

# Analysis of the Origin of Through-Space Proton NMR Deshielding by Selected Organic Functional Groups

Ned H. Martin,\* Justin D. Brown, Kimberly H. Nance, Henry F. Schaefer, III,<sup>†</sup>  
Paul v. R. Schleyer,<sup>†</sup> Zhi-Xiang Wang,<sup>†</sup> and H. Lee Woodcock<sup>†</sup>

Department of Chemistry, University of North Carolina at Wilmington,  
Wilmington, North Carolina, 28403-5932, and Center for Computational Quantum  
Chemistry, University of Georgia, Athens, Georgia 30602-2525

*martinn@uncwil.edu*

Received July 26, 2001 (Revised Manuscript Received October 9, 2001)

## ABSTRACT



GIAO-HF and IGLO-DFT computations of isotropic magnetic shieldings were used to map the NMR shielding environments of small molecules exemplifying selected organic functional groups. Two different probes were employed: a methane molecule and NICS (nucleus-independent chemical shifts) based on computed absolute isotropic shieldings. The reason for the different results obtained using these two probes is perturbation of the wave function by the proximity of methane to the  $\pi$  bond, as analyzed by the localized orbital contributions to the shieldings.

It has long been known that common organic functional groups containing  $\pi$  bonds exert through-space magnetic shielding or deshielding effects.<sup>1</sup> These can influence NMR chemical shifts in molecules quite noticeably. McConnell's equation, based on the anisotropy of the magnetic susceptibility,<sup>2</sup> quantified these proximity effects and predicted the long-range shielding influences. This treatment gives rise to the familiar "shielding cones" over functional groups represented in NMR spectroscopy textbooks.

However, the predictions of this model do not agree with recent experimental and computational results. These results show substantial deshielding (rather than shielding) of hydrogens located over alkenes.<sup>3</sup> Such findings have led to the development of a new graphical representation to predict the chemical shifts of covalently bonded hydrogens located at various positions above a carbon-carbon double bond.<sup>4</sup>

We now report more detailed results of Hartree-Fock (HF) and density functional theory (DFT) calculations of the magnetic shielding effects of ethene, as well as simple models for additional functional groups: ethyne for the carbon-carbon triple bond; HCN for the nitrile group; formaldehyde for the carbonyl group; and HNO<sub>2</sub> ( $C_{2v}$  symmetry) for the nitro group. Methane was employed as the probe molecule, and one hydrogen was oriented toward each functional group (as shown in Figure 1).

(3) (a) Martin, N. H.; Allen, N. W., III; Minga, E. K.; Ingrassia, S. T.; Brown, J. D. *J. Am. Chem. Soc.* **1998**, *120*, 11510–11511. (b) Martin, N. H.; Allen, N. W., III; Minga, E. K.; Ingrassia, S. T.; Brown, J. D. *Struct. Chem.* **1998**, *9*(6), 403–410. (c) Alkorta, I.; Elguero, J. *New J. Chem.* **1998**, *22*, 381–385. (d) Martin, N. H.; Allen, N. W., III; Minga, E. K.; Ingrassia, S. T.; Brown, J. D. In *Modeling NMR Chemical Shifts: Gaining Insights into Structure and Environment*; Facelli, J. C., deDios, A. C., Eds.; ACS Symposium Series 732; American Chemical Society: Washington, DC, 1999; pp 207–219. (e) Martin, N. H.; Allen, N. W., III; Minga, E. K.; Ingrassia, S. T.; Brown, J. D. *Struct. Chem.* **1999**, *10*(5), 375–380. (f) Attention is called to a related, recent study on ethene, acetylene, HCN, and formaldehyde: Klod, S.; Kleinpeter, E. *J. Chem. Soc., Perkin Trans. 2* **2001**, advance article.

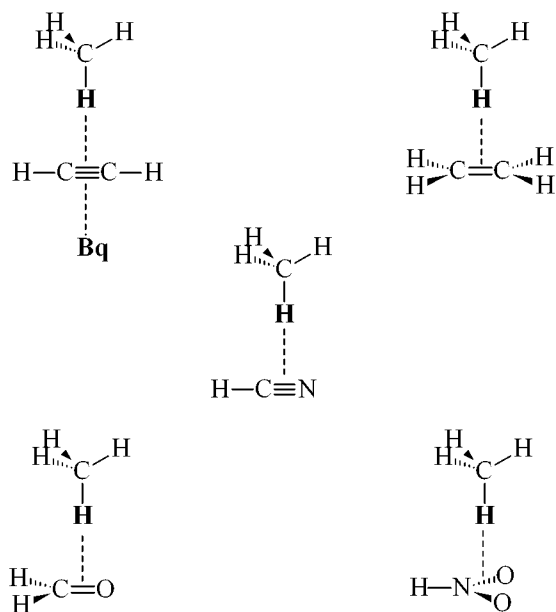
(4) Martin, N. H.; Allen, N. W., III; Brown, J. D.; Ingrassia, S. T.; Minga, E. K. *J. Mol. Graphics Mod.* **2000**, *18*(1), 1–6.

\* University of North Carolina at Wilmington.

<sup>†</sup> University of Georgia.

(1) Günther, H. *NMR Spectroscopy: Basic Principles, Concepts, and Applications in Chemistry*, 2nd ed.; Wiley: Chichester, 1995; pp 78–84.

(2) McConnell, H. M. *J. Chem. Phys.* **1957**, *27*, 226–229.



**Figure 1.** Structures used in the calculations. The proximal proton of methane was fixed at a 2.0 Å distance with the C–H bond perpendicular to the center of each functional group multiple bond, but further optimizations of the individual structures were not carried out. The location of a “ghost atom” (Bq) is shown for ethyne.

The isotropic magnetic shielding of this proximal proton of methane fixed at a point 2.0 Å above the center of the  $\pi$  bond was computed for each of the model structures. These calculations employed IGLO<sup>5a</sup>-DFT (in deMon<sup>5b</sup>) with the PW91 functional and a large (IGLO III TZ2P)<sup>5a</sup> basis set and also GIAO-HF (in Gaussian 98<sup>6</sup>) with the 6-31G(d,p) basis set. The IGLO method<sup>5a</sup> has the interpretive advantage of giving the shielding contributions of the individual localized orbitals (which correspond, e.g., to bonds and lone

(5) (a) IGLO program. See: Fleischer, U.; Kutzelnigg, W.; Lazzaretto, P.; Muehlenkamp, V. *J. Am. Chem. Soc.* **1994**, *116*, 5298. (b) DeMon program: Malkin, V. G.; Malkina, O. L.; Casida, M. E.; Salahub, D. R. *J. Am. Chem. Soc.* **1994**, *116*, 5898.

(6) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(7) Quantum chemical programs compute absolute shieldings (but not chemical shifts) directly. More positive values mean greater shielding (i.e., the resonances are more *upfield*). Note that the signs are reversed in the NMR chemical shift convention: more positive chemical shifts are *downfield*. Thus, NICS is based on the negative of the absolute shieldings computed at selected points in space designated by “ghost atoms” (Bq’s).

(8) (a) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. R. v. E. *J. Am. Chem. Soc.* **1996**, *118*, 6317–6318. (b) Schleyer, P. v. R.; Jiao, H.; Hommes, N. J. R. v. E.; Malkin, V. G.; Malkina, O. L. *J. Am. Chem. Soc.* **1997**, *119*, 12669. (c) Schleyer, P. v. R.; Manoharan, M.; Kiran, B.; Jiao, H.; Puchta, R.; Hommes, N. J. R. v. E. *Org. Lett.* **2001**, *3*(16), 2465–2468.

pairs of electrons). Absolute shieldings<sup>7,8</sup> also were computed at selected points (positions designated by ghost atoms, i.e., the same procedure used to obtain nucleus-independent chemical shifts (NICS)<sup>8</sup>). The results are summarized in Tables 1–5.

The differences in behavior summarized in Table 1 are striking! The negative values in the first row indicate that

**Table 1.** IGLO Isotropic Shielding Data (in ppm) for the Model Compounds as Shown in Figure 1<sup>a</sup>

isotropic shielding	C <sub>2</sub> H <sub>2</sub>	C <sub>2</sub> H <sub>4</sub>	HCN	H <sub>2</sub> CO	HNO <sub>2</sub>
shielding of the proximal CH <sub>4</sub> proton (as in Figure 1)	−4.3	−4.0	−3.0	−1.1	0.1
absolute shielding 2.0 Å above $\pi$ bond (no CH <sub>4</sub> )	0.8	1.5	0.4	1.3	0.9

<sup>a</sup> Row 1 gives the shielding of each proximal proton of methane relative to the value for isolated methane. Row 2 gives the absolute (ghost atom) shieldings<sup>7</sup> at the same 2.0 Å points in the absence of CH<sub>4</sub>.

the proximal methane protons shown in Figure 1 are *deshielded* (i.e., downfield, relative to the proton value in isolated methane)<sup>7</sup> by the adjacent  $\pi$  system. In sharp contrast, the values in the second row (computed at the same position (2.0 Å above the center of each  $\pi$  bond, but without a methane probe) are all positive (i.e., *shielded*, upfield).<sup>7</sup> It is evident that the absolute magnetic shieldings computed by the McConnell equation (and by modern ab initio and DFT methods) should not be used to predict through-space effects on proton chemical shifts.

Such large discrepancies between the computed relative magnetic shielding for a methane hydrogen probe and the absolute shielding at the same position have been noted previously.<sup>3d</sup> Experimental and computational findings show substantial deshielding of covalently bonded hydrogens located intramolecularly over carbon–carbon double and triple bonds.<sup>3a–f</sup> These effects are very similar to those modeled intermolecularly by the methane probe.

To analyze the reasons for the discrepancies in Table 1, we first examine the effect of the methane probe in detail. Table 2 summarizes the localized orbital contributions (rows

**Table 2.** IGLO-DFT Absolute Shielding Contributions (in ppm) from Localized Orbitals of Ethyne at Points 2.0 Å above the Center of the  $\pi$  Bond of Ethyne, Computed without and with Methane Positioned Similarly on the Opposite Side<sup>a</sup>

shielding contribution from ethyne	with CH <sub>4</sub> opposite	without CH <sub>4</sub>	difference
sum, C–H bonds	0.4	0.4	0.0
C–C $\sigma$ bond	−0.2	0.0	−0.2
sum, C–C $\pi$ bonds	0.7	0.3	0.4
<b>net shielding<sup>b</sup></b>	<b>0.8</b>	<b>0.8</b>	<b>0.0</b>

<sup>a</sup> The difference gives the orbital perturbation effect on the absolute shielding due to the remote methane. <sup>b</sup> Rounding errors and core electron contributions account for the slight discrepancy between the sum of the first three rows and the final net shielding values.

1–3) to the net absolute shielding values (row 4). These data were computed at a point (ghost atom) 2.0 Å away from the center of the CC bond of ethyne (“without CH<sub>4</sub>”). In a second calculation, a methane probe was located on the opposite side (as in Figure 1) (“with CH<sub>4</sub> opposite”). Note that the net shielding (which corresponds to the 0.8 ppm absolute shielding for C<sub>2</sub>H<sub>2</sub> in Table 1, row 2) is the same with and without the methane probe. However, the data in rows 1–3 of Table 2 reveal that this is due to the cancellation of the influences on the various localized orbitals (corresponding to the different CC bonds).

The presence of a methane probe on one side of ethyne deforms the electron density of the  $\pi$  bond, which then contributes more to the absolute shielding on the opposite side (Table 2, row 3). An analogous methane– $\pi$  electron perturbation effect has been suggested previously for ethene.<sup>3b,d–f</sup> The illustration above the abstract depicts the change in the HOMO of an ethene–methane pair (at the 2.0 Å distance of Figure 1). The severe distortion of the  $\pi$  cloud of ethene in the presence of methane (compared to the HOMO of ethene, shown by the wire mesh) is evident. We conclude that a methane probe at a 2.0 Å separation can be expected to perturb the wave function of functional groups significantly.

Next we analyze the contributions of the functional group model to the shielding of the proximal proton of a methane probe 2.0 Å above the center of each  $\pi$  bond (Table 3). The

**Table 3.** IGLO-DFT Contributions (in ppm) of the Localized Orbitals of the Functional Group Model Compounds to the Shielding of the Proximal Proton of Methane Placed 2.0 Å above the  $\pi$  Bonds (as in Figure 1)

shielding contribution from	C <sub>2</sub> H <sub>2</sub>	C <sub>2</sub> H <sub>4</sub>	HCN	H <sub>2</sub> CO	HNO <sub>2</sub>
sum of X–H bonds	0.2	0.8	0.1	0.0	0.0
X–Y $\sigma$ bonds	0.1	1.2	1.1	1.1	–1.4
X–Y $\pi$ bonds	–2.9	–4.1	–3.0	–2.7	0.3
lone pairs of electrons			–0.2	0.8	1.2
<b>sum of model compound</b>	<b>–2.6</b>	<b>–2.1</b>	<b>–2.0</b>	<b>–0.8</b>	<b>0.1</b>

sums (last row) are dominated by the  $\pi$  contributions, but contrary to conventional expectations, the effect is deshielding rather than shielding.

The effects of the proximity of the functional group model on methane’s localized orbital contributions to the shielding

**Table 4.** IGLO-DFT Contributions (in ppm) of the Localized Orbitals of the Methane Probe to the Isotropic Shielding of the Proximal Proton of Methane Held 2.0 Å above the Center of the  $\pi$  Bond

shielding contribution from	C <sub>2</sub> H <sub>2</sub>	C <sub>2</sub> H <sub>4</sub>	HCN	H <sub>2</sub> CO	HNO <sub>2</sub>
proximal C–H bond	–2.1	–2.3	–1.2	–0.7	–0.1
sum of other C–H bonds	0.2	0.5	0.3	0.4	0.3
<b>total of all C–H bonds</b>	<b>–1.9</b>	<b>–1.8</b>	<b>–0.9</b>	<b>–0.3</b>	<b>0.2</b>

the proximal proton of methane are listed in Table 4. The effects on the proximal C–H bond of methane are quite large. This reinforces the conclusion that the deshielding of the systems in Figure 1 (and also those observed experimentally in through-space intramolecular situations<sup>1</sup>) is due to the mutual perturbation of the wave functions of the interacting moieties.

Table 5 summarizes the analysis. The sum of the total localized orbital contributions from each model compound

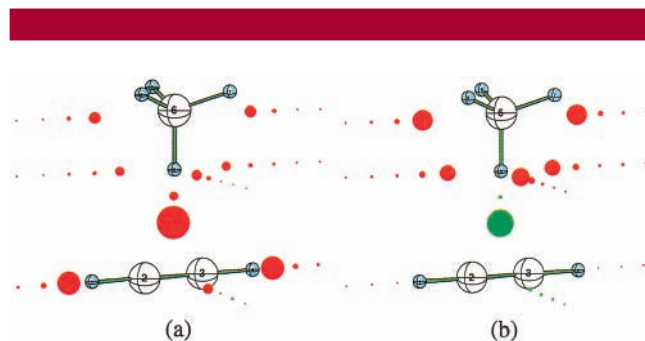
**Table 5.** Summary of the Localized Orbital Contributions (in ppm) of Methane and the Model Compounds to the Isotropic Shielding of the Proximal Proton of Methane 2.0 Å above the  $\pi$  Bonds

shielding contribution from	C <sub>2</sub> H <sub>2</sub>	C <sub>2</sub> H <sub>4</sub>	HCN	H <sub>2</sub> CO	HNO <sub>2</sub>
model compound (Table 3)	–2.6	–2.1	–2.0	–0.8	0.1
methane (Table 4)	–1.9	–1.8	–0.9	–0.3	0.2
<b>total: model + methane<sup>a</sup></b>	<b>–4.5</b>	<b>–3.9</b>	<b>–2.9</b>	<b>–1.1</b>	<b>0.3</b>
$\Delta\delta$ , model compound (Table 1, row 1) <sup>a</sup>	–4.3	–4.0	–3.0	–1.1	0.1

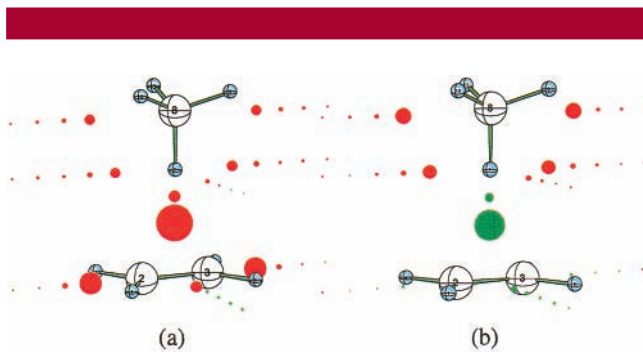
<sup>a</sup> The slight differences between the data in rows 3 and 4 are due to core electron effects and rounding errors.

(Table 3, row 5) and from its methane probe (Table 4, row 3) matches the difference in the shielding of isolated methane and the proximal proton of methane 2.0 Å above the model compounds (Table 1, row 1). Thus, the net absolute shielding of –4.3 ppm for methane–C<sub>2</sub>H<sub>2</sub> (Table 1) corresponds to the –4.5 ppm sum of the individual contributions (–2.6 ppm from C<sub>2</sub>H<sub>2</sub>, Table 3 and –1.9 ppm from methane, Table 4).

GIAO-HF calculations also were performed to assess absolute shieldings in the presence and absence of a methane probe molecule. Several series of points at 0.5 Å intervals radiating parallel and laterally about the multiple bond centers were used to construct “shielding maps” in the vicinity of ethyne–CH<sub>4</sub> (Figure 2) and of ethene–CH<sub>4</sub> (Figure 3)



**Figure 2.** (a) GIAO-HF absolute shieldings computed with methane held 2.0 Å above ethyne. (b) Differences in absolute shieldings between ethyne in the presence of methane (a) and isolated ethyne. Red denotes positive (shielding), green negative (deshielding) values. The sizes of the colored dots are proportional to the magnitude.



**Figure 3.** (a) GIAO-HF absolute shieldings computed in the presence of methane held 2.0 Å above ethene. (b) Differences in absolute shieldings between ethene in the presence of methane (a) and isolated ethene. Red denotes positive (shielding), green negative (deshielding) values. The sizes of the colored dots are proportional to the magnitude.

The absolute shieldings in the presence of a methane probe molecule are shown for ethyne and ethene in Figures 2a and 3a, respectively. These correspond to NICS representations, where red dots denote shielding and green dots deshielding values. The sizes of the colored dots are proportional to the magnitude. Note that the shielding effects 1.0 Å above both  $\pi$  bonds are large but are much smaller at 1.5 Å. (The proximal hydrogens at 2.0 Å separations are deshielded.)

A second set of calculations was performed on ethyne and ethene at exactly the same positions but without the methane probe (results not shown). These shielding values (in the absence of methane) were subtracted from those with methane present; the *differences* are plotted in Figures 2b and 3b. Note that most of the red points in the vicinity of ethyne and ethene in Figures 2a and 3a practically vanish in

Figures 2b and 3b as a result of cancellation of effects. However, the points above both  $\pi$  bonds change dramatically. The color switches from red (shielding, upfield) to green (deshielding, downfield)!

Indeed, the absolute shieldings 1.0 Å above the center of the  $\pi$  bonds of ethyne (Figure 2b) and of ethene (Figure 3b) decrease by 4.4 and 5.0 ppm, respectively, when methane is present. (These changes correspond to the large green dots.) Likewise, our calculations show that a covalently bonded hydrogen (such as the proximal proton of methane) 2.0 Å above a  $\pi$  bond is strongly deshielded. Again, this demonstrates the inappropriateness of using absolute shieldings to predict the chemical shifts of hydrogens located above functional group multiple bonds.

In summary, the results of GIAO-HF and IGLO-DFT computations stress that *the through-space chemical shift effects produced by  $\pi$  bonded functional groups on covalently bonded hydrogens in their proximity should be predicted by employing a methane or similar probe and that absolute shielding values should not be used for this purpose.* The mutual perturbations of the C–H orbital and of the functional group  $\pi$  orbital in proximity are largely responsible for the deshielding effect on hydrogens located above  $\pi$  bonds. These effects are not included when absolute shielding values are computed by using ghost atoms.

**Acknowledgment.** Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, the National Science Foundation, the North Carolina Supercomputing Center, the University of North Carolina at Wilmington, and the University of Georgia for support of this research.

OL016500U