

A comparison of calculated NMR shielding probes

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Abstract

In a strong magnetic field, covalently bonded hydrogen nuclei located over the plane of an anisotropic π bond-containing functional group experience magnetic shielding (or deshielding) that results from the combined effect of the magnetic anisotropy of the functional group and other nearby covalent bonds plus other intramolecular shielding effects. These effects can now be calculated with reasonable accuracy using ab initio methods. We have investigated several computational probes of the magnetic shielding surface near anisotropic functional groups and compared the results to previous reports of experimental observations in example structures. GIAO-HF in Gaussian 03 was employed to calculate isotropic shielding values and to predict the net NMR shielding increment for several computational probes: methane, diatomic hydrogen, a hydrogen atom, a helium atom, or a ghost atom, each held in various positions over simple test molecules (ethene, ethyne, benzene and HCN) that contain the functional groups studied. Also, the effect of performing single point calculations versus constrained geometry-optimized calculations was examined. In addition, the effect of the angle of the orientation of the probe molecule (in the case of CH_4 and H_2) relative to the π bond in the test molecule was studied. Finally, the atomic charges in the molecular probes (CH_4 and H_2) were computed to investigate the nature of the interaction of the probe with the test molecule. The optimal, most economical computational results were obtained using single point calculations of a diatomic hydrogen probe oriented perpendicular to the surface (or axis) of the test molecule.

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1. Introduction

The long-held model for NMR shielding by anisotropic functional groups, which can cause shielding or deshielding in the NMR spectrum of nearby protons, is based on the McConnell equation [1], which gives rise to the familiar “shielding cones” found in most textbooks on NMR spectroscopy [2]. However, the McConnell equation predicts the distance and directional effect of (only) the anisotropy of the magnetic susceptibility of a given bond. The values of the magnetic anisotropy of bonds are not known with much certainty. For example, Pople [3] and Flygare [4] each calculated quite different values of the magnetic anisotropy of the carbonyl group and its principal susceptibilities. Furthermore, Zürcher [5] demonstrated that the chemical shifts observed in ketosteroids could only be accounted for if

both the long-range magnetic anisotropy and electrostatic shielding effects of the carbonyl group are considered. It has been shown, furthermore, 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 [6–8], and therefore it is not appropriate for predicting chemical shifts. We have developed models based on ab initio calculations using methane (CH_4) as a computational probe that predict chemical shift values quite close to those observed experimentally for protons near aromatic rings [9,10], alkenes [11–14], the ethynyl, cyano and nitro groups [15], and the carbonyl group in aldehydes and ketones [16]. Elguero et al. have also used methane as a computational probe of the remote shielding effects of several functional groups [7]. Our approach differs substantially from the McConnell method in the assumptions involved. The McConnell model considers *only* the anisotropy of the magnetic susceptibility of one structural feature (in the case of alkenes, the $\text{C}=\text{C}$) on the magnetic

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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* computations incorporate all of these effects, to the extent that they are computed by the HF/6-31G(d,p) calculations. Thus, the latter are preferable for predicting chemical shift effects.

Other approaches for mapping the NMR shielding surface of functional groups include the use of a ‘ghost atom’, designated in Gaussian 03 [17] by the symbol Bq; it is simply a position in space with no mass, charge or size. Klod and Kleinpeter [18] used ghost atom calculations for the prediction of through-space shielding effects on chemical shifts. An advantage of using ghost atoms is that a single computation can be performed using an array of ghost atoms so that an entire shielding surface can be computed at once very efficiently. However, detailed analysis of the origins of through-space (de)shielding effects has shown that nearly 40% of the deshielding effect observed in close proximity to π bond-containing functional groups is attributable to the sigma bond to the affected proton [19]. Ghost atom calculations cannot model this important contribution to (de)shielding.

The use of either a hydrogen atom or a helium atom as the probe has been suggested in the interest of computational simplicity and efficiency. However, neither of these probes have covalent bonds that are needed to mimic the shielding effect of a covalently bonded proton, therefore it is unlikely that they would accurately model through-space shielding effects on chemical shifts.

In this paper we describe the results of our study of several computational probes of NMR shielding based on quantum mechanical calculations of a simple model system: the computational probe placed sequentially at each of four distances (from 2.0 Å to 3.5 Å) above the molecular plane (or axis) of the simple test molecules containing the π -bonded anisotropic functional group. The computational probes studied were CH₄, H₂, a hydrogen atom, a helium atom, and a ghost atom. The simple test molecules employed in this study were ethene, ethyne, benzene, and HCN. In addition, the effect of performing constrained geometry-optimized calculations versus single point calculations was checked. Also, the effect of the orientation of the computational probe relative to the test molecule in the case of the molecular probes (CH₄ and H₂) was examined. Finally, the atomic charges in the molecular probes (CH₄ and H₂) were computed to investigate the nature of the interaction of the probe with the test molecule.

2. Computational methods

Input geometries for each computational probe and test molecule were created using Titan [20] molecular modeling software running on an Dell Optiplex 2.4 GHz computer and

were optimized at an *ab initio* level using Hartree–Fock theory with a basis set of 6-31G(d,p) [21]. The geometry-optimized structures were then converted to Cartesian coordinate files, and the two text files were merged in GaussViewW [22] to create a Gaussian input file representing the geometry of a computational probe-test molecule pair shown in Fig. 1 for a general probe and ethene.

The Cartesian coordinates of the probe portion of the input file were modified in copies of the original file to move the computational probe incrementally in the Z direction above the plane (or axis) of the test molecule placing the proximate atom of the probe molecule at 2.0 Å, 2.5 Å, 3.0 Å, or 3.5 Å from the center of the surface (or axis) of the test molecule.

Using the same theory and basis set (HF/6-31G(d,p)) as employed in the geometry optimization calculations of the molecular computational probes and test molecules, single point calculations of isotropic magnetic shielding were performed using the NMR keyword in Gaussian 03W [17]. This level of theory and basis set were selected because this is widely used for NMR calculations. We have observed [23] that inclusion of electron correlation effects by using MP2 in calculations of methane at various positions 2.0 Å over ethene does not substantially change the results; the mean of the absolute differences in the calculated isotropic shielding values between HF and MP2 was 0.1 ppm (even when the magnitude of the computed shielding increment exceeded 4 ppm). Our previous calculations of this type have also shown that corrections due to basis set superposition error (BSSE), made using the counterpoise method of Boys and Bernardi [24], were less than 0.01 ppm [12,15,16], which is far less than the uncertainty in the method. Therefore, BSSE corrections were not made in the present study. Isotropic shielding values were calculated using the GIAO (gauge-invariant atomic orbital) method, developed by Ditchfield [25] and improved by Chesnut and Foley [26] and Wolinski et al. [27]. The isotropic shielding values for the proximal atom of the atomic and molecular computational probes over the test structure were recorded and transformed into a shielding increment ($\Delta\sigma$, in ppm) by subtracting from each the isotropic shielding value calculated for the computational probe alone using the same level of theory and basis set. In the case of the ghost atom (Bq) the isotropic shielding value was used directly. In this analysis and all subsequent discussions, only the shielding values for the *proximal* proton of methane and diatomic hydrogen were considered.

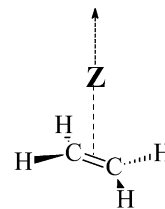


Fig. 1. Position of shielding probe (Z) over a test molecule, illustrated here by ethene.

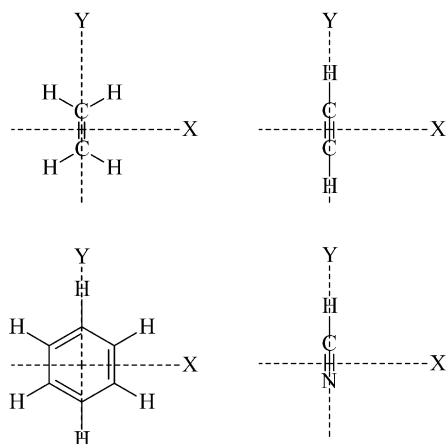


Fig. 2. Test molecules and their Cartesian coordinates.

In order to better assess the effects on NMR shielding of any structural changes due to the close proximity of the probe to the test molecule, constrained geometry-optimized calculations were also performed on each of the probe-test molecule pairs using Z-matrix input files. In these calculations, the position of the proximate atom of each probe was placed at a fixed distance directly above the origin of the Cartesian space for each test molecule as described in Fig. 2. All other geometric features of the probe and test molecule were allowed to optimize. Then a single point GIAO calculation of the isotropic shielding (keyword, NMR) was performed on that geometry. Shielding increments were calculated as above.

It has been reported previously that the angle of orientation of the C–H bond of the computational probe molecule methane relative to the π electron system has a negligible effect on the calculated isotropic shielding value for ethene [11], benzene [9], and formaldehyde [16]. In this study we also examined the effect of the angle of orientation of diatomic hydrogen relative to the surface or axis of the test molecules studied (Fig. 2). The diatomic hydrogen probe was oriented with its axis 30° relative to and with the proximal proton 2.0 \AA above the center of the plane (or axis) of each of the test molecules (Fig. 3). The diatomic hydrogen probe was angled above the X-axis and above the Y-axis in separate calculations. Single point calculations of isotropic shielding values were performed as noted previously.

The overall shielding experienced by a probe is the sum of all shielding influences due to nearby groups and their interactions [19]. The ab initio computation-based model

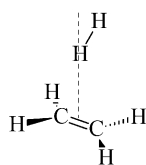


Fig. 3. Orientation of diatomic hydrogen probe 30° from perpendicular to the plane of ethene.

presented here considers not only the magnetic anisotropy of the π bond but also the shielding influences due to the covalently bonded protons in the cases of the molecular probes methane and diatomic hydrogen, and the interactions of the probe and test molecules, which may lead to orbital perturbations, especially at close proximity. Such perturbations should be reflected in changes in the charge on atoms. To investigate this possibility, the atomic charges were calculated according to the natural population analysis method.

3. Results and discussion

The calculated shielding increments ($\Delta\sigma$) for each of the probes were graphed against their distance (Z) from the center of the plane (or axis) of each of the test molecules. The results of both the single point calculations and the constrained geometry optimized calculations are presented in the same graph for a given test molecule. Positive values of $\Delta\sigma$ represent shielding; negative values represent deshielding. The results are shown in Figs. 4–7.

The calculated shielding increments for the various probes over ethene are shown in Fig. 4. All probes except the H atom and the ghost atom (Bq) show deshielding at close proximity to ethene (2.0 \AA), but helium shows the least deshielding effect, and at all greater distances from the center of the plane of ethene, the hydrogen atom, the ghost atom and the helium atom show only shielding, in contradiction to experimental observations [6–8,11–13]. In contrast, both the diatomic hydrogen and methane probes display deshielding that is substantial close to ethene but which diminishes with distance from ethene, with methane giving slightly larger shielding increments at each distance from ethene. This is consistent with experimental NMR results [6–8,11–13]. There is essentially no difference in the shielding increment between the single point calculation and the constrained geometry optimization.

The calculated shielding increments for the various probes over ethyne are shown in Fig. 5. All probes except the ghost atom show deshielding at close proximity to ethyne (2.0 \AA), with the hydrogen atom and the helium atom again showing the least deshielding effect. As with ethene, both

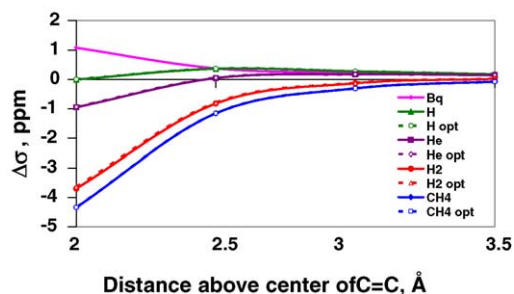


Fig. 4. Calculated shielding increments for various probes vs. distance above the center of ethene.

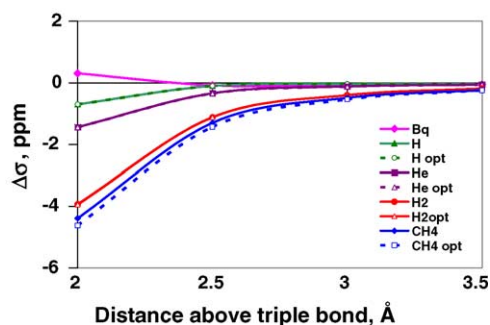


Fig. 5. Calculated shielding increments for various probes vs. distance above the center of ethyne.

the diatomic hydrogen and methane probes show similar shielding behavior, with methane giving slightly larger shielding increments at each distance from ethene. The diatomic hydrogen probe and the methane probe provide shielding increments that are comparable to those observed experimentally ([15] and references cited therein). There is little difference in the calculated shielding increment between the single point calculation and the constrained geometry optimization, regardless of the probe employed.

All of the shielding probes used in this study show shielding over the center of benzene that diminishes with distance (Fig. 6). The ghost atom, the hydrogen atom, and the helium atom predict a similar shielding increment, which is greater than that calculated using either diatomic hydrogen or methane. As noted over the other test molecules, use of methane as a probe leads to less shielding than obtained using hydrogen as a probe. The magnitude of the shielding effect over benzene predicted by both the diatomic hydrogen and by methane is consistent with that observed experimentally [9,10]. The non-molecular probes predict somewhat greater shielding effects than what are observed experimentally over aromatic rings.

The shielding curve over HCN (Fig. 7) is similar to that over ethyne except that the shielding increments are slightly more positive (less deshielding). Again, only the diatomic hydrogen and the methane probes provide shielding increments that match those observed experimentally ([15] and references cited therein).

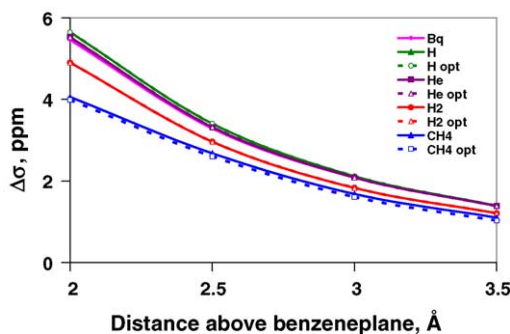


Fig. 6. Calculated shielding increments for various probes vs. distance above the center of benzene.

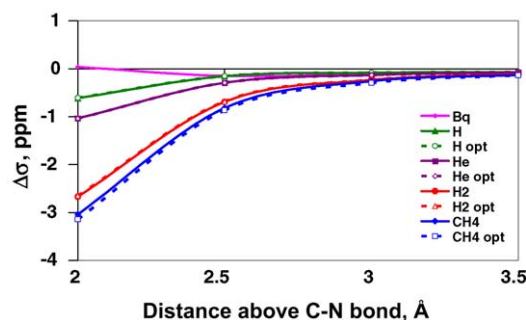


Fig. 7. Calculated shielding increments for various probes vs. distance above the center of HCN.

Use of methane as a computational probe has been successful at reproducing experimental NMR chemical shift effects of the test molecules in this study [9–15] and others [16]. Among the other probes investigated in this study, only diatomic hydrogen gives results uniformly similar to those of methane, which has previously been shown to give good agreement with observed chemical shift effects in model systems [9–16]. In fact, the ratio of isotropic shielding values calculated using diatomic hydrogen to those obtained using methane as a probe is 0.85 ± 0.01 for all calculations reported in this paper. Thus, the two molecular probes (diatomic hydrogen and methane) that have covalent bonds (unlike all other probes in this study) give comparable results. Furthermore, the isotropic shielding values calculated using the operationally and computationally simpler diatomic hydrogen probe could easily be converted to values that would be obtained using methane if necessary.

It has been demonstrated [11,12,19] that there is severe distortion of the highest occupied molecular orbital (HOMO) of the ethane–methane pair when one hydrogen atom of methane is positioned 2.0 Å above ethene. Such close approach of a covalently bonded proton to the π electron cloud might be expected to result in polarization of the methane C–H bond. To examine this possibility we also computed the Weinhold natural (npa) charges [28–30] on the

Table 1

Calculated natural population analysis (npa) charges (in unit charges) on each atom of the diatomic hydrogen probe and the resulting polarization (in unit charges, see text) as a function of distance over various test molecules

Test molecule	Distance (Å)	Proximal H	Distal H	Polarization (Δ)
Ethene	2.0	0.012	−0.036	0.048
	2.5	0.013	−0.021	0.034
	3.0	0.011	−0.014	0.025
	4.0	0.007	−0.009	0.016
Ethyne	2.0	0.016	−0.036	0.052
	2.5	0.015	−0.021	0.036
	3.0	0.012	−0.014	0.026
	4.0	0.008	−0.009	0.017
HCN	2.0	−0.001	−0.015	0.016
	2.5	0.003	−0.008	0.011
	3.0	0.004	−0.005	0.009
	4.0	0.003	−0.003	0.006

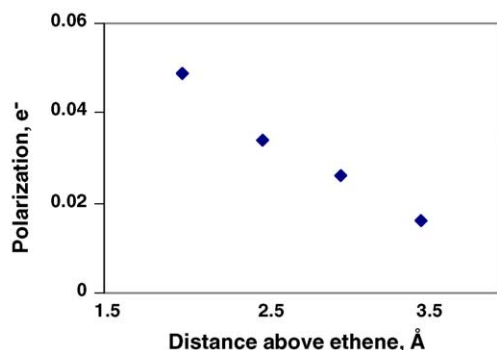


Fig. 8. Calculated polarization (Δ) of diatomic hydrogen vs. distance above the center of the plane of ethene.

proximal and distal protons of the diatomic hydrogen probes as a function of distance from the center of the test molecule. Table 1 shows how these charges vary with distance from the test molecules ethene, ethyne, and HCN when diatomic hydrogen is the probe. Charge on the computational probe is not conserved as it encounters a test molecule (some charge is shifted to or from the test molecule). Therefore, we have defined the term 'polarization' (Δ) in the case of diatomic hydrogen to be the sum of the absolute values of the computed npa charges on the proximal hydrogen and the distal hydrogen. The 'polarization' diminishes with distance from the test molecule as shown in Table 1. This is as expected if the interaction of the probe with the test molecule perturbs the electron distribution of the H–H covalent bond, as this effect would diminish with distance. This is illustrated for the test molecule ethene in Fig. 8.

4. Conclusions

Several probes of the magnetic shielding surface near anisotropic functional groups have been investigated computationally using GIAO-HF in Gaussian 03 to calculate isotropic shielding values and to predict the net NMR shielding increment. The probes studied were methane, diatomic hydrogen, a hydrogen atom, a helium atom, or a ghost atom, each held in various positions over simple test molecules (ethene, ethyne, benzene and HCN). The effect of performing single point calculations versus constrained geometry-optimized calculations was also examined; there was little difference. In addition, the effect of the angle of the orientation of the probe molecule (in the case of CH₄ and H₂) relative to the π bond in the test molecule was studied; it too, was found to be negligible. Finally, the computation of the atomic charges in the molecular probe H₂ showed slight polarization of the H–H bond, which diminished with increasing separation between the probe molecule and test structure. This is as expected, and is consistent with the NMR (de)shielding effect observed. Of the probes examined, only the molecular probes diatomic hydrogen and methane give results consistent with experimental

chemical shift observations previously reported. Interaction of a covalent bond with the test molecule seems to be needed to most accurately model the observed chemical shift effects. Diatomic hydrogen is computationally and operationally simpler and more economical to employ than methane as a probe of shielding. We conclude the optimal and most economical computational results were obtained using single point calculations of a diatomic hydrogen probe oriented perpendicular to the surface (or axis) of the test molecule.

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