

An algorithm for predicting proton nuclear magnetic resonance deshielding over a carbon–carbon double bond

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Hydrogen nuclei located over a carbon–carbon double bond in a strong magnetic field experience NMR shielding effects that result from the magnetic anisotropy of the nearby double bond and various other intramolecular shielding effects. We have used GIAO, a subroutine in Gaussian 98, to calculate isotropic shielding values and to predict the proton NMR shielding increment for a simple model system: methane held in various orientations, positions, and distances over ethene. The average proton NMR shielding increments of several orientations of methane have been plotted versus the Cartesian coordinates of the methane protons relative to the center of ethene. A single empirical equation for predicting the NMR shielding experienced by protons over a carbon–carbon double bond has been developed from these data. The predictive capability of this equation has been validated by comparing the shielding increments for several alkenes calculated using our equation to the experimentally observed shielding increments. This equation predicts the NMR shielding effects more accurately than previous models that were based on fewer geometries of methane over ethene. In fact, deshielding is predicted by this equation for protons over the center and within about 3 Å of a carbon–carbon double bond. This result is in sharp contrast to predictions made by the long-held McConnell “shielding cone” model found in nearly every textbook on NMR, but is consistent with experimental observations. The algorithm for predicting the (de)shielding increment for a proton over an alkene can be used in a spreadsheet on a PC or incorporated into software that estimates chemical shifts using additive substituent constants or a database of structures. In either application its

use can substantially improve the accuracy of the estimated chemical shift of a proton in the vicinity of a carbon–carbon double bond, and thus assist in spectral assignments and in correct structure determination. © 2000 by Elsevier Science Inc.

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INTRODUCTION

Anisotropic functional groups can cause shielding (upfield shift) or deshielding (downfield shift) in the NMR spectrum of nearby protons. The long-held model for NMR shielding by anisotropic groups is based on the McConnell equation,¹ which gives rise to the familiar “shielding cone” found in most textbooks on NMR spectroscopy.² The McConnell equation predicts shielding for protons above the center of the double bond. The unexpected deshielding of a proton held over the center of a carbon–carbon double bond and within about 3 Å of the double bond was predicted by ab initio calculations.^{3,4} Molecules having this structural feature are not uncommon. Indeed, deshielding is observed experimentally for the protons labeled H_a in structures **1**, **2**, **4**, and **5** in Figure 1. Sorensen and Whitworth⁵ reported an inverse relation between the downfield shift of the *in*-proton in the NMR spectra of a series of bridged tricyclic olefins including structure **5** and the mean distance from the alkene carbon atoms as measured from MNDO-optimized structures.

We have developed a model for predicting the NMR shielding effect of an alkene carbon–carbon double bond based on ab initio calculations of a simple model system: methane in one orientation moved over the surface of ethene at several distances above the plane of ethene.^{6,7} Differences in the assumptions employed in the McConnell model and those used in our computational model have been discussed.^{6,7} Subsequently, an improved model for predicting proton NMR shielding over a

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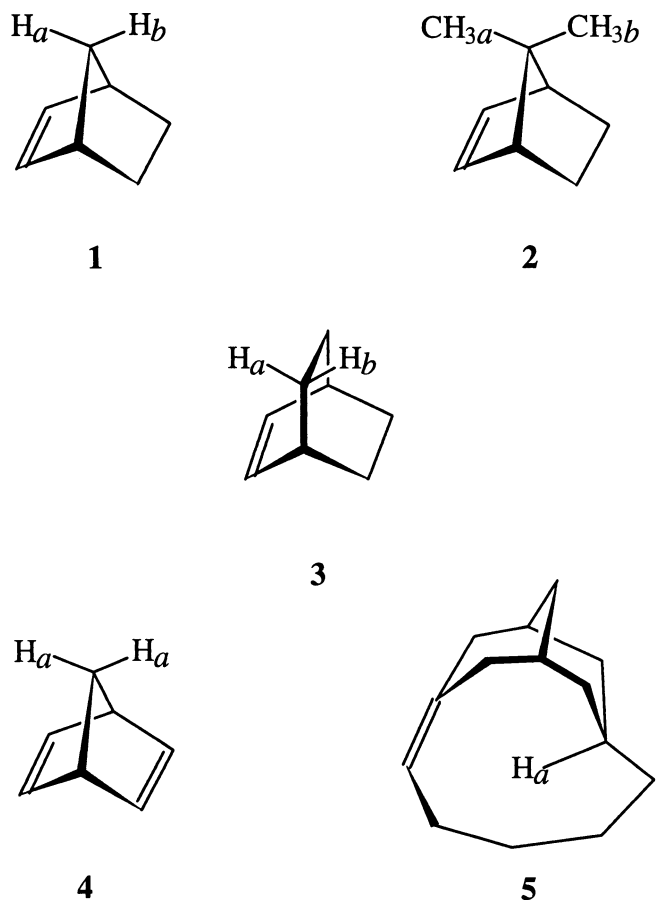


Figure 1. Examples of structures having protons over a carbon-carbon double bond.

carbon-carbon double bond was developed using three geometries of methane at three distances above ethene.⁸ That model predicted (de)shielding increments well when protons were more distant than 2 Å, but underestimated the deshielding effect for protons closer than 2 Å. In this article we present an improved empirical model for predicting the NMR (de)shielding effect on a proton over a carbon-carbon double bond based on ab initio calculations of an extension of that simple model system. The improved model presented herein utilizes the average shielding increment experienced by an ensemble of three orientations of methane over ethene at four distances above ethene, from 2.0 to 3.5 Å.

COMPUTATIONAL METHODS

Input geometries of methane and ethene were generated using Spartan⁹ 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).¹⁰ The geometry-optimized structures were then exported to a Brookhaven Protein DataBank file format (.pdb) file, at which point two files were textually merged to create one of the three geometries indicated in Figure 2. 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 keep ethene (in the XY plane) stationary as the methane molecule was moved over the face of the ethene molecule incrementally in the X and Y directions, keeping the Z distance above the plane of ethene fixed. The symmetry of ethene reduced the number of geometries to be calculated; only one quadrant over one face of ethene was considered. The X and Y coordinates of methane were adjusted in 0.25 Å (geometry a, Figure 2) or 0.5 Å (geometries b and c, Figure 2) increments. At least 30 different positions were calculated for each of 3 orientations of methane at each of 4 distances (2.0, 2.5, 3.0, and 3.5 Å) of the proximate protons of methane above ethene.

Using the same theory and basis set [HF/6-31G(d,p)] as employed in the geometry optimization calculations of the individual structures of methane and ethene, each of these input files was submitted for a single point computation using Gaussian 98¹¹ on a Cray T90 supercomputer. The NMR shielding values were calculated using the utility GIAO (gauge including atomic orbital), developed by Ditchfield¹² and later modified by Chesnut¹³ and Wolinski.¹⁴ The isotropic shielding values for each proton on the methane molecule over ethene were recorded and transformed into the shielding increment $\Delta\sigma$ (in ppm) by subtracting from each data point the shielding value calculated for methane alone. In this analysis and all subsequent discussions only the data for the protons of methane indicated in boldface in Figure 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-carbon double bond of ethene separately at each of four distances of separation (Z) from the plane of ethene. Positive values of $\Delta\sigma$ represent shielding; negative values represent deshielding.

Corrections due to basis set superposition error (BSSE) were not made on these data. In previous calculations of this type it has been demonstrated that corrections made by the counterpoise method of Boys and Bernardi¹⁵ affected the predicted

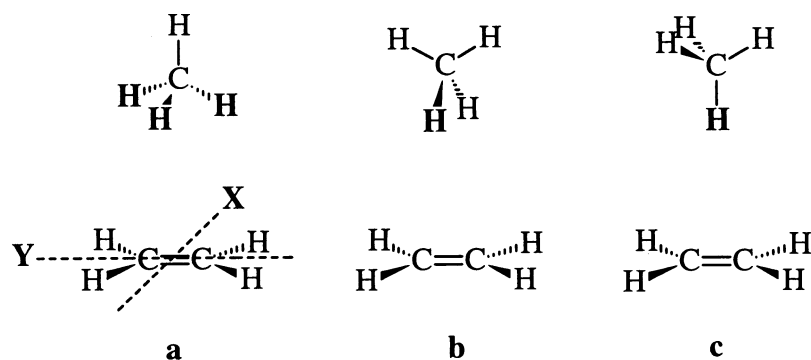


Figure 2. Three orientations of methane over ethene.

shielding increment by about 0.01 ppm.⁷ This is substantially less than the uncertainty in the present model, and therefore correction for BSSE was deemed unnecessary.

Equations were fitted to each of the resulting three-dimensional surfaces using the statistical modeling software TableCurve3D.¹⁶ One equation type [Eq. (1)],

$$\Delta\sigma = a + bX + cY + dX^2 + eY^2 + fXY \quad (1)$$

was found to give a good fit to the shielding surfaces for each orientation of methane at each of the four distances above ethene (Table 1). To obtain a more general shielding surface that is less dependent on the orientation of methane, the shielding increments for the three different orientations of methane were combined at each of four distances over ethene, and the resulting mean shielding surfaces were graphed (Color Plate 1). Each of these surfaces was fit by an equation of the same form as Eq. (1); values of the parameters are listed in Table 2. 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 ethene was determined by least-squares fit to quadratic equations (Table 3) using MSeExcel.¹⁷ 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)] to predict the $\Delta\sigma$ values as a function of the lateral displacement (X and Y) from the center of the carbon–carbon double bond and the vertical distance (Z) above the plane of ethene.

$$\begin{aligned} \Delta\sigma = & (-1.76Z^2 + 11.5Z - 18.6) \\ & + (0.916Z^2 - 6.140Z + 10.5)X \\ & + (1.37Z^2 - 8.87Z + 14.4)Y \\ & + (-0.0336Z^2 + 0.311Z - 0.775)X^2 \\ & + (-0.0489Z^2 + 0.393Z - 0.811)Y^2 \\ & + (-0.519Z^2 + 3.36Z - 5.40)XY \end{aligned} \quad (2)$$

The overall shielding experienced by a proton is the sum of all shielding influences due to nearby groups. In our previous study we reported that the orientation of the C–H bond relative to the plane of ethene could cause as much as a 9% deviation in the GIAO-calculated shielding increments.^{6,7} The present model considers both the anisotropy of an ethene carbon–carbon double bond and the average shielding influence experienced by protons in an ensemble of three different orienta-

Table 1. The correlation coefficients (r) for the fit of the shielding increments calculated by GIAO to the shielding surface described by Eq. (1) for each orientation of methane over ethene (Fig. 2) at each distance

Distance (Å)	Orientation a	Orientation b	Orientation c
2.0	0.92	0.98	0.99
2.5	0.91	0.98	0.98
3.0	0.89	0.98	0.98
3.5	0.88	0.98	0.99

Table 2. The values of the constant a and the coefficients b , c , d , e , and f in the equation $\Delta\sigma = a + bX + cY + dX^2 + eY^2 + fXY$ for the mean shielding surface as a function of the distance above the plane of ethene

Parameter	Distance above ethene (Å)			
	2.0	2.5	3.0	3.5
a	-2.726	-0.793	-0.119	0.0509
b	1.877	0.815	0.345	0.199
c	2.20	0.696	0.230	0.0916
d	-0.286	-0.216	-0.138	-0.102
e	-0.218	-0.142	-0.0649	-0.0374
f	-0.773	-0.213	-0.0379	0.00350

Table 3. 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 ethene^a

Equation
$a = -1.76Z^2 + 11.5Z - 18.6$
$b = 0.916Z^2 - 6.14Z + 10.5$
$c = 1.37Z^2 - 8.87Z + 14.4$
$d = -0.0336Z^2 + 0.311Z - 0.775$
$e = -0.0489Z^2 + 0.393Z - 0.811$
$f = -0.519Z^2 + 3.36Z - 5.40$

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

tions of a methane molecule. This model should be generally applicable to predicting deshielding effects on protons held in various orientations over a carbon–carbon double bond.

RESULTS AND DISCUSSION

The applicability of Eq. (2) was tested by predicting the shielding increments of protons in several rigid molecular systems (1–5, Figure 1) and comparing the results with experimentally observed shielding increments (Table 4). Note that for four of these five structures this function predicts deshielding (a downfield, or paramagnetic shift) for the protons over the carbon–carbon double bond. The traditional “shielding cone” model based on the McConnell equation^{1, 18} predicts the opposite sign of shielding from that observed experimentally and predicted by Eq. (2) in three of the five structures in Figure 1. For structure 5, the shielding cone model predicts slight shielding whereas Eq. (2) predicts substantial (ca. 2 ppm) deshielding, consistent with the downfield shift that is observed experimentally. In these examples, the calculated shielding increment is defined as the difference in the isotropic shielding value of protons in similar environments except for their relationship to a carbon–carbon double bond, and is given by $\Delta\sigma = \sigma H_a - \sigma H_b$, where proton a is located over the carbon–carbon double bond. The observed chemical shift difference is defined as the difference in the chemical shifts of protons in similar environments except for their relationship to a carbon–carbon double

Table 4. Shielding increments^a ($\Delta\sigma$) of protons over a carbon–carbon double bond in structures in Fig. 1 as calculated by GIAO, predicted by Eq. 2, predicted by McConnell's equation, and experimentally observed chemical shift differences ($\Delta\delta$)^b

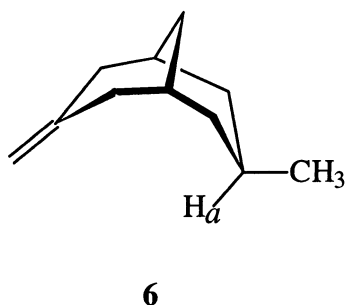
Structure	GIAO (calculated)	Eq. (2) (predicted)	McConnell (predicted) ^c	Experimental (observed)
1	−0.33	−0.28	−0.10	−0.24
2	−0.06	−0.09	0.05	−0.09
3	0.15	0.30	−0.06	0.27
4	−0.66	−0.46	−0.10	−0.80
5	−1.83	−1.99	0.12	−2.12

^a The shielding increment is defined by $\Delta\sigma = \sigma H_a - \sigma H_b$, where proton *a* is located over the carbon–carbon double bond. For methyl protons, $\Delta\sigma = \sigma CH_{3a} - \sigma CH_{3b}$, where the protons labeled *a* are those located over the carbon–carbon double bond.

^b The chemical shift difference is defined by $\Delta\delta = \delta H_b - \delta H_a$, where proton *a* is located over the carbon–carbon double bond. For methyl protons, $\Delta\delta = \delta CH_{3b} - \delta CH_{3a}$, where the protons labeled *a* are those located over the carbon–carbon double bond.

^c Calculated using a value of $140 \times 10^{-36} \text{ m}^3/\text{molecule}$ for the magnetic anisotropy of the carbon–carbon double bond.¹⁸

bond, and is given by $\Delta\delta = \delta H_b - \delta H_a$, where proton *a* is located over the carbon–carbon double bond. These are defined so that if proton “a” is downfield or deshielded relative to proton “b” both $\Delta\sigma$ and $\Delta\delta$ are negative. For structure **4**, H_b in structure **1** was used as reference; for structure **5**, a bicyclic alkene (**6**) that does not place H_a over a carbon–carbon double bond was employed as reference.⁵



Structures in which a methyl group is held over an alkene double bond (Figure 1, **2**) 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; the error introduced by neglecting other rotamers is less than 0.05 ppm, which is less than the uncertainty in the model. These data are found along with the experimentally observed $\Delta\sigma$ ($= \delta CH_{3b} - \delta CH_{3a}$) in Table 4, where the protons labeled *a* are those located over the carbon–carbon double bond. A negative value of $\Delta\sigma$ means that CH_{3a} (over the double bond) is downfield of CH_{3b} .

Table 4 also includes the predicted value of shielding based on the McConnell equation, in which shielding (+) is predicted for a proton within the 54.7° shielding cone and deshielding (−) is predicted for protons outside the cone.¹⁸ As previously in the case of methyl groups, only the lowest energy conformation was considered. Table 4 clearly shows that the predicted values of shielding based on the McConnell equation differ in several instances from the values predicted by Eq. (2), those calculated directly by GIAO, or the experimentally observed chemical shift differences. The difference in the shielding effect predicted by GIAO or by Eq. (2) and those of the McConnell equation arises from the fundamental difference in the two approaches. The McConnell equation predicts the theoretical shielding effect of the anisotropic group (carbon–carbon double bond, in this case) on the nucleus of a hydrogen atom as a function of its position relative to the anisotropic group. The method described in this article predicts the average net shielding effect on a covalently bonded hydrogen of methane held at some position relative to a carbon–carbon double bond. Although very simple, this model is more realistic than that employed by McConnell. Furthermore, because the present model incorporates an ensemble of methane orientations, it should be more generally applicable than the shielding model previously described.^{6,7} The present algorithm is based on calculations of proton positions as close as 2.0 Å from the plane of a carbon–carbon double bond, and is therefore better able to model bicyclic systems that have protons that close to a double bond. The method described herein should prove useful for predicting the effect of position relative to a carbon–carbon double bond on the NMR chemical shift of a proton attached to carbon.

It should be noted that predictions based on Eq. (2) have limitations. The model was developed from shielding data for protons from 2.0 to 3.5 Å above ethene, yet all of the structures in Figure 1 have at least one proton closer than 2.0 Å from the plane of the carbon–carbon double bond. Predictions of shielding increments beyond the 2.0 to 3.5 Å range over which this equation was developed may be in error. It has been demonstrated^{6,7} 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 Å above ethene. The effect of orientation of methane relative to ethene is also much greater at this proximity.¹⁹ It is for this reason that calculations for the current model were not extended closer than 2.0 Å. Two structures (**1** and **4**) have an angle of the deshielded C–H bond that is geometrically impossible to model with a methane–ethene pair. All of the example structures are strained bicyclic or tricyclic ring systems, yet the equation is based on a strain-free system. This method was developed using methane and ethene, yet all example structures to which it has been applied involve more highly substituted double bonds than ethene and protons attached to more highly substituted carbon than methane. Nonetheless, despite these limitations, the equation predicts shielding increments which, when used in conjunction with conventional additive substituent effects, lead to much better estimates of chemical shifts than any other currently available correction.

The shielding increment at each methane proton position used in generating the shielding 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 that calculated directly by GIAO is

Table 5. 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 ethene

Distance (Å)	rms deviation (ppm)
2.0	0.47
2.5	0.18
3.0	0.11
3.5	0.08

reported in Table 5; this is a measure of the fit of the shielding function to the GIAO-calculated shielding values, and provides an indication of the precision of the predictions made using this equation. As expected, the largest deviation is found at the closest distance between methane and ethene, where the predicted shielding increment is also largest and where orientation effects are greatest.

Deshielding is predicted by Eq. (2) for protons closer than 3 Å above the center of a carbon–carbon double bond (X and Y values less than 1 Å). Similar deshielding observed for protons held close over an aromatic ring has been attributed to high-order orbital compression effects, which generate deshielding by deformation of the electron clouds.²⁰ This effect has been shown graphically in a visualization of the distortion of the HOMO of an ethene–methane pair at 2.0 Å.^{6, 7, 21} It should be noted that the van der Waals thickness of half of the electron cloud in an aromatic ring (vdW radius) is 1.85 Å²²; the value for an alkene π bond should be similar. The sum of this value and the vdW radius of hydrogen (1.11 Å) is 2.96 Å, comparable to the distance below which deshielding is predicted, thus supporting the suggestion²⁰ of orbital compression as a major cause of deshielding.

A dramatic example of the difference between the shielding increment predicted by Eq. (2) and that predicted by the McConnell shielding cone model is seen in structure 5, *in*-tricyclo-[7.3.1.1^{7,11}]tetradec-1-ene. Equation (2) predicts a shielding increment of -1.99 ppm; the observed shielding increment is -2.16 ppm.⁵ The McConnell “shielding cone” equation predicts a shielding increment of $+0.12$ ppm.

CONCLUSIONS

The (de)shielding increment $\Delta\sigma$ has been calculated for protons of methane held in various orientations and at various positions over the plane of ethene using GIAO in Gaussian 98. A plot of the mean of the calculated $\Delta\sigma$ values for an ensemble of methane orientations against X and Y distance from the center of the ethene molecule gives a smooth curved surface for each of four distances Z above ethene. Each of these surfaces was fitted well by an equation of the general form: $\Delta\sigma = a + bX + cY + dX^2 + eY^2 + fXY$. The constant (a) and the coefficients (b , c , d , e , and f) were related to the distance Z above the plane of ethene by simple quadratic equations. Substitution of these equations for a , b , c , d , e , and f provides a single equation for predicting the shielding increment experienced by protons held over ethene. Application of this equation to several more complex alkene structures demonstrates its predictive validity, even in cases where the position of the

proton results in deshielding. This is in sharp contrast to the traditional “shielding cone” model, which predicts upfield shifts for protons over the center of a carbon–carbon double bond. Utilization of the (de)shielding equation in a spreadsheet or after incorporation into software that estimates chemical shifts from a database of substituent effects should provide valuable assistance to chemists in making proper spectral assignments and correct structure determinations.

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