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Interpretation of Conformational Effects on 2-*endo*-Norborneol by Natural Chemical Shielding Analysis

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This paper represents an extension of our work on the ^1H and ^{13}C NMR chemical shifts of norbornane and 2-*endo*-norborneol. NCS−NBO analysis was employed to probe contributions of bond orbitals and orbitals of lone pairs to nuclear shielding in conformers of the alcohol generated by rotation of the C−O bond. Variations in ^1H and ^{13}C chemical shifts with the dihedral angle are discussed in terms of Lewis and non-Lewis partitioning and their respective importance is evaluated. In addition to hyperconjugation of the lone pair in a p orbital of oxygen that was previously reported, a sizable participation of the lone pair which is in an sp orbital is also observed and their combined effect dominates the carbon chemical shifts of the C_1-C_2-OH and C_3-C_2-OH fragments. Both lone pairs on oxygen also contribute to localized, though-space effects on nuclei in the vicinity, these effects answering for the largest deviations in hydrogen chemical shifts on rotation around the C−O bond. On the other hand, for conformers in which nonbonded repulsions lead to distortions in the molecular framework, variations in chemical shifts may be attributed to angular effects.

Introduction

Stereo-electronic effects provide an efficient probe for the investigation of factors that affect NMR chemical shifts.[1−4] The rotation about a C−O bond can lead to significant variations in ^1H and ^{13}C chemical shifts in alcohols and, according to the dihedral angle of the C−O rotation, relative contributions of different factors to the shielding of the respective nuclei can be interpreted in terms of steric and electronic effects.

The recent detailed investigation of effects of C−C and C−H bonds on the shielding of *axial* and *equatorial* hydrogens in cyclohexane by natural chemical shielding−natural bond orbital (NCS−NBO) analysis[5] has clearly shown the various contributions of C−C and C−H bonds to the nuclear shieldings of the hydrogens in cyclohexane. A similar approach was applied to the steric effects that arise from the introduction of a methyl group in cyclohexane and bicyclo[2.2.1]heptane (or norbornane) as well as those of *n*-pentane in different conformations.[6] NCS analysis clearly shows that substituent effects that are attributed to steric interactions are the result of distortions in molecular structure that lead to bond stretching or compression as well as to angular distortions.[6] To verify how electronic effects, such as those introduced by a hydroxyl substituent, affect nuclear shielding we calculated the ^1H and ^{13}C chemical shifts of all nuclei in norbornane (Figure 1; X = H) and compared them to those of 2-*endo*-norborneol (Figure 1; X = OH). For the latter, the dependence of chemical shifts on the dihedral angle formed by the hydroxyl group and the C_2-C_3 bond at 30° intervals was carefully analyzed, both in terms of the structural variations of the norbornyl skeleton and of the relative contributions of chemical bonds/lone pairs to the nuclei that are affected by C−O rotation.

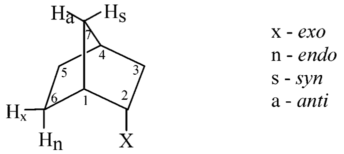

Figure 1. Norbornyl systems.

Our results show significant contributions of both lone pairs on oxygen to the shieldings of almost all nuclei of 2-*endo*-norborneol. They may be transmitted through space, through bonds, or both and are strongly orientation-dependent as predicted by current descriptions of lone pair directionality. This approach removes most of the ambiguities in the qualitative interpretation of the origin of stereo-electronic effects of the corresponding lone pairs[1−4] and confirms most of our previous observations on 2-norborneol to a large extent. Additionally, as was verified for a pentacyclic alcohol,[7] both the p and sp lone pairs on oxygen affect chemical shielding and both their relative localized and nonlocalized contributions are much larger than expected, reinforcing or canceling each other. In fact, when the hydroxyl hydrogen is pointing in the direction of a certain nucleus, the shielding of that nucleus is owing to attenuation of the localized effect of the corresponding lone pair and not to polarization of the O−H bond.

Calculations. The quantum mechanical calculations were carried out on SGI octane and SGI origin 2000 workstations using the GAUSSIAN 98 program package[8] at the B3LYP/6-

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31G(d)[9] level of theory. The conformations obtained result from unrestricted optimization of all degrees of freedom except the torsional angle for the 12 rotamers of the hydroxyl group. The population analysis and the natural chemical shielding (NCS)[5] analysis were done using the NBO 5.0[10] module linked to the GAUSSIAN 98[8] program. All chemical shifts were calculated as differences in magnetic shieldings between the corresponding nucleus and TMS using the GIAO method at the B3LYP/6-31G(d) level of theory.

Results and Discussion

Natural Chemical Shielding (NCS) Analysis of Norbornane. The theoretical NMR shieldings of the ^1H and ^{13}C nuclei in norbornane were partitioned into contributions from the various bonds using NCS analysis based on the NBO method.[10] This type of analysis applied to cyclohexane revealed that contributions of C−C and C−H bonds to the chemical shifts of a certain nucleus depend on the stereochemistry of these bonds.[5] Since all carbon nuclei of cyclohexane are equivalent and the hydrogens bonded to them occupy either equatorial or axial positions, only one type of C−C bond and two types of C−H bonds had to be considered. In contrast, for norbonane, there are several bonds that must be taken into account,[6] such as those formed by the three types of carbon and four types of hydrogen. They correspond to bonds formed by bridgehead carbons C_1 and C_4; those that are part of ethano bridges C_2, C_3, C_5, and C_6; and the methano bridge carbon, C_7. Whereas ethano hydrogens may occupy exo (H_x) or endo (H_n) positions, methano hydrogens may be syn (H_s) or anti (H_a) to one of the ethano bridges (Figure 1; X = H).

In norbornane, the contributions to the shielding of carbon and hydrogen nuclei by distinct C−C and C−H bonds are considerably different, as is given in Table 1. The C_1-C_2 bond contributes −13.74 ppm to the chemical shift of C_2 while this value is reduced to −10.46 ppm for C_2-C_3. Contributions from C−H bonds are also distinct. For C_2, these values are −8.68 ppm from C_2-H_{2x} and −7.97 ppm from C_2-H_{2n}, while for C_1 these contributions are −11.79 ppm from C_1-C_2 and −13.24 ppm from C_1-C_7, and the contribution from C_1-H is −12.64 ppm. Thus, the relative magnetic contributions of a certain substituent (2-*endo*-OH in this case) must be taken into account when evaluating the magnitude of its effect on chemical shifts.

Conformational Effects of the Hydroxyl Group on Shielding Contributions. DFT B3LYP calculations using the 6-31G(d) basis set were used to obtain isotropic shielding values by the GIAO method for twelve rotamers of 2-*endo*-norborneol that are found at 30° intervals of the C_3-C_2-O-H dihedral angle. Energy minima occur at 60°, 180°, and 300° (Figure 2) and correspond approximately to conformers **2A**, **2B**, and **2C**, respectively, of ref 1 (Figure 3).

On rotation about the C−O bond, largest variations in chemical shielding for carbon nuclei were observed for C_1, C_3, and C_4 while for hydrogen these nuclei are H_1, H_{3x}, H_{3n}, H_{5n}, H_{6x}, and H_{6n}.[1] Figures 4 and 5 show the respective variations in carbon and hydrogen chemical shifts for these nuclei with the C_3-C_2-O-H dihedral angle.

This approach reveals that certain differences in chemical shifts are still larger than those that had been reported (only the lowest energy rotamers are considered in ref 1). For C_3, for example, there is a 6 ppm difference between the 0° rotamer and the 180° rotamer, while for H_{3n} this difference between 0° and 120° rotamers is over 0.8 ppm. In addition, shielding of almost all nuclei proved to be strongly dependent on the C_3-C_2-OH dihedral angle. Each nucleus is affected differently, however. For example, C_1 is found at lowest field at $\Phi = 180°$ (the global minimum) but, at this angle, C_3 and H_1 are observed at highest field. The chemical shifts of other carbon and hydrogen nuclei depicted in Figures 4 and 5 vary in distinct ways, but their dependence on the dihedral angle is quite regular, a strong hint that this behavior can be properly accounted for.

TABLE 1: Magnetic Shielding Contributions to Chemical Shifts of Norbornane (ppm)

NBO	C_1	C_2	C_7	H_1	H_{2x}	H_{2n}	H_7
C_1-C_2 L	−11.47	−13.01	0.13	0.23	0.06	0.07	0.00
NL	−0.32	−0.73	−0.01	0.24	0.01	0.01	−0.09
C_1-C_6 L	−11.47	0.06	0.13	0.23	0.23	0.19	0.13
NL	−0.32	−0.11	−0.01	0.24	−0.08	−0.03	−0.06
C_1-C_7 L	−13.29	0.47	−11.68	0.08	0.19	0.16	0.86
NL	0.05	−0.41	−0.45	0.28	−0.06	0.00	0.13
C_1-H_1 L	−13.20	0.56	0.82	26.99	0.02	0.01	0.14
NL	0.56	−1.15	−1.39	0.09	0.02	0.01	−0.01
C_2-C_3 L	0.01	−10.19	−0.89	0.10	0.04	0.17	0.06
NL	0.46	−0.27	−0.08	−0.16	0.06	0.03	0.04
C_2-H_{2x} L	0.96	−9.74	−0.03	0.23	0.00	−0.01	0.03
NL	−1.11	1.06	0.09	−0.12	0.01	0.00	0.01
C_2-H_{2n} L	0.81	−8.60	−0.43	0.36	0.02	−0.01	0.05
NL	−0.76	0.63	0.05	−0.09	0.01	0.02	−0.05
C_3-C_4 L	−1.23	0.12	0.13	0.07	−0.08	−0.04	0.00
NL	0.00	0.13	−0.01	0.01	−0.17	−0.13	−0.09
C_3-H_{3x} L	−0.14	0.86	−0.03	0.00	0.06	−0.02	0.03
NL	0.05	−1.14	0.09	0.01	−0.07	0.04	0.01
C_3-H_{3n} L	−0.30	0.61	−0.43	0.04	0.04	−0.12	0.05
NL	0.36	−1.05	0.05	−0.02	−0.02	0.07	−0.05
C_4-C_5 L	−1.23	0.16	0.13	0.07	0.80	1.09	0.13
NL	0.00	−0.02	−0.01	0.01	0.05	0.01	−0.06
C_4-C_7 L	0.33	−0.01	−11.67	0.33	0.11	−0.02	0.86
NL	0.51	−0.45	−0.45	−0.18	−0.09	−0.06	0.13
C_4-H_4 L	−0.93	−0.52	0.82	0.06	0.13	0.22	0.14
NL	0.55	0.36	−1.39	−0.07	−0.07	−0.03	−0.01
C_5-C_6 L	0.01	0.16	−0.89	0.10	0.82	0.94	0.21
NL	0.46	0.09	−0.08	−0.16	−0.06	−0.04	−0.02
C_5-H_{5x} L	−0.14	−0.02	−0.03	0.00	26.89	1.32	−0.04
NL	0.05	0.03	0.09	0.01	−0.01	0.25	0.02
C_5-H_{5n} L	−0.30	0.02	−0.43	0.04	1.39	26.76	−0.03
NL	0.36	0.06	0.05	−0.02	0.17	0.02	0.01
C_6-H_{6x} L	0.81	−0.95	−0.43	0.36	0.18	−0.07	−0.03
NL	−0.76	0.04	0.05	−0.09	−0.12	−0.07	0.01
C_6-H_{6n} L	0.96	−0.67	−0.03	0.23	−0.08	0.16	−0.04
NL	−1.10	0.03	0.09	−0.12	−0.15	−0.10	0.02
C_7-H_{7a} L	0.37	−0.63	−12.67	0.19	−0.03	0.04	27.01
NL	−0.68	0.07	1.00	−0.06	0.04	0.03	−0.03
C_7-H_{7s} L	0.37	−0.56	12.66	0.19	−0.04	0.00	1.08
NL	−0.68	0.22	1.01	−0.06	0.03	−0.04	0.16
C_1 (core) L	202.92	−0.15	−0.20	0.88	−0.04	0.00	−0.04
NL	0.21	0.03	0.04	−0.25	0.01	0.00	0.01
C_2 (core) L	−0.27	202.98	−0.14	−0.05	0.44	0.66	−0.07
NL	0.04	0.14	0.03	0.00	−0.10	−0.14	0.02
C_3 (core) L	−0.15	−0.13	−0.14	0.07	−0.05	−0.03	−0.07
NL	0.04	0.04	0.03	0.01	0.01	0.01	0.02
C_4 (core) L	−0.17	−0.13	−0.20	−0.07	−0.08	−0.06	−0.04
NL	0.05	0.04	0.04	0.02	0.02	0.02	0.01
C_5 (core) L	−0.15	−010	−0.14	−0.07	−0.07	−0.06	−0.07
NL	0.04	0.02	0.03	0.01	0.02	0.01	0.01
C_6 (core) L	−0.27	−0.12	−0.27	0.05	0.07	−0.06	−0.07
NL	0.04	0.03	0.04	0.00	0.01	0.01	0.01
C_7 (core) L	−0.27	−0.13	203.00	−0.04	−0.07	−0.05	0.52
NL	0.04	0.03	0.13	0.00	0.01	0.01	−0.10
$\sum$ Lewis	152.57	160.29	151.91	30.46	31.16	30.88	30.78
$\sum$ non-Lewis	−1.88	−2.30	−0.96	−0.45	−0.57	−0.01	0.07
$\sum$ total	150.69	157.99	150.96	30.01	30.59	30.88	30.86
^{13}C or ^1H (TMS)	189.69	189.69	189.69	32.18	32.18	32.18	32.18
chemical shift	39.00	31.70	38.73	2.17	1.59	1.30	1.32
experiment[a,b]	36.3	29.6	38.3	2.192	1.471	1.162	1.181

[a] ^{13}C chemical shifts, Barfield, M. *J. Am. Chem. Soc.* **1995**, *117*, 2862. [b] ^1H chemical shifts, ref 14.

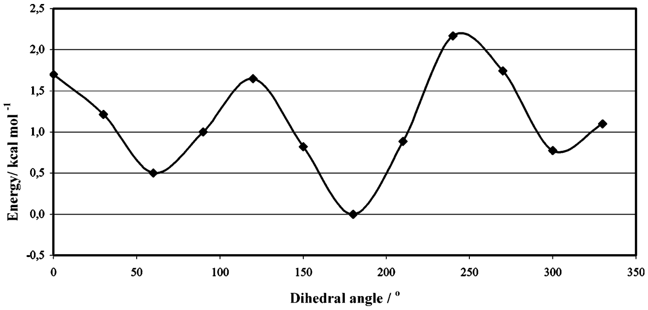
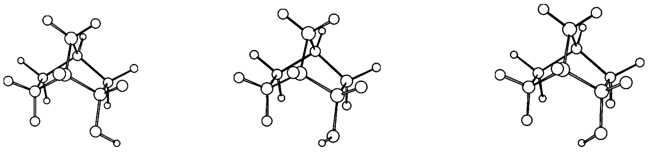


Figure 2. Variation in energy of 2-*endo*-norborneol conformers with the C_3-C_2-O-H dihedral angle.



A (60º) B (180º) C (300º)

Figure 3. Lowest energy conformers of 2-*endo*-norborneol.

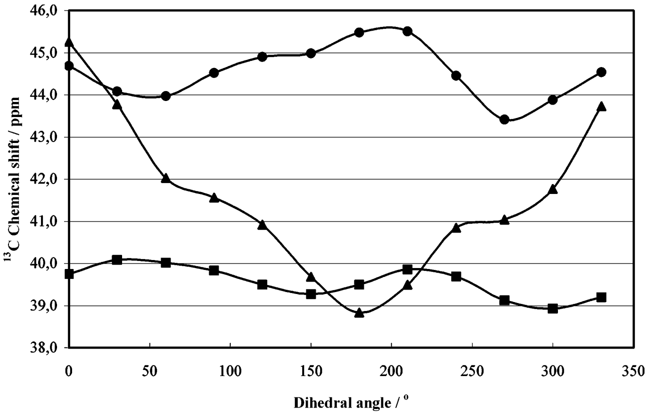


Figure 4. Variation of ^{13}C chemical shifts of selected nuclei of 2-*endo*-norborneol with the C_3-C_2-O-H dihedral angle. ●, C_1; ▲, C_3; ■, C_4.

Our previous results on norborneol indicated that hyperconjugation with the lone pair on oxygen was mainly responsible for variations in chemical shifts of C_1 or C_3.[1,4] Alignment of the p-orbital on the oxygen with the C_1-C_2 or C_2-C_3 bonds should result in lengthening of these bonds and deshielding of the corresponding nucleus. However, the chemical shift of C_1 for **2C**, where hyperconjugation was favored, was comparable to that of **2A**, where hyperconjugation was absent. Attenuation of the effect of hyperconjugation as well as deshielding of C_4 were attributed to electrostatic effects of the hydroxyl group.[1]

To verify these hypotheses, C_1-C_2 and C_2-C_3 bond lengths, those that would be most strongly affected by hyperconjugation of their σ^*_{C-C} antibonding orbitals with the lone pairs are plotted against the C_3-C_2-O-H dihedral angles in Figure 6. Comparison of the behavior of the C_1 chemical shift (Figure 4) and C_1-C_2 bond length (Figure 6) on rotation around the C−O bond shows a general agreement, as is the case with the chemical shift of C_3 and the C_2-C_3 bond distance. This qualitative agreement led to a more detailed study of the effects of hyperconjugation on chemical shifts of the norbornyl alcohol (Figure 1; X = OH) by NBO analysis.

Hyperconjugation of the oxygen lone pairs with the antibonding orbitals on certain C−C or C−H bonds in 2-norborneols is conveniently described by natural bond orbitals (NBO).[4] The NBO approach of Reed and Weinhold[12] has been used in conjugation with calculated ^{13}C chemical shifts to quantify the amount of intramolecular charge-transfer interactions in some strained bicyclic pentanes.[13] This led to the conclusion that lone pair electron delocalizations toward neighboring C−C antibonding orbitals, as quantified by the NBO approach, have a significant effect on the chemical shift of the carbon nucleus that is involved. In the present work, NBO analysis is used as a probe for the extent that hyperconjugation contributes to shielding or deshielding of specific ^{13}C or ^{1}H nuclei.

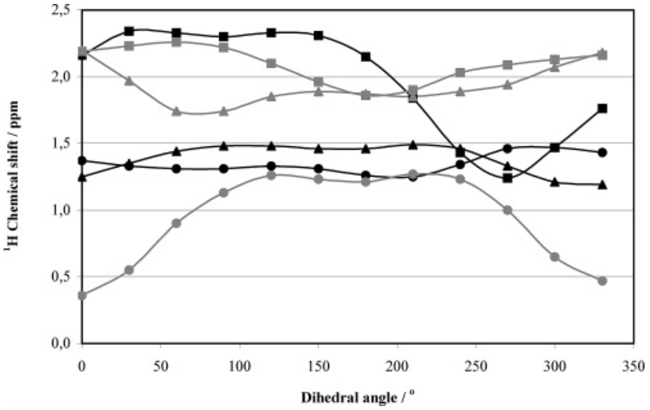


Figure 5. Variation in ^{1}H chemical shifts of selected nuclei of 2-*endo*-norborneol with the C_3-C_2-O-H dihedral angle. Black: ●, H (6*x*); ■, H (6*n*); ▲, H (5*n*); gray: ▲, H (3*x*); ●, H (3*n*); ■, H (1).

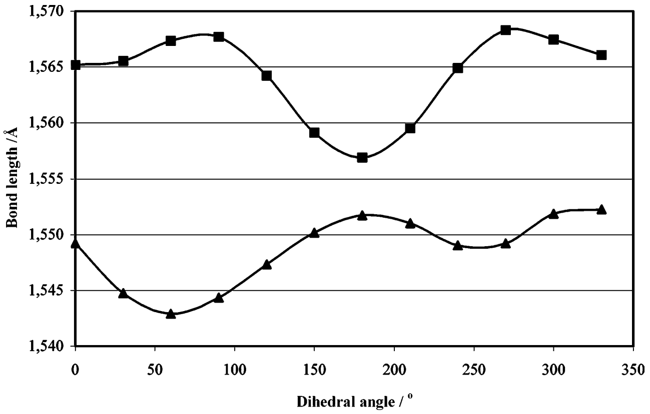


Figure 6. Variation of selected bond lengths of 2-*endo*-norborneol with the C_3-C_2-O-H dihedral angle. ▲, C_1-C_2; ■, C_2-C_3.

Hyperconjugation can be in quantified in terms of the energy of the second-order perturbation interaction as obtained in the NBO analysis.[12] In this approach, the noncovalent bonding−antibonding interaction is expressed by means of the second-order perturbation interaction energy (E^2) involving neighboring orbitals. This energy represents an estimate of the off-diagonal NBO Fock matrix elements. For example, the E^2 interaction involving the p-type lone pair on the oxygen as donor and one of the antibonding $\sigma(C-X)^*$ orbitals of a vicinal CX_3 group as acceptor is strongly dependent on the $H-O-C_2-C_1(C_3)$ dihedral angle. As shown in ref 4, for 2-*exo*- and 2-*endo*-norborneols the highest value for E^2 (up to 9.11 kcal/mol), corresponding to the conformation of strongest lone pair-C−C antibonding interaction, is found for those conformations where the p-type oxygen lone pair is perfectly aligned with the C−C bond (corresponding to C_3-C_2-O-H dihedral angles of 180° and 360° for C_1 and 90° and 270° for C_3, respectively), while vanishing interactions are found for those dihedral angles where the p-type oxygen lone pair and the C−C bond are perpendicular

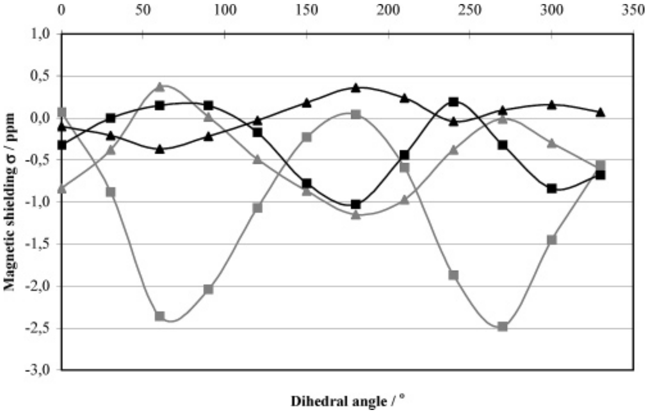


Figure 7. Variations of non-Lewis contributions from oxygen lone pairs, LP(1) and LP(2), respectively, to natural chemical shieldings of C_1 and C_3 in 2-*endo*-norborneol with the C_3-C_2-O-H dihedral angle. The sign denotes shielding (+) or deshielding (−). ▲, LP(1) O C_1 NL (black). ■, LP(2) O C_1 NL (black). ▲, LP(1) O C_3 NL (gray). ■, LP(2) O C_3 NL (gray).

to one another (corresponding to H−O−C−C dihedral angles of 60° and 240° for C_1 and 180° or 360° for C_3, respectively).

DFT calculations show that the oxygen lone pairs occupy two different orbitals, one with a high p character and the other of sp-type.[7] Thus, in addition to hyperconjugation with the lone pairs in a p-type orbital, interactions of a similar nature should be expected with lone pairs that occupy an sp-type orbital. Analysis of the natural chemical shieldings of C_1 and C_3 (see Supporting Information) reveals the significant non-Lewis contributions of both the sp-type orbital, denoted LP(1), and the p-type orbital, denoted LP(2), as expected if both participate in hyperconjugation with neighboring C−C bonds. The correlation between the non-Lewis contributions of the oxygen lone pairs to the shieldings of C_1 and C_3, respectively, and the C_3-C_2-O-H dihedral angle Φ shown in Figure 7 reveal that the two different types of lone pair have distinct angular effects. LP(1), which is mostly of sp character, is delocalized most strongly at a dihedral angle of 60°, deshielding C_1 by about 0.4 ppm and shielding this nucleus by almost the same amount at 180°. It has an inverse effect on C_3, shielding this other nucleus by about 0.4 ppm at 60° and deshielding it by almost 1.2 ppm at 180°. LP(2) occupies an orbital which is essentially of p character. Its contribution to the shielding of C_1 assumes its maximum values at dihedral angles of 180° and 300°, deshielding this nucleus by just over 1 and 0.8 ppm, respectively. The contribution of LP(2) to the chemical shift of C_3 is much larger, deshielding this nucleus by almost 2.5 ppm at 60° and 270°. Thus, the angular dependence of non-Lewis contributions of both lone pairs on oxygen is in good agreement with our previous interpretations based on hyperconjugative interactions.[1,4] Those of LP(2) to the chemical shifts of C_1 and C_3 are stronger, probably owing to its better overlap with the antibonding σ^* orbital of the adjacent C−C bond.

The effect of hyperconjugation on ^{13}C chemical shifts is best observed for dihedral angles between 60° and 270° and was attributed to the lengthening of C−C bonds.[4] In this region, the C_1-C_2 bond reaches its maximum length at a C_3-C_2-OH dihedral angle of 180° (Figure 6). In this conformation, overlap between the lone pair in a p orbital corresponding to LP(2) and the antibonding orbital on C_1 is most favorable and σ^* back-donation is strongest, lengthening the C_1-C_2 bond. This is the position in which deshielding of C_1 by LP(2) is at a maximum (Figure 7). However, it also coincides with the position in which shielding by LP(1) reaches its maximum and the resulting effect of LP(1) and LP(2) is to partially cancel each other. The C_2-C_3 bond reaches its maximum length at 90° and 270° (Figure 6), the positions in which overlap between LP(2) and the antibonding orbital on C_3 is most favorable and deshielding reaches its maxima as well (Figure 7). At a dihedral angle of 90°, the effect of LP(1) is slightly shielding (0.4 ppm) while at 270° it is negligible so the chemical shift for C_3 will correspond almost solely to deshielding by LP(2). Thus, the larger conformational effect on C_3 over C_1 can be attributed to a combination of better overlap of the corresponding antibonding orbital with LP(2) on oxygen as well as the absence of a contrary effect by LP(1).

NCS analysis of *endo* 2-norboneol conformers provides further insight into the relative importance of these contributions. Substituent effects based on comparisons of norbornane and its 2-endo hydroxy derivative in different conformations can be used to evaluate relative contributions of distinct factors. For example, the C_3-C_4 bond has stronger influence on the chemical shift of C_3 than the C_2-C_3 bond while for C_1 the stronger effect is owing to the C_1-C_7 bond. Analysis of the shielding contributions reveals that for C_3 there is a difference of more than 6 ppm between chemical shifts of 180° and 0° conformers. Here, the localized effects of the oxygen lone pair on C_3 are reinforced by the deshielding contributions of C_2-C_3, C_3-C_4, C_3-H_{3x}, and C_3-H_{3n} bonds (contributions from the latter three bonds are comparable to those from C_2-C_3). On the other hand, for C_1 the difference between conformers is only ca. 2 ppm. Here, not only is the contribution from the C_1-C_2 bond relatively smaller, but there is a still larger one from the C_1-C_6 bond (it is affected by the position of the hydroxyl group).

Relative magnitudes of localized and delocalized effects of the oxygen lone pairs on shielding carbon nuclei may be evaluated by comparing conformational effects on C_3 and C_4. Whereas for C_3 the largest contribution is observed for positions in which either LP(1) or LP(2) is favorably aligned for delocalization and corresponds to non-Lewis deshielding contributions of about 2.5 ppm, contributions to C_4 are much smaller (about 1.0 ppm) and are of a localized nature. Maxima are observed for conformations in which LP(1), LP(2), or both are closest in space to C_4 and a minimum corresponds to the rotamer for which the hydroxyl hydrogen points toward the inside of the ring system, in the general direction of this nucleus.

NCS analysis thus partially confirms some of the previous observations related to the effect of hyperconjugation on ^{13}C NMR chemical shifts.[1−4] Hyperconjugation can account for some of the largest variations in ^{13}C chemical shifts on rotation around the C−O bond. Nevertheless, there are significant differences among contributions from different bonds and these must be taken into account on comparison of substituent effects.

In our previous work on norborneol,[1] hyperconjugative interactions did not seem to make significant contributions to hydrogen chemical shifts. In fact, the chemical shift of H_2 appeared to be relatively insensitive to conformational effects. The difference in chemical shifts for conformations **A** and **B**, where the C−H bond is properly aligned with LP(2), and **C**, where this alignment is unfavorable, are less than 0.1 ppm, a fraction of that observed for H_{3n} or H_{6n}, for example. Figure 8 shows the variation of the non-Lewis contribution of LP(1) and LP(2), respectively, to the shielding of H_2 with the C_3-C_2-O-H dihedral angle. Deshielding reaches its maximum value at 60° and 180° (conformations **A** and **B**, respectively) and its minimum at 300° (conformation **C**), the maximum difference being about 0.3 ppm. Deshielding also reflects an increase in the C_2-H_2 bond length but, in this case, its effect on hydrogen

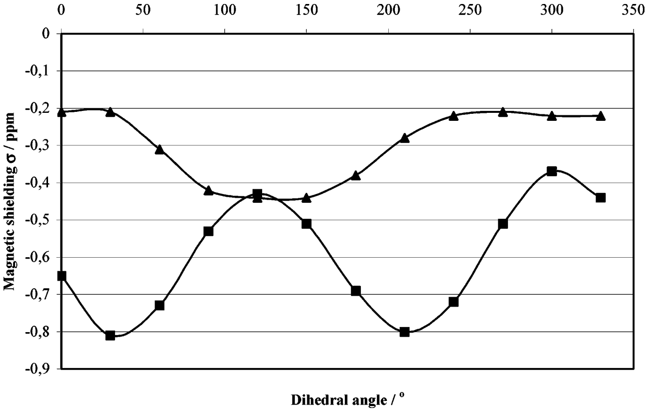


Figure 8. Variations of non-Lewis contributions from oxygen lone pairs, LP(1) and LP(2), respectively, to natural chemical shieldings of H_2 in 2-*endo*-norborneol with the C_3-C_2-O-H dihedral angle. The sign denotes shielding (+) or deshielding (−). ▲, LP(1) O (H_2) NL. ■, LP(2) O (H_2) NL.

chemical shifts is not as large as that observed for H_{3n} or H_{6n} (Figure 5). Both these nuclei reveal broad maxima for regions where either LP(1) or LP(2) is close in space to one of them and minima for the conformer in which the hydroxyl hydrogen is pointing in their direction. Thus for hydrogens, the main shielding contribution is of a localized (Lewis) type, the non-Lewis contributions being small for all hydrogens except H_2 but it, too, is relatively small compared to the localized contributions.

The orientation dependence of substituent effects on ^1H chemical shifts of norbornane had already been noted, those of 2-*endo*-norborneol having been attributed mainly to electric field mechanisms.[14] Our results reveal that there are several effects operating simultaneously and that their relative importance depends on stereo-electronic interactions and can be evaluated by theoretical methods.

There is a still another type of conformational effect that must be considered. Rotation around the C−O bond brings some atoms in close contact and may lead to distortions in the molecular framework. For C_3, for example, severe repulsions between the hydroxyl hydrogen and H_{3n} result in streching the C_2-C_3 bond and deshielding C_3, as is observed for an *endo*-2-methyl group and is discussed in ref 6. This must be the case in the region below 60° and above 270° where angular effects are probably responsible for chemical shift variations.

Another important point that arises from this type of analysis is relative to the directional character of lone pair orbitals on oxygen. It can be traced to delocalization into antibonding orbitals of suitably aligned C−C or C−H bonds in the neighborhood of the substituent or to through-space interactions of a localized nature associated with the sp or p lone pairs on oxygen. Rather than polarization of the O−H bond that was originally proposed,[1] it appears that this directionality depends on the type of orbital that is occupied by the lone pair on oxygen and its position relative to other nuclei in the vicinity of the one that is affected by its presence.

Conclusions

Natural chemical shielding−natural bond analysis is particularly well-suited for tracing the origins of conformational effects on carbon and hydrogen chemical shifts of 2-*endo*-norborneol. Delocalization of both lone pairs on oxygen accounts for the largest variations in carbon chemical shifts while localized through-space interactions have the largest effect on hydrogen chemical shifts; nevertheless, there are significant differences among contributions from distinct bonds and these must be taken into account on comparisons of substituent effects. Anisotropic effects of the C−O bond do not make a significant contribution to hydrogen chemical shifts.

The strong directional character of the effects that can be traced to oxygen is evident from these studies. It is also quite clear that both lone pairs on oxygen can affect shielding of carbon and hydrogen nuclei, the magnitude of their respective contributions depending on their hybridization and position relative to that of the nucleus under consideration.

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Supporting Information Available: Natural chemical shieldings for all ^{13}C, ^1H, and ^{17}O nuclei of 0°, 30°, 60°, 90°, 120°, 150°, 180°, 210°, 240°, 270°, 300°, 330° rotamers of 2-*endo*-norborneol are given. This material is available free of charge via the Internet at http://pubs.acs.org.

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