshielding) that results from the combined effect of the magnetic anisotropy of the carbon–oxygen double bond and various other intramolecular shielding effects. GIAO-HF in Gaussian 98 was employed to calculate isotropic shielding values and to predict the net proton NMR shielding increment for a simple model system: the proximate proton of methane held in various positions over formaldehyde. The net shielding increments of the proximate proton of methane, plotted against its Cartesian coordinates relative to the center of the carbon–oxygen double bond, led to the development of a single empirical equation for predicting the NMR shielding experienced by a covalently bonded proton over the plane of a carbonyl group. The predictive capability of this equation has been validated by calculating the shielding increments of protons over the plane of a carbonyl group in known structures, using this as a correction to the chemical shift estimated by substituent effects and comparing the result to experimentally observed chemical shifts. Shielding is predicted by this equation for protons located in the region from over the center of the carbon–oxygen double bond to beyond the carbon atom; deshielding is predicted for protons located above and beyond the oxygen atom. This prediction differs from those made by the long-held “shielding cone” model found in nearly every textbook on NMR, but is consistent with experimental observations. The algorithm for predicting the shielding increment for a proton over a carbonyl group can be used in a spreadsheet or incorporated into software that estimates chemical shifts using additive substituent constants or a database of structures. Its use can improve the accuracy of the estimated chemical shift of a proton in the vicinity of a carbon–oxygen double bond, and thus assist in spectral assignments and in correct structure determination.

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1. Introduction

The diamagnetic (de)shielding effect on the chemical shift of protons that lie in or near the plane of the carbonyl group is well known. The large (~ 10 ppm) chemical shift of an aldehyde proton is an example. Less thoroughly studied is the effect of a carbonyl group on the chemical shift of protons that lie above (or below) the plane of the carbonyl group. The long-held model for NMR shielding by anisotropic groups, which can cause shielding or deshielding in the NMR spectrum of nearby protons, is based on McConnell equation [1], which gives rise to the familiar “shielding cones” found in most textbooks on NMR spectroscopy (for example, [2]). However, the McConnell equation predicts the distance and directional effect of (only) the anisotropy of the magnetic susceptibility of a bond. Pople [3] and Flygare [4] each calculated quite different values of the anisotropy of the car-

bonyl group and its principal susceptibilities. Furthermore, Zürcher [5] demonstrated that the chemical shifts observed in ketosteroids could only be accounted for if both the electrostatic and long-range magnetic anisotropy shielding effects are considered.

Examples of molecules having protons located over the plane of a carbon–oxygen double bond are shown in Fig. 1. In each of these examples, a proton positioned over the plane of a carbonyl group (and just beyond the carbonyl carbon atom, away from oxygen) experiences an upfield shift (shielding) in the NMR spectrum arising from its position over the carbonyl group. The McConnell equation predicts shielding for protons above the *center* of a carbon–oxygen double bond, but deshielding for protons within a cone aligned with the carbon–oxygen bond axis [6].

It has been shown, however, that the McConnell equation is inaccurate in predicting the net shielding experienced by a covalently bonded proton over a carbon–carbon double bond in alkenes [7–9]. Models based on *ab initio* calculations have been developed [10–13] that predict chemical

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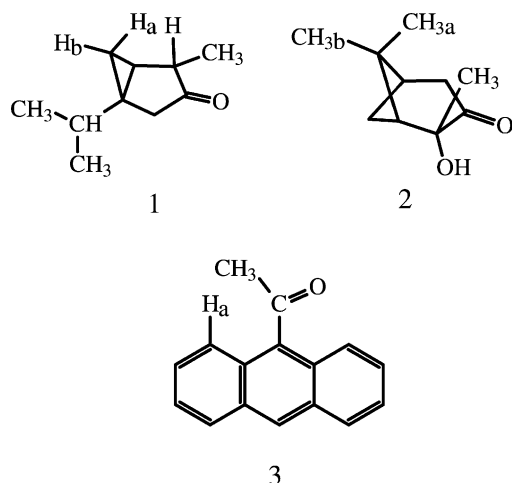


Fig. 1. Examples of structures with a proton above the plane of a carbonyl group.

shift values quite close to those observed. The two approaches differ quite substantially in the assumptions involved. The McConnell model considers only the anisotropy of the magnetic susceptibility of one structural feature (in the case of alkenes, $C=C$) on the magnetic shielding. Thus, it ignores other significant contributors to the overall chemical shift, such as electric field effects, orbital interactions, dispersion, and the effects of the anisotropy of all of the other bonds. The *ab initio*-derived functions incorporate all of these effects, to the extent that they are computed by HF/6-31G(d,p) calculations on which they are based.

In this paper, we describe a model for predicting the proton NMR shielding effect of a carbonyl group based on *ab initio* gauge-including atomic orbital (GIAO)-HF calculations of a simple model system: methane placed in various positions above formaldehyde at four distances above the molecular plane (from 2.5 Å to 4.0 Å).

2. Computational methods

Input geometries for methane and formaldehyde were each created using Spartan [14] molecular modeling software running on an SGI Indigo2 R4000 computer and were optimized at an *ab initio* level using Hartree-Fock theory with a basis set of 6-31G(d,p) [15]. The geometry-optimized structures were then converted to Cartesian coordinate files, and the two files were textually merged to create the geometry of a methane-formaldehyde pair indicated in Fig. 2.

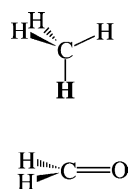


Fig. 2. Orientation of methane over formaldehyde.

After creating the merged file, multiple copies of each file were made. The coordinates of the methane portion of the input file were manipulated in these copies to move the methane molecule incrementally (in the XY plane) over the face of formaldehyde keeping the Z distance above the plane of formaldehyde fixed. The symmetry of formaldehyde reduced the number of geometries to be calculated; only one half of the surface over one face of formaldehyde was considered. The X and Y coordinates of methane were adjusted in 0.5 Å increments. Seventy-eight positions of methane were calculated at each of four distances (2.5, 3.0, 3.5, and 4.0 Å) between the proximal proton of methane and the molecular plane of formaldehyde.

As has been reported previously [10], the angle of incidence of the methane $C-H$ bond to the π -electron system (in ethene) has relatively negligible effect on the calculated isotropic shielding value. A methane probe was oriented in three mutually perpendicular directions with the proximal proton fixed at a position 3 Å above the plane of formaldehyde and located 3 Å in the X -direction and 3 Å in the Y -direction from the center of the $C=O$ bond (beyond the carbonyl oxygen). The isotropic shielding values of the proximal proton in the three methane orientations varied by less than 0.07 ppm. We therefore conclude that the orientation of the $C-H$ bond of the methane probe is of relatively minor importance, and can be ignored in the development of our current model for shielding by the carbonyl group.

Using the same theory and basis set (HF/6-31G(d,p)) as employed in the geometry optimization calculations of methane and formaldehyde, single point calculations were performed using Gaussian 98 [16] on a Cray T90. The difference in computed isotropic shielding between single point and constrained geometry optimization calculations was found to be less than 0.05 ppm [17]. Corrections due to basis set superposition error (BSSE) were made using the counterpoise method of Boys and Bernardi [18]. Each BSSE correction for this series of calculations was less than 0.01 ppm, which is far less than the uncertainty in the method. The isotropic shielding values were calculated using the subroutine GIAO, developed by Ditchfield [19] and improved by Chesnut and Foley [20] and Wolinski et al. [21]. The isotropic shielding values for the proximal proton of methane over formaldehyde were recorded and transformed into a shielding increment ($\Delta\sigma$) in ppm by subtracting from each data point the isotropic shielding value calculated for methane alone using the same level of theory and basis set. In this analysis and all subsequent discussions, only the data for the proximal proton of methane (indicated in bold in Fig. 2) were used.

The shielding increments ($\Delta\sigma$) for these protons were graphed against their distance (X and Y) from the center of the carbon-oxygen double bond of formaldehyde separately at each of four distances of separation (Z) from the plane of formaldehyde (Fig. 3). Positive values of $\Delta\sigma$ represent shielding; negative values represent deshielding. Fig. 4

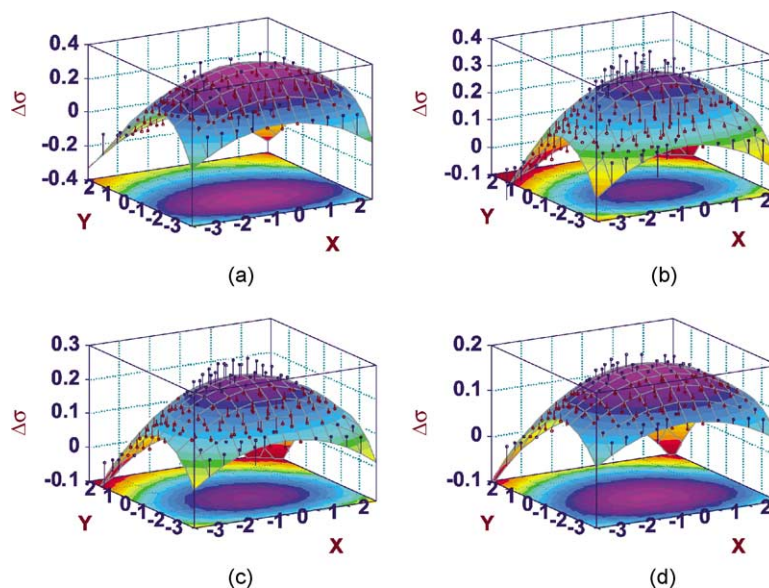


Fig. 3. Surfaces of the shielding increment in ppm at (a) 2.5, (b) 3.0, (c) 3.5, and (d) 4.0 Å.

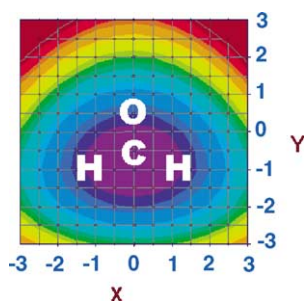


Fig. 4. Shielding increment surface at 3.0 Å above formaldehyde with atom positions of formaldehyde noted.

shows the orientation of formaldehyde in the Cartesian coordinate system.

Equations were fitted to each of the resulting three-dimensional shielding increment surfaces using the statistical modeling software TableCurve3D [22]. A polynomial equation (Eq. (1)) fit well the shielding surfaces for methane at each of the four distances above formaldehyde (Table 1).

Table 1

The values of the constant a and the coefficients b , c , d , e , and f in the equation $\Delta\sigma = a + bY + cX^2 + dY^2 + eY^3 + fX^2Y$ for the shielding surface as a function of the distance (Z) above the plane of formaldehyde, and the correlation coefficients (r)

| Parameter | Distance above formaldehyde (Å) | | | |
|-----------|---------------------------------|----------|----------|----------|
| | 2.5 | 3.0 | 3.5 | 4.0 |
| a | 0.3299 | 0.3113 | 0.2416 | 0.1817 |
| b | -0.1086 | -0.05243 | -0.0335 | -0.02373 |
| c | -0.02293 | -0.0218 | -0.01568 | -0.01043 |
| d | -0.03566 | -0.02909 | -0.02035 | -0.01383 |
| e | 0.00770 | 0.00293 | 0.00153 | 0.00097 |
| f | -0.00072 | -0.00202 | -0.00144 | -0.00101 |
| r | 0.96 | 0.96 | 0.97 | 0.98 |

$$\Delta\sigma = a + bY + cX^2 + dY^2 + eY^3 + fX^2Y \quad (1)$$

Values of the parameters are listed in Table 1. A mathematical relationship between the constant (a) and coefficients (b , c , d , e , and f) in the equation for each surface and the distance (Z) above formaldehyde was determined by least-squares fit to quadratic equations (Table 2) in MSExcel [23]. Substituting the appropriate quadratic equations for the constant (a) and each of the coefficients (b , c , d , e , and f) into Eq. (1) provided a single equation (Eq. (2)). This equation predicts the shielding increment ($\Delta\sigma$) values in ppm for protons as a function of their lateral displacement (X and Y , in Å) from the center of the carbon–oxygen double bond and the vertical distance (Z , in Å) above the plane of formaldehyde.

$$\begin{aligned} \Delta\sigma = & (-0.0413Z^2 + 0.166Z + 0.177) \\ & + (-0.0463Z^2 + 0.356Z - 0.707)Y \\ & + (0.0041Z^2 - 0.018Z - 0.0039)X^2 \\ & + (-0.00007Z^2 + 0.0153Z - 0.0737)Y^2 \\ & + (0.042Z^2 - 0.0316Z + 0.0604)Y^3 \\ & + (0.0017Z^2 - 0.0114Z + 0.0167)X^2Y \end{aligned} \quad (2)$$

Table 2

Equations relating the values of a , b , c , d , e , and f in Eq. (1) for the mean shielding surface to the distance (Z) above the plane of formaldehyde^a

| Equation |
|--------------------------------------|
| $a = -0.0413Z^2 + 0.166Z + 0.177$ |
| $b = -0.0463Z^2 + 0.356Z - 0.707$ |
| $c = 0.0041Z^2 - 0.018Z - 0.0039$ |
| $d = -0.00007Z^2 + 0.0153Z - 0.0737$ |
| $e = 0.042Z^2 - 0.0316Z + 0.0604$ |
| $f = 0.0017Z^2 - 0.0114Z + 0.0167$ |

^a The correlation coefficient (r) of each equation was 0.99 or greater.

Table 3

Shielding increments ($\Delta\sigma$) predicted by Eq. (1) for protons over the plane of a carbon–oxygen double bond in the structures in Fig. 1, estimated chemical shifts^a of those protons, chemical shift estimates corrected by the shielding increments^b, and experimentally observed chemical shifts

| Structure | Proton label | Predicted shielding increment ($\Delta\sigma$) | Estimated chemical shift | Corrected chemical shift estimate | Observed chemical shift |
|-----------|-----------------|--|--------------------------|-----------------------------------|-------------------------|
| 1 | H _a | 0.36 | 0.22 | −0.14 | −0.05 |
| | H _b | −0.40 | 0.22 | 0.62 | 1.39 |
| 2 | H _a | 0.28 | 8.00 | 7.72 | 7.81 |
| 3 | H _{3a} | 0.18 ^c | 1.00 | 0.82 | 0.90 |
| | H _{3b} | −0.30 ^c | 1.00 | 1.30 | 1.40 |

All values are in ppm.

^a Chemical shifts were estimated using additive substituent constants [25].

^b Corrections were made by subtracting the shielding increment calculated by Eq. (2) from the estimated chemical shift. Cartesian coordinates were obtained using Spartan [14].

^c Mean value of three H positions in the lowest energy conformation.

The overall shielding experienced by a proton is the sum of all shielding influences due to nearby groups and their interactions [24]. The *ab initio*-derived model presented here considers not only the magnetic anisotropy of the carbon–oxygen double bond but also the shielding influences due to the covalently bonded proton of methane and the interactions of the two molecules, which may lead to orbital perturbations, especially at close proximity. This model should be generally applicable to predicting the net chemical shielding effects on protons held over a carbonyl group of an aldehyde or ketone.

3. Results and discussion

The shielding increments of protons in several rigid molecular systems (structures 1–3, Fig. 1) calculated using Eq. (2) were used to correct chemical shifts estimated by additive substituent effects [25]. Corrected chemical shift estimates are compared to experimentally observed chemical shifts in Table 3.

Structures in which a methyl group is held over a carbonyl group (Figs. 1 and 3) pose a special problem. Rapid rotation of the methyl group results in NMR chemical shifts for the methyl groups representing the time-weighted average environment of the three protons. Both GIAO and the shielding equation presented herein utilize a specific geometry (single conformation). Only the lowest energy conformation was used in this study to predict the shielding increment. In another study [13], it was determined that the error introduced by neglecting other rotamers is less than 0.05 ppm, which is less than the uncertainty in the model. Mean shielding increment data for the three protons in each methyl group are found in Table 3.

It should be noted that predictions based on Eq. (2) have limitations. The model was developed from shielding data for protons from 2.5 Å to 4.0 Å above formaldehyde, and laterally within 3.0 Å of the center of the carbonyl group. Predictions of shielding increments beyond the range over which this equation was developed are meaningless. It has

Table 4

The RMS deviation of the $\Delta\sigma$ values calculated by Eq. (2) from the values calculated by GIAO as a function of the distance from formaldehyde

| Distance (Å) | RMS deviation (ppm) |
|--------------|---------------------|
| 2.5 | 0.04 |
| 3.0 | 0.03 |
| 3.5 | 0.02 |
| 4.0 | 0.01 |

been demonstrated [10,11,24] that there is severe distortion of the highest occupied molecular orbital (HOMO) of the ethene–methane pair when one hydrogen atom of methane is positioned 2.0 Å above ethene. The effect of the orientation of methane relative to formaldehyde is also greater at this proximity [26]. It is for this reason that calculations for the current model were not extended closer than 2.5 Å to the plane of the carbonyl group. Despite these limitations, the equation predicts shielding increments, which, when used in conjunction with conventional additive substituent effects, lead to improved estimates of chemical shifts.

Each proton position of methane used in the GIAO calculation to generate the shielding increment surfaces was also calculated using the shielding function (Eq. (2)). The root mean square (RMS) deviation between the chemical shift increment calculated by Eq. (2) and the shielding increment calculated directly by GIAO for each proximal proton position is reported in Table 4; this measure of the fit of the shielding function to the GIAO-calculated shielding values is an indication of the precision of predictions made using this equation. As expected, the largest deviation is found at the closest distance between methane and formaldehyde, where the predicted shielding increment is also largest and where orientation effects are greatest.

4. Conclusions

Plotting the through-space shielding increment ($\Delta\sigma$), calculated using GIAO-HF in Gaussian 98 for protons of

methane held at various positions over the plane of formaldehyde, against X and Y distance from the center of the formaldehyde molecule gives a smooth curved surface for each of four distances (Z) above formaldehyde. An equation of the general form $\Delta\sigma = a + bY + cX^2 + dY^2 + eY^3 + fX^2Y$ fit each of these surfaces well. Simple quadratic equations relate the distance Z to the constant (a) and the coefficients (b , c , d , e , and f). Substitution of these equations for a , b , c , d , e , and f provides a single equation for predicting the through-space shielding increment experienced by protons held over formaldehyde. Application of this equation to several structures having a proton over the plane of a carbonyl group demonstrates its general predictive validity. Utilization of the shielding increment equation in a spreadsheet or after incorporation into software that estimates chemical shifts from a database of substituent effects as a chemical shift correction should provide valuable assistance to chemists in making proper spectral assignments and correct structure determinations.

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