Ab-initio quantum-mechanical GIAO calculation of the anisotropic effect of C–C and X–C single bonds—application to the ^{1}H NMR spectrum of cyclohexane

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The anisotropic effects of the C–C single bond in ethane and various other X–C single bonds (X = OH, SH, NH_2) have been quantitatively calculated as nuclear independent chemical shieldings (NICSs) in a three-dimensional grid of lattice atoms around the single bonds using the GIAO method integrated into the GAUSSIAN 98 calculation program. The shielding/deshielding areas due to the anisotropic effect have been plotted as *iso-chemical-shift-surfaces (ICSSs)*; hereby, both direction and scale of the anisotropic effect were quantified and visualized. The results obtained are *not* in agreement with McConnell's point dipole model; the influence of the anisotropic effect of C–C and X–C single bonds on especially ^{1}H chemical shifts must be reevaluated. The various magnetic contributions to the theoretical NMR shielding tensors of the *axial/equatorial* protons in cyclohexane were calculated by a detailed NCS-NBO analysis. The partition of the C(2)–C(3) [C(5)–C(6)] bonds at the C(1)–H_{ax}/H_{equ} magnetic shielding tensors determines both position and chemical shift difference, dominated by *hyperconjugation*.

Introduction

McConnell ascribed the magnetic anisotropy in hydrocarbons solely to the C–C bonds,[1] however, it was found that other factors affecting the chemical shift were still important.[2] The C–H bond anisotropy gave negligible chemical shift contributions only.[3] If both sign and magnetic anisotropy of an axially symmetrical group are known, its contribution to the chemical shift of each nearby proton can be calculated employing McConnell's equation.[1] On this basis the anisotropic effect of the C–C single bond was calculated, represented by means of an anisotropy cone (visualizations can be found in common text books—*cf.* Fig. 1),[4] and employed *e.g.* to assign the chemical shift difference Δδ = 0.5 ppm of the *axial/equatorial* protons of cyclohexane at low temperature, as well as the high field position of *axial* protons in saturated 6-membered rings in the conformational analysis of the latter.

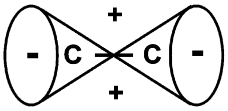

Fig. 1 Anisotropy cone of the C–C single bond,[4] classically used for signal assignment in ^{1}H NMR spectroscopy.

Previously, Klod and Kleinpeter[5] calculated the anisotropic effect of C,C and hetero-analogous double and triple bonds as well as the ring current effect of aromatic and anti-aromatic ring systems. These *ab initio* quantum-mechanical calculations, based on the nuclear independent chemical shieldings (NICSs) as employed by P. v. R. Schleyer,[6] resulted in quantitative information about the spatial extension, sign and scope of the corresponding anisotropic/ring current effects and were visualized as iso-chemical-shift-surfaces (ICSSs).

In the present study, employing the same method,[5] the anisotropic effects of the C–C single bond in ethane and of a number of heteroanalogous X–C single bonds (X = OH, SH, NH_2) have been calculated.

Computational details

The *ab-initio* quantum-mechanical calculations were performed on SGI Octane and SGI Origin 2000 work stations using GAUSSIAN 98.[7] Geometry optimization was carried out using HF/6-31G* without constraints[8] [the quality of the basis set (6-31+G**, 6-31++G**, 6-311G**) was found to be of no significant influence on shape and size of the anisotropic effect]. The shielding constants were calculated with the GIAO method[9,10] at the same level of theory; since the GIAO approach is gauge-invariant, it can be applied for the calculation of NICS.

The studied single bond was placed in the centre of a grid of lattice points, ranging from −10 to +10 Å in all three dimensions (step width 0.5 Å), resulting in a cube of 68921 lattice points; the symmetries of the compounds calculated were taken into account. The coordinates and shielding values of the lattice points around the studied single bond were transformed into SYBYL[11] contour files and the anisotropic effect visualized as *iso-chemical-shift-surfaces (ICSSs)*. In this way, it is possible to map the spatial extension, the sign and scope of the corresponding anisotropic effect in the studied molecules at each certain stereochemical position.[5]

The NBO 5.0[12] was used linked to the GAUSSIAN 98 calculation program. The natural chemical shielding (NCS)-NBO analysis partitions quantitatively the magnetic shielding of a certain nucleus into magnetic contributions from chemical bonds and lone pairs. The shielding and deshielding contributions are divided into Lewis and non-Lewis parts (non-Lewis portions point out hyperconjugation).

Results and discussion

The anisotropic effect of the C–C single bond

The anisotropic effect of the C–C single bond in ethane, calculated as just mentioned, is given in Fig. 2; the red ICSS visualizes deshielding of +0.1 ppm, the yellow one −0.1 ppm

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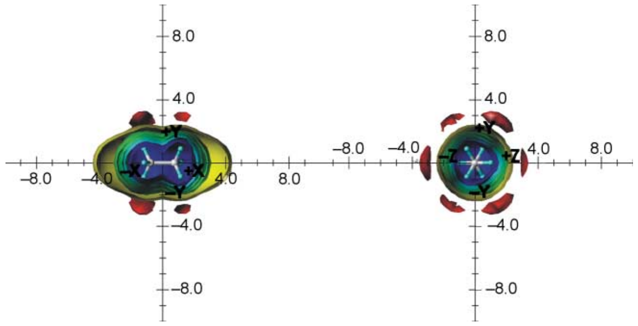

Fig. 2 Calculated anisotropic effect of the C–C single bond (shielding ICSS of −0.1 ppm—yellow, of −0.5 ppm—green, of −1 ppm—green-blue, of −2 ppm—cyan and of −5 ppm—blue; deshielding ICSS of 0.1 ppm—red). View from perpendicular to the C–C single bond (left) and in the C–C bond direction (right).

shielding (the green–blue surfaces, nearer to the C–C single bond, state even higher shielding influences, however, at these distances heavy van der Waals effects can already be expected).[5] Thus, the anisotropic effect of the C–C single bond proves to be −0.1 ppm shielding at *ca.* 4 Å from the centre in the C–C bond direction. This result reverses the classical picture (*cf.* Fig. 1) but is in line with *ab initio* calculations of Alkorta and Elguero.[13] These authors calculated the super molecule ethane.methane and found a shielding of a similar amount at nearly the same position of one methane proton with respect to ethane. The deshielding of one methane proton positioned perpendicularly to the C–C single bond at a distance of 2.5 Å as calculated by Alkorta and Elguero,[13] has also been confirmed (*cf.* Fig. 2). Additionally, from our calculation now the whole anisotropic effect of the C–C single bond is available quantitatively.

The anisotropic effect of X–C single bonds

The anisotropic effect of the single bond doesn't change very much if one carbon is replaced by a heteroatom; the corresponding anisotropic effects of the O–C bond (in methanol), of the S–C bond (in methanethiol) and of the N–C bond (in methylamine), as calculated by the same method, are visualized in Figs. 3–5. As found for ethane, in the direction of the X–C single bond there is generally a high field shift; the intensity proved to be different: with respect to the C–C single bond, the ICSSs of −0.1 ppm of the X–C single bonds were extended to 5–6 Å (also the shielding ICSSs nearer to the centre of the bonds proved to be spatially more extended). Thus, qualitatively the same anisotropic effect has been obtained. This result is completely in line with the anisotropic effect of multiple bonds:[5] if one carbon atom was replaced by a heteroatom, the anisotropic effect of double and triple bonds was significantly strengthened.

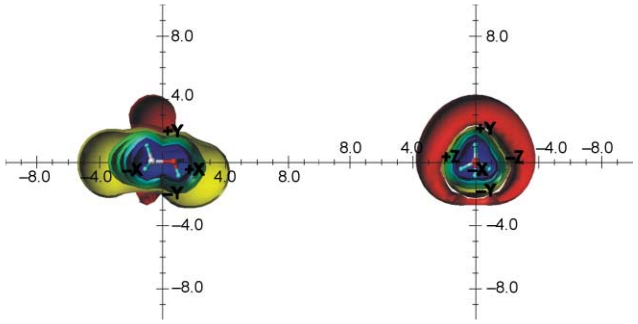

Fig. 3 Calculated anisotropic effect of the O–C single bond (shielding ICSS of −0.1 ppm—yellow, of −0.5 ppm—green, of −1 ppm—green-blue, of −2 ppm—cyan and of −5 ppm—blue; deshielding ICSS of 0.1 ppm—red). View from perpendicular to the C–O single bond (left) and in the O–C bond direction (right).

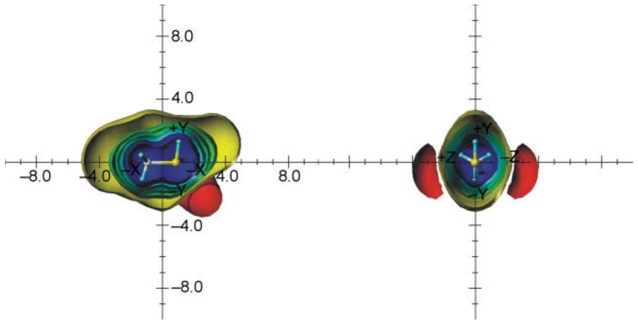

Fig. 4 Calculated anisotropic effect of the S–C single bond (shielding ICSS of −0.1 ppm—yellow, of −0.5 ppm—green, of −1 ppm—green-blue, of −2 ppm—cyan and of −5 ppm—blue; deshielding ICSS of 0.1 ppm—red). View from perpendicular to the C–S single bond (left) and in the S–C bond direction (right).

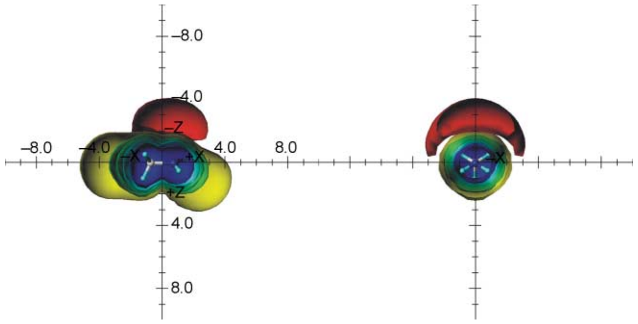

Fig. 5 Calculated anisotropic effect of the N–C single bond (shielding ICSS of −0.1 ppm—yellow, of −0.5 ppm—green, of −1 ppm—green-blue, of −2 ppm—cyan and of −5 ppm—blue; deshielding ICSS of 0.1 ppm—red). View from perpendicular to the C–N single bond (left) and in the N–C bond direction (right).

The same result was obtained for the deshielding ICSSs perpendicular to the single bonds: the red ICSS of +0.1 ppm is extended to *ca.* 4 Å. It should be kept in mind that only the global minimum conformation was considered and therefore is visualized in Figs. 3–5.

Finally, it ought to be repeated that the present *ab-initio* calculations reverse the classical picture of the anisotropic effect of the single bond (*cf.* Fig. 1). This should be taken into account if the anisotropic effect of C–C and C–X single bonds on especially protons in the ^{1}H NMR spectrum is estimated when they are stereochemically positioned on different ICSSs of the anisotropic effect.

The anisotropic effect of the C–C single bonds in cyclohexane on the 0.5 ppm chemical shift difference of the axial/equatorial protons in ^{1}H NMR spectroscopy

Employing the classical point dipole model,[1] shielding for the *axial* proton (−0.168 ppm)[2] and deshielding for the *equatorial* proton (+0.141 ppm)[2] due to the anisotropic effect of the C–C single bonds were calculated, both in fair agreement with experiment ($\Delta\delta$ *ca.* 0.5 ppm).[4] As a result of the present *ab-initio* calculations of the anisotropic effect of the C–C single bonds on the *axial/equatorial* protons in cyclohexane, only shielding influences on the two protons were obtained (*cf.* Fig. 6). The chemical shift difference ($\Delta\delta = 0.24$ ppm per C–C single bond) proved to be in excellent agreement with experiment, but the sign is reversed: the *equatorial* proton is more high field shifted than the *axial* one. Thus, in the light of the present calculations, the anisotropic effect of the C–C single bonds proved not to be responsible for the chemical shift difference of the two different protons in the ^{1}H NMR spectrum of cyclohexane at low temperature.

Employing the same optimized geometry of cyclohexane (HF/6-31G*) and calculating the ^{1}H chemical shifts of the axial (δ_{ax} = 1.16 ppm, exp. 1.12 ppm) and the equatorial protons (δ_{equ} = 1.49 ppm, exp. 1.60 ppm) in cyclohexane with the GIAO

Table 1 Magnetic shielding contributions (ppm)

		H(1)eq	H(1)eq L + NL	H(1)ax	H(1)ax L + NL
C1–C2	L (Lewis)	0.47	0.70	1.24	1.29
	NL (non-Lewis)	0.23		0.05	
C1–C6	L	0.47	0.70	1.24	1.29
	NL	0.23		0.05	
C1–Heq	L	26.95	27.15	1.71	1.82
	NL	0.20		0.11	
C1–Hax	L	1.84	2.02	27.11	27.05
	NL	0.18		−0.06	
C2–C3	L	0.06	−0.19	0.16	0.05
	NL	−0.25		−0.11	
C2–Heq	L	0.29	0.17	0.14	0.06
	NL	−0.12		−0.08	
C2–Hax	L	0.26	0.16	0.02	−0.05
	NL	−0.10		−0.07	
C3–C4	L	0.07	0.05	0.15	0.11
	NL	−0.02		−0.04	
C3–Hax	L	0.01	0.03	−0.10	−0.05
	NL	0.02		0.05	
C3–Heq	L	0.09	0.02	0.01	0.03
	NL	−0.07		0.02	
C4–C5	L	0.07	0.05	0.15	0.11
	NL	−0.02		−0.04	
C4–Heq	L	0.02	0.00	0.04	0.03
	NL	−0.02		−0.01	
C4–Hax	L	0.00	0.02	0.06	0.09
	NL	0.02		0.03	
C5–C6	L	0.06	−0.19	0.16	0.05
	NL	−0.25		−0.11	
C5–Hax	L	0.01	0.03	−0.10	−0.05
	NL	0.02		0.05	
C5–Heq	L	0.09	0.02	0.01	0.03
	NL	−0.07		0.02	
C6–Hax	L	0.26	0.16	0.02	−0.05
	NL	−0.10		−0.07	
C6–Heq	L	0.29	0.17	0.14	0.06
	NL	−0.12		−0.08	
C1 core	L	0.69	0.55	0.24	0.19
	NL	−0.14		−0.05	
C2 core	L	−0.01	−0.01	−0.07	−0.06
	NL	0.00		0.01	
C3 core	L	−0.05	−0.04	−0.07	−0.06
	NL	0.01		0.01	
C4 core	L	−0.05	−0.04	−0.07	−0.06
	NL	0.01		0.01	
C5 core	L	−0.05	−0.04	−0.07	−0.06
	NL	0.01		0.01	
C6 core	L	−0.01	−0.01	−0.07	−0.06
	NL	0.00		0.01	
	Σ Lewis	31.80		32.02	
	Σ non-Lewis	−0.38		−0.28	
	Σ Total	31.41		31.74	
	^{1}H (TMS)	32.90			
	Chem. shift	1.49		1.16	
	Experiment	1.60		1.12	

method,[9,10] both the sequence and the amount of the chemical shift differences prove to be correct (taking into account that cyclohexane was calculated at 0 K, as a single molecule and in the gas phase). So the calculations done so far are correct, but the reason for the ^{1}H chemical shift difference of the cyclohexane protons seems to be not the classical anisotropic effect of the C–C single bonds.

On the other hand, there are clear hints at the activity of stereoelectronic effects in cyclohexane; the *axial* C–H bond is longer than the *equatorial* C–H bond, adequately different are the direct H,C coupling constants [$^1J_{H,C}$ (ax) < $^1J_{H,C}$ (equ)],[14] referred to as the normal Perlin effect.[15] These experimental facts were also theoretically calculated and were related to the various hyperconjugative interactions in cyclohexane and, finally, to the electron donor ability of C–H and C–C bonds; actually, C–H bonds are better electron donors than C–C bonds and the partial positive charge, due to hyperconjugation, proved higher at H_{equ}.[16]

Along with the present GIAO calculation of cyclohexane (HF/6-31G*), the theoretical NMR shielding tensors of the *axial/equatorial* protons were partitioned into magnetic contributions from the bonds of this molecule by employing the natural chemical shielding (NCS) analysis, based on the NBO method.[12] Both the localized contributions from chemical bonds as well as the delocalized contributions (from *hyperconjugation*) to the shieldings of the two different protons in cyclohexane were calculated and are collected in Table 1.

As Table 1 shows, the orbital contribution of the σ_{C-H} bond, in which the *axial/equatorial* protons are involved, causes the greatest shielding (27.15 ppm for the *equatorial* proton and 27.05 ppm for the *axial* one), being very similar for the two protons considered. However, both localized and delocalized contributions of the other C–C and C–H bonds of cyclohexane proved much more different (*cf.* Table 1); especially the adjacent C–C bond contributions were found to be very diverse (0.70 ppm shielding per C–C bond on the *equatorial* proton but

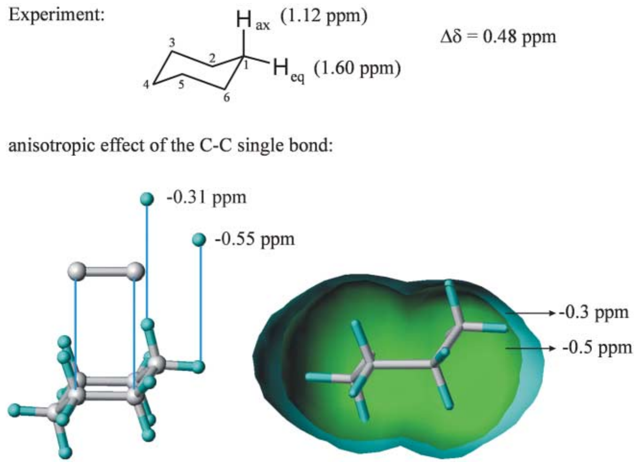

Fig. 6 Experimental ^{1}H chemical shifts of the *axial*/*equatorial* protons of cyclohexane (above); anisotropic effect of the C(2)–C(3) single bond on the *axial*/*equatorial* protons at C(1)—calculated values (left below), and within the ICSS of −0.3 ppm—blue and −0.5 ppm—green (right below).

1.29 ppm shielding on the *axial* proton). In the case of the contribution of the second $\sigma_{C–H}$ bond, the effect is reversed: 2.02 ppm shielding on the *equatorial* and 1.82 ppm on the *axial* proton. Also the shielding contributions of the other C–C and C–H bonds, more distant from the protons considered, are different, nevertheless, the sum of all magnetic contributions to the theoretical NMR shielding tensors (which correspond to *the chemical shift*) of the *axial*/*equatorial* protons of cyclohexane is correct both in sign and in amount even when being a rather complex term which consists of a large number of localized and non-localized contributions (*cf.* Table 1). So it seems rather difficult to isolate only a single magnetic effect which will be responsible for the different chemical shifts of the *axial*/*equatorial* protons in cyclohexane; certainly, it is not the anisotropic effect of the C–C single bonds in the 2,3- and 5,6-positions (*vide supra*).

However, it is evident that both sign and amount of the chemical shift difference of the *axial*/*equatorial* protons are dependent on these bonds. If the sum of localized and delocalized contributions from the C(2)–C(3) bond to the shielding tensors of the two protons at C1 is considered, a shielding of 0.05 ppm on the *axial* proton and a deshielding of −0.19 ppm on the *equatorial* proton were calculated, if doubled due to the same effects of the C(5)–C(6) bond the difference $\Delta\delta$ = 0.48 ppm proved to be in excellent agreement with experiment. The low field position of the *equatorial* proton is reproduced correctly.

If the corresponding non-localized contributions (due to *hyperconjugation*) are considered only (in this case the effects of the $\sigma_{C–H}$ bond C(2)–H$_{ax}$ and C(6)–H$_{ax}$ also have to be taken into account) the result is as follows: a deshielding contribution of −0.18 ppm on the *axial* proton and a larger deshielding contribution of −0.35 ppm on the *equatorial* proton were calculated (*cf.* Table 1). The difference $\Delta\delta$ = 0.17 ppm (doubled to 0.34 ppm, with the *equatorial* proton at low field) is 0.14 ppm smaller than the sum of the Lewis and non-Lewis contributions but seems to dominate to present chemical shift difference.

Thus, it can be concluded from the present study that the magnetic contributions from the C(2)–C(3) [C(5)–C(6)] bonds to the magnetic shielding tensors of the *axial*/*equatorial* protons at C(1) determine both position and difference of the chemical shifts of the latter protons; *hyperconjugation* seems to dominate this effect.

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