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Anomeric Effect on Geminal and Vicinal J_{HH} NMR Coupling Constants

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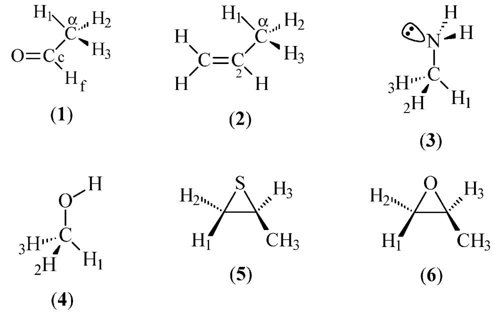
Trends for geminal ($^{2}J_{HH}$) and vicinal ($^{3}J_{HH}$) nuclear magnetic resonance indirect spin−spin coupling constants, SSCCs, for 2-methylthiirane (**5**) and 2-methyloxirane (**6**) are studied both from experimental and theoretical points of view to determine the influence of hyperconjugative interactions on these couplings. These two analogous compounds were chosen because it was expected that they exhibit quite different anomeric effects. Hyperconjugative interactions are investigated using the "natural bond orbital" method. Coupling constants are calculated within the density functional theory including all four scalar contributions, that is, the Fermi contact, the spin−dipolar, and the paramagnetic and diamagnetic spin−orbital contributions. Solvent dielectric effects are taken into account using Tomasi's polarizable continuum model. Results for geminal couplings are consistent with linear correlations connecting $^{2}J_{HH}$ with the coupling pathway occupation numbers taken from the literature. The present analysis suggests that both $^{2}J_{HH}$ and $^{3}J_{HH}$ coupling constants are sensitive probes to gauge the anomeric effect, as well as other hyperconjugative interactions.

Introduction

The importance of a lone-pair (LP) orientation in the conformational stability for several types of compounds, such as acetals, sugars, and nucleotides, is very well known.[1−5] For many years, the interaction that defines such lone-pair orientation was called the anomeric effect; now, it is also known, following Schleyer et al.,[6] as "negative hyperconjugative interaction". One rationalization of the nature of the anomeric effect is to consider it also to be a two-electron stabilizing shift from a lone pair of electrons on one oxygen atom to an antibonding σ^* orbital, adjacent to the C−O bond, one in the case of sugars and acetals. A similar effect is known for other types of lone-pair-bearing atoms (X); in this case, the σ^* antibonding orbital corresponds to a bond adjacent to the C−X bond, where X is an electronegative lone-pair bearing atom such as nitrogen. Although this interaction is strongest for an antiperiplanar arrangement between the LP and the σ^* antibonding orbital, it has also been observed for other conformations.[7] The anomeric effect is a fundamental stereoelectronic interaction and presents a profound influence on the molecular electronic structure, not limited to either acetals or ring systems.[1−3] At present, the natural bond orbital (NBO) approach of Weinhold et al.[8] has been frequently used to quantify the anomeric effect, as well as other hyperconjugative interactions.[9]

$^{1}J_{CH}$ couplings are known to be sensitive to the anomeric effect, and many authors[10] studied them from both experimental and theoretical approaches. Such studies show that, at least in many cases, $^{1}J_{CH}$ couplings are an adequate probe to gauge this interaction. Very early in the history of NMR spectroscopy, interproton couplings were recognized as powerful tools for elucidating molecular structures.[11] Since the pioneering work of Ramsey,[12] it has been considered that couplings involving not only protons but also other light atoms are dominated by the Fermi contact term. Now, high-level ab initio calculations tend to confirm such a trend, although in some instances noncontact contributions can have a non-negligible influence, even in interproton couplings. Several cases were reported where, individually, noncontact contributions are more important than the FC term, but they almost cancel each other.[13]

SCHEME 1



The influence of the anomeric effect on $^{2}J_{HH}$ coupling constants was, by far, less studied than the influence of such interactions on $^{1}J_{CH}$ couplings.[14] It is known that experimental $^{2}J_{HH}$ couplings cover a very wide range of values from about −24 to +43 Hz,[15] and it is accepted that they depend on a variety of factors.[16,17] Recently,[18] for a CH_2 moiety placed α to an sp^2 carbon atom, for example, a carbonyl moiety such as acetaldehyde (**1**) or a C=C double bond such as that in propene (**2**) (Scheme 1), eq 1 was written for different values of φ, the rotation angle around the $C(sp^2)-C(sp^3)$ bond, to account for the DFT-calculated FC contribution to the $^{2}J_{HH}$ coupling constant

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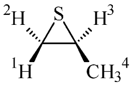
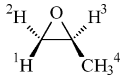
$$^2J_{H_2,H_3}\,(\mathrm{Hz}) = J_0 + A\Sigma\Delta\mathrm{occ}(\sigma_{C_\alpha-H_{2,3}}) + B\Sigma\Delta\mathrm{occ}(\sigma^*_{C_\alpha-H_{2,3}}) \quad (1)$$

where ΣΔocc is the sum of the differences between the NBO occupancies of the $\sigma_{C_\alpha-H_{2,3}}$ bonding orbitals containing both coupled protons for an angle φ and those corresponding to $\varphi = 0°$ (and the analogous quantity for the respective ($\sigma^*_{C_\alpha-H_{2,3}}$) antibonding orbitals). For **1**, we obtained $J_0 = -19.38$, $A = 324$, and $B = 1249$, whereas for **2**, the following eq 1 parameters were reported: $J_0 = -18.30$, $A = 616$, and $B = 720$. These parameters for eq 1 indicate that for compounds **1** and **2** hyperconjugative interactions from the coupling pathway yield negative increases in the $^2J_{HH}$ coupling, whereas hyperconjugative interactions into the coupling pathway yield positive increases in the $^2J_{HH}$ coupling. As examples of how the anomeric effect affects $^2J_{HH}$ couplings, methylamine (**3**) and methanol (**4**) were taken as model compounds,[18] and the FC term of $^2J_{H_2,H_3}$ was calculated for different rotation angles, φ, around the C−N and C−O bonds, respectively. It should be recalled that the inductive effect is not expected to depend on φ; therefore, the plots shown in Figure 27 of ref 18 mainly reflect the influence of the anomeric effect (negative hyperconjugative interactions) on $^2J_{H_2,H_3}$. A plot of these couplings versus the sum of the NBO occupancies of the ($\sigma^*_{C_\alpha-H_{2,3}}$) antibonding orbitals shows that for both compounds $^2J_{H_2,H_3}$ increases monotonically when that sum was increased.[18] This indicates that negative hyperconjugative interactions, as well as other hyperconjugative interactions, qualitatively affect $^2J_{HH}$ couplings in the same way. However, the influence of the former is notably more important than that of the latter.

Vicinal proton−proton coupling constants, $^3J_{HH}$, in H−C−C−H fragments are a powerful tool for structural elucidation and conformational analysis of molecules in solution[19] because of their Karplus-type dependence[20] on the corresponding dihedral angle. During the last two decades, several factors that affect the standard Karplus curve, such as bond angles, bond lengths, substituent electronegativity, and orientation, were studied.[15,21] It is already known that hyperconjugative interactions involving either bonding or antibonding orbitals belonging to the coupling pathway could have a significant influence on the respective FC term of such vicinal couplings,[18] although it seems that the relationship between hyperconjugative interactions and vicinal couplings is more complicated than the effect of such interactions on geminal couplings. Apparently, the FC term of other types of couplings involving ^{13}C and ^{15}N nuclei are similarly influenced by hyperconjugative interactions.[13]

To gain further insight into the effect of hyperconjugative interactions on $^2J_{HH}$ and $^3J_{HH}$ coupling constants, we report the study of 2-methylthiirane (**5**) and 2-methyloxirane (**6**) (Scheme 1), which were chosen as model compounds. This choice was based on the following considerations. (1) The antibonding orbitals corresponding to the C−H bonds, bound to these small, strained, cyclic heteroatom compounds, are expected to be very good electron acceptors for hyperconjugative interactions. There are two reasons for expecting such behaviors, and both of them are based on Bent's rule,[22] namely, (i) an electronegative atom is bound α to the CH_2 moiety; and (ii) the strained ring C−C bond presents low s % character. Therefore, the ring C−H bonds in **5** and **6** should show high s % character at the C atom (vide infra), and their antibonding orbitals are good electron acceptors. (2) Both heteroatoms belong to group VI of the periodic table, but they are expected to show notably different anomeric effects because they belong to different rows of the periodic table. Such a difference in the anomeric effect for O and for S atoms is observed when comparing the relation between the axial-$^1J_{C_2H_2}$ and equatorial-$^1J_{C_2H_2}$ couplings, which is reversed when going from *cis*-4,6-dimethyl-1,3-dioxane to the 1,3-dithiane analogue.[10d] Therefore, compounds **5** and **6** can be considered to be test cases, and the trends observed in this study could be expected to hold for the FC term of other geminal and vicinal couplings involving either ^{13}C or ^{15}N isotopes. The proton spectra of **5** and **6** were taken at 500 MHz, and the corresponding experimental $^{2,3}J_{HH}$ couplings were determined. The coupling constants were calculated within the DFT framework, and the hyperconjugative interactions were studied with the NBO method.[8]

TABLE 1: Proton Chemical Shifts (ppm) and Coupling Constants (Hz) for 2-Methylthiirane (5) and 2-Methyloxirane (6) in $CDCl_3$[a,b]

compounds		
H^1	2.12	2.43
H^2	2.51	2.75
H^3	2.92	3.00
H^4	1.51	1.32
$^2J_{H_1H_2}$	1.07 (−1.37)[c]	5.11 (5.66)[d]
$^3J_{H_1H_3}$	5.72 (5.54)[c]	2.71 (2.52)[d]
$^3J_{H_2H_3}$	6.34 (6.60)[c]	4.27 (4.06)[d]
$^3J_{H_3H_4}$	5.72	5.23

[a] Only absolute values of SSCCs were measured in this work. [b] Manatt et al.[37] reported for styrenimine: $^2J_{H_1H_2} = 0.87$ Hz, $^3J_{H_1H_3} = 3.29$ Hz, and $^3J_{H_2H_3} = 6.12$ Hz. [c] Measured by Manatt et al.[37] in styrene sulfide. [d] Measured by Manatt et al.[36] in styrene oxide.

Experimental Details

NMR Measurements. Compounds **5** and **6** are commercially available (Acros) and were used without further purification because they did not show any impurity in the proton NMR spectra. The ^1H NMR spectra were obtained on a Varian INOVA spectrometer operating at 499.88 MHz for solutions of ca. 20 mg in 0.8 mL of $CDCl_3$, with a probe temperature of ca. 25 °C. ^1H spectra were referenced to internal TMS, and typical conditions for taking the spectra were 48 transients, and spectral width of 4000 Hz, with 32k data points and zero filled to 128k to give a digital resolution of 0.06 Hz. Under such conditions, the spectra of both compounds are first order; therefore, the chemical shifts and the absolute values of the coupling constants were taken directly from the spectra (Table 1).

Computational Approach. All DFT calculations were carried out with the Gaussian 98 package of programs[23] using the B3LYP functional.[24,25] The aug-cc-pVTZ basis set was employed for geometry optimizations, and occupancy numbers and energies of hyperconjugative interactions were calculated with the NBO program.[26] All four isotropic contributions to SSCCs, that is, Fermi contact, J^{FC}, spin−dipolar, J^{SD}, diamagnetic spin−orbit, J^{DSO}, and paramagnetic spin−orbit, J^{PSO}, were calculated within the DFT framework. Their calculation was implemented within the Gaussian 98 program, where all three second-order terms were evaluated either within the FPT single-perturbation[27] approach (J^{FC} and J^{SD}) or within the coupled perturbed Kohn−Sham approach,[28] CP−KS (J^{FC} and J^{PSO}). Both types of approaches correspond to the same approximation, and for the implementation used in this work, it was verified that J^{FC} numerical values for FPT and CP−KS approaches are equal within 0.01 Hz. A detailed description of the corresponding implementation is presented in Peralta et al.'s paper.[29] The J^{DSO} term was obtained as the mean value of the DSO operator in the unperturbed reference state. The one-electron integrals for

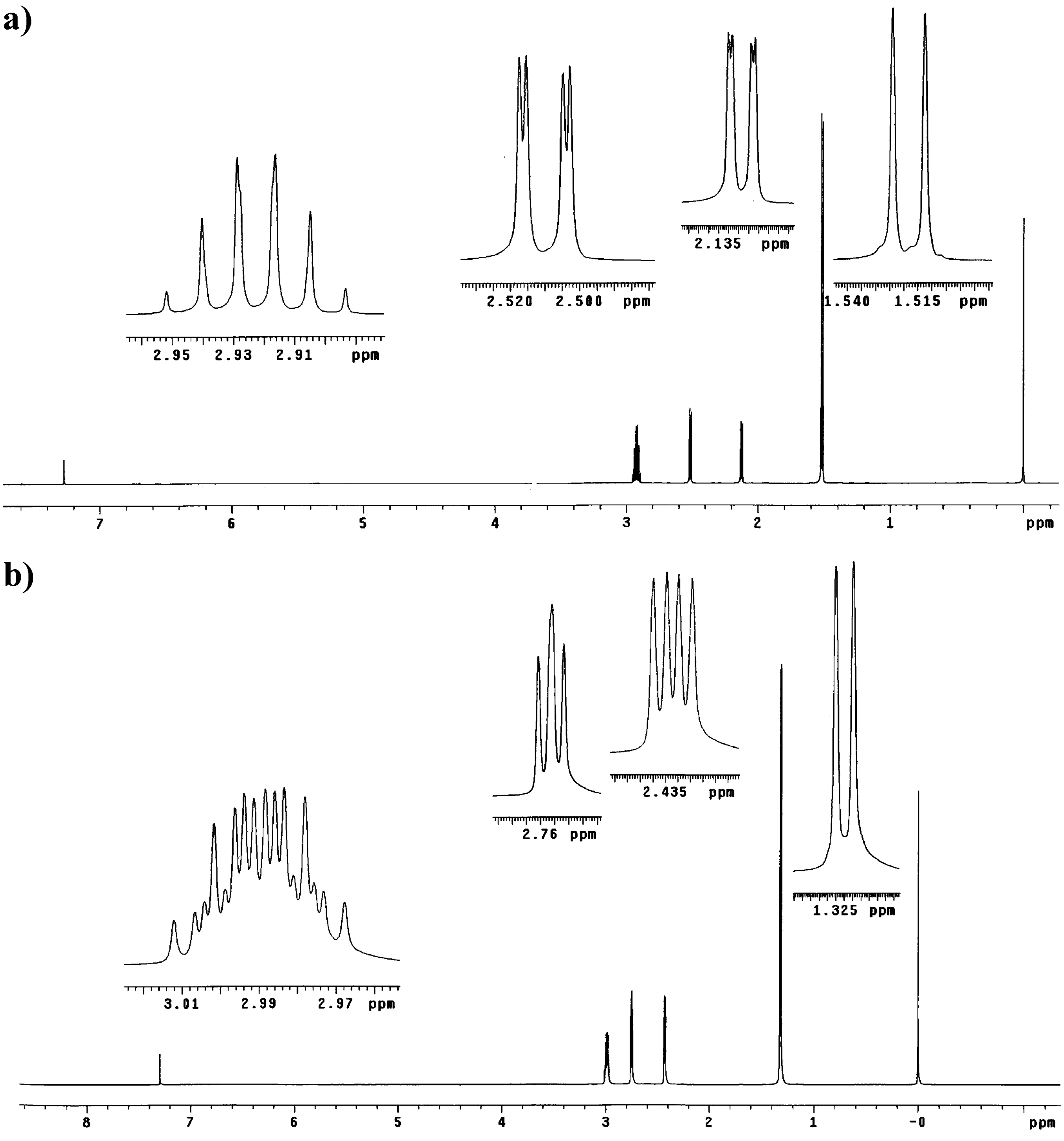


Figure 1. ^{1}H NMR spectrum in CDCl$_3$ at 500 MHz for (a) 2-methylthiirane (**5**), and (b) 2-methyloxirane (**6**).

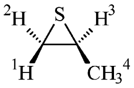
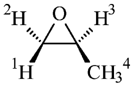
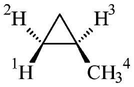
the PSO and DSO operators were computed with the Dalton 1.1 program.[30]

To calculate SSCC contributions, we used two different types of basis sets. The J^{PSO} and J^{DSO} contributions were calculated by employing the correlation-consistent triple-ζ basis sets (cc-pVTZ). The J^{FC} and J^{SD} terms were calculated using the aug-cc-pVTZ-J[31] basis set, which is essentially the aug-cc-pVTZ[32] basis set, but it was optimized for calculating SSCC by augmenting it with four tight s functions with very large exponents, which are crucial for a correct description of the J^{FC} term.[33] The aug-cc-pVTZ-J basis set performance within the DFT framework was recently studied, and its potential to calculate SSCCs was determined.[34] The dielectric medium effect is included in the FPT calculation of the FC term using the polarizable continuum model, PCM, of Tomasi et al.[35]

Results and Discussion

Under the conditions described above, the ^{1}H NMR spectra for compounds **5** and **6**, Figure 1, show, as expected, four different signals, one for each ring hydrogen and one for the three methyl protons, although they present different coupling patterns. The corresponding chemical shifts and coupling constants are displayed in Table 1. These coupling constants are compared, respectively, with those reported for styrene sulfide[36] and styrene oxide,[37] which are compounds that are analogous to **5** and **6**, where the methyl group is replaced by a

TABLE 2: Comparison between Calculated[a] and Experimental ($CDCl_3$) $^nJ_{HH}$ Couplings (Hz) in 5, 6, and 7

Compounds	$^nJ_{HH}$	$J^{FC\,a}$	J^{SD}	J^{PSO}	J^{DSO}	$J_{cal.}$	$J_{exp.}$
	$^2J_{H_1H_2}$	-1.37	0.36	3.12	-2.92	-0.81	-1.07
	$^3J_{H_1H_3}$	6.09	0.00	2.48	-2.80	5.77	5.72
(5)	$^3J_{H_2H_3}$	7.13	0.16	0.24	-0.10	7.34	6.34
	$^3J_{H_3H_4}$	6.52	0.05	1.32	-1.34	6.55	5.72
	$^2J_{H_1H_2}$	5.46	0.35	2.94	-3.10	5.65	5.11
	$^3J_{H_1H_3}$	2.40	0.02	2.72	-3.11	2.03	2.71
(6)	$^3J_{H_2H_3}$	4.05	0.12	0.37	-0.42	4.12	4.27
	$^3J_{H_3H_4}$	5.82	0.05	1.31	-1.46	5.72	5.23
	$^2J_{H_1H_2}$	-5.52	0.29	3.14	-3.11	-5.20	-3.0[b]
	$^3J_{H_1H_3}$	5.36	0.00	2.56	-2.85	5.07	5.0[b]
	$^3J_{H_2H_3}$	9.14	0.14	0.29	-0.29	9.28	8.5[b]
(7)	$^3J_{H_3H_4}$	6.68	0.07	1.18	-1.30	6.63	

[a] The FC and SD terms were calculated at the FPT-B3LYP/aug-cc-pVTZ-J level for H and C atoms and FPT-B3LYP/aug-cc-pVTZ for O and S atoms. [b] Predicted by Manatt et al.[36]

phenyl group. It is observed that the three-bond ring J_{HH} SSCCs are similar for analogous compounds. As expected from the different patterns of their ^1H NMR spectra, two- and three-bond J_{HH} SSCCs are notably different for compounds **5** and **6**, although the bond angles and dihedral angles are similar. In fact, optimized $H_1-C-C-H_3$ and $H_2-C-C-H_3$ dihedral angles are 149.6 and 154.7° and 2.8 and 1.1° for **5** and **6**, respectively.

The calculated J^{FC}, J^{SD}, J^{PSO}, and J^{DSO} contributions to isotropic J_{HH} SSCCs in **5**, **6**, and methylcyclopropane (**7**), considering an isolated molecule are shown in Table 2, being that the following features of such data deserve comment. Both geminal and vicinal coupling constants are dominated by the FC term, although for the geminal coupling in **5**, the absolute values of the J^{PSO} and J^{DSO} terms are larger than that of the J^{FC} term; however, they are of opposite sign and almost cancel each other. In **6**, the J^{PSO} and J^{DSO} terms of $^2J_{HH}$ are similar in magnitude to those in **5**, but the algebraic value of the corresponding J^{FC} term is notably larger. The J^{DSO} term follows a well-known trend; that is, if the space spanned by the electrons of a given molecule is partitioned into two regions considering a sphere whose diameter is determined by the distance separating both coupled protons, then electrons inside such a sphere yield a negative contribution, whereas those outside the sphere yield a positive contribution.[38] In concordance with such a trend, the J^{DSO} term of the $^2J_{HH}$ SSCC in **6** is more negative than that in **5** because the C−O bond is shorter than the C−S bond. The marked difference between the J^{DSO} contribution to $^3J_{H_1H_3}$ and $^3J_{H_2H_3}$, in each compound, can also be rationalized on the same grounds, remembering the difference in the respective H−C−C−H dihedral angles. A J^{DSO} term, similar to that calculated for $^3J_{H_1H_3}$ SSCCs was reported by Sauer et al.[39] for $^3J_{HH}$ in ethane in the 180° dihedral angle conformation (−3.13 Hz).

TABLE 3: Comparison of Significant NBO Interactions (in kcal mol^{-1}) for 2-Methylthiirane (5) and 2-Methyloxirane (6)

	energy	
orbital interactions	**5**	**6**
$LP_2(X) \rightarrow s^*_{C_6-H_3}$	2.70	5.62
$LP_2(X) \rightarrow s^*_{C_4-H_1}$	2.92	5.24
$LP_2(X) \rightarrow s^*_{C_4-H_2}$	2.90	5.42
$LP_2(X) \rightarrow s^*_{C_6-C_7}$	2.74	4.78
$^a\sigma_{X5-C6} \rightarrow s^*_{C_4-H_1}$	1.62	1.40
$^a\sigma_{X5-C6} \rightarrow s^*_{C_4-H_2}$	1.86	1.40

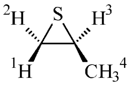
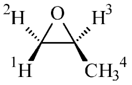
[a] X = S for compound **5** and X = O for compound **6**.

The very large difference between the J^{FC} term of $^2J_{HH}$ couplings in **5** (−1.37 Hz), **6** (+5.46 Hz), and **7** (−5.52 Hz) suggests that besides an electronegativity effect such differences are influenced by the stronger negative hyperconjugative interactions into the ($\sigma^*_{C_4-H_{1,2}}$) antibonding orbitals in **6** than in **5**, which are absent in **7**. The difference in these interactions can be quantified by comparing the energies of the interactions $LP_2(O) \rightarrow (\sigma^*_{C_4-H_{1,2,3}})$ and $LP_2(S) \rightarrow (\sigma^*_{C_4-H_{1,2,3}})$ (LP_2 corresponds to the lone pair NBO orbital with higher energy), which are presented in Table 3. Energies of $(\sigma_{O-C_6}) \rightarrow (\sigma^*_{C_4-H_{1,2}})$ and $(\sigma_{S-C_6}) \rightarrow (\sigma^*_{C_4-H_{1,2}})$ hyperconjugative interactions are also displayed, which are notably smaller than the negative hyperconjugative interactions. Moreover, the occupancies of the NBO LP_2 and $(\sigma^*_{C_4-H_{1,2,3}})$ orbitals also convey an idea about the importance of such interactions, which are compared for **5**, **6**, and **7** (Table 4). In the same Table, the s % character at the C atom of the $(\sigma_{C-H_{1,2,3}})$ bond orbitals is also shown. The high s % character indicates that the respective antibonding orbitals are very good electron acceptors. The negative hyperconjugative interactions are notably more important in **6** than in **5**, and this fact is also appreciated by comparing the respective occupancies

TABLE 4: NBO Carbon s % Character of the C−H Bonds and Occupancy of the σ^*_{C-H} Antibonding Orbitals and the LP$_2$(X) (10^{-4}), Calculated at the B3LYP/aug-cc-pVTZ Level for Compounds 5 (X = S), 6 (X = O), and 7

	carbon **s** % character			occupancy			
	C_4-H_1	C_4-H_2	C_6-H_3	σ^*_{C4-H1}	$\sigma^*_{C_4-H_2}$	$\sigma^*_{C_6-H_3}$	LP$_2$(X)
5	28.75	28.80	26.59	190	184	262	19 460
6	29.70	29.64	27.22	216	212	292	19 285
7	27.84	27.78	25.44	122	114	204	

TABLE 5: Comparison between Experimental ($CDCl_3$) and Calculated $^nJ_{HH}{}^a$ Couplings (Hz) Including Solvent Effect (PCM)

Compounds	$^nJ_{HH}$	ε = 1	$CHCl_3$	Acetone	$J_{exp}{}^b$
 (**5**)	$^2J_{H_1H_2}$	-0.81	-1.07	-1.15	-1.07
	$^3J_{H_1H_3}$	5.77	5.94	5.91	5.72
	$^3J_{H_2H_3}$	7.34	7.47	7.48	6.34
	$^3J_{H_3H_4}$	6.50^c	6.52^c	6.52^c	5.72
 (**6**)	$^2J_{H_1H_2}$	5.65	5.33	5.22	5.11
	$^3J_{H_1H_3}$	2.03	2.10	2.12	2.71
	$^3J_{H_2H_3}$	4.12	4.28	4.37	4.27
	$^3J_{H_3H_4}$	5.72^c	5.71^c	5.72^c	5.23

[a] The FC term was calculated at the FPT-B3LYP/aug-cc-pVTZ-J level for H and C atoms and at the FPT-B3LYP/aug-cc-pVTZ level for O and S atoms. [b] Samples prepared in $CDCl_3$. Only the absolute values of couplings were determined. [c] Average value of coupling with the three methyl protons.

$$J_{av} = \frac{H_3H_8 + H_3H_9 + H_3H_{10}}{3} = \frac{3.38 + 13.50 + 2.63}{3} = 6.50 \text{ Hz}$$

of the ($\sigma^*_{C_4-H_{1,2,3}}$) antibonding orbitals. This observation is compatible with the more positive $^2J_{HH}$ SSCC in **6** than those in **5** and **7**.[18] It should be noted that although $^2J^{FC}$ in **7** is notably more negative than $^2J^{FC}$ in **5** and $^2J^{FC}$ in **6** it is notably more positive than in unstrained saturated hydrocarbons, where it is known that $^2J_{HH}$ is ca. -12 Hz.[13] It should be recalled that methylcyclopropane is a strained compound where (σ_{C-C}) → (σ^*_{C-H}) = 2.40 kcal mol^{-1} hyperconjugative interactions take place.

It is known that for a given compound the negative hyperconjugative interactions are slightly inhibited by the solvent dielectric effect.[40] NBO analysis of such interactions taking into account solvent effects yields the following results. The energies of the LP$_2$ → ($\sigma^*_{C_4-H_{1,2}}$) interactions are 2.90 kcal mol^{-1} in compound **5** for $\epsilon = 1$, whereas for ϵ corresponding to chloroform, the energy for the same interaction is 2.84 kcal mol^{-1} and for ϵ corresponding to acetone, is 2.80 kcal mol^{-1}. Similar differences were also observed for compound **6**. The J^{FC} term of the J_{HH} couplings, in **5** and **6**, was also calculated including the solvent dielectric effect, which was taken into account using the PCM model.[31] Solvent effects on the remaining three terms of SSCCs were not taken into account. Results for **5** and **6** considering solvent dielectric constants corresponding to chloroform and acetone are compared in Table 5, where the FC term (including the solvent dielectric effect) plus all other three contributions calculated in an isolated molecule ($\epsilon = 1$), are compared with experimental SSCCs. The following features of data shown in Table 5 are noted.

Geminal Couplings. This type of SSCC becomes more negative, both for **5** and **6**, when increasing the solvent dielectric constant, that is, when inhibiting slightly the negative hyperconjugative interactions. This result is then compatible with assuming that the anomeric effect causes an algebraic increase in the $^2J_{HH}$ SSCC. This is further supported when noting that the solvent dielectric effect on $^2J_{HH}$ in **6** is larger than that in **5**. It is also noted that the total $^2J_{HH}$ SSCCs are in better agreement with experimental values when taking into account the solvent dielectric effect on the J^{FC} term. It is noteworthy that the J^{FC} term of $^2J_{HH}$ in **5** and **6** shows a solvent influence similar to that reported by Webb et al.[41] for the $^2J_{CH}$ coupling across the carbonyl group in acetaldehyde and on the absolute value of $^2J_{NH}$ coupling in formamide.[42] Recently,[43] it was shown that in acetaldehyde this trend originates in the J^{FC} term of this $^2J_{CH}$ coupling, which, like other geminal SSCCs through a carbonyl group,[44] is unusually large and positive, provided the magnetogyric ratios of both coupled nuclei are of the same sign. This feature of geminal SSCCs through a carbonyl carbon atom is originates in part from the strong hyperconjugative interactions involving the p-type carbonyl oxygen lone pair and the antibonding orbitals belonging to the coupling pathway.[13,16]

Vicinal Couplings. The calculated solvent dielectric effects for **5** and **6** on the J^{FC} term for both $^3J_{H_1H_3}$ and $^3J_{H_2H_3}$ are of opposite sign to those for the geminal couplings, and their absolute values are smaller. Moreover, for compound **5**, the calculated solvent effect on $^3J_{H_1H_3}$ (dihedral H−C−C−H is about 150°) is slightly more important than that on $^3J_{H_2H_3}$ (dihedral H−C−C−H about 0°), but this trend is reversed for compound **6**. Such a trend suggests that the influence of negative hyperconjugative interactions on $^3J_{HH}$ SSCCs is more important for a 0° conformation than for a 150° conformation. The influence of hyperconjugative interactions on $^3J_{HH}$ couplings are known to be more complicated than that on the $^2J_{HH}$ couplings.[15] The first distinction to be made is between hyperconjugative interactions (a) within the coupling pathway and (b) involving nearby bonds or antibonding orbitals. Those of type a seem to enhance $^3J_{HH}$ couplings,[15b] as well as the J^{FC} term of $^3J_{CH}$ couplings.[45] Those of type b in an H−C−C−H fragment and corresponding to either hyperconjugative interactions into the (σ^*_{C-H}) antibonding orbitals or hyperconjugative interactions from the C−H bond orbitals cause a decrease in the $^3J_{HH}$ coupling.[13] Hyperconjugative interactions into the (σ^*_{C-C}) antibonding orbital also cause a decrease in $^3J_{HH}$ coupling, as is well known.[46,13] These considerations can shed some light on the trends observed for the values reported in Table 2, both for the $^3J^{FC}$ and experimental $^3J_{HH}$ SSCCs. It is noted that there is a remarkable difference in $^3J_{H_2,H_3}$ couplings along the series **7** > **5** > **6**, which parallels the increase in the negative hyperconjugative interactions involving the ($\sigma^*_{C-H_{2,3}}$) antibonding orbitals. Moreover, $^3J_{H_1H_3}$ is notably smaller in **6** than in **5**, which is slightly larger than in **7**. This suggests that the Karplus-like relationship must be markedly affected when the corresponding (σ^*_{C-H}) antibonding orbitals are involved in strong negative hyperconjugative interactions with nearby nonbonding electron pairs; $^3J_{HH}$ SSCCs for an almost cis configuration seem to be more affected than for a 150°

configuration. Furthermore, ${}^3J_{H_3HMe}$ in **6** is only slightly smaller than ${}^3J_{H_3HMe}$ in **5**. A different sensitivity between cis and trans ${}^3J_{HH}$ SSCCs through the H−C−N−H pathway was reported in formamide where Vaara et al.[46c] measured 2.25 and 13.90 Hz for cis and trans ${}^3J_{HH}$ SSCCs, respectively. The last coupling was also measured recently by Farrar et al.[47] in a dilute solution of CCl_4, trans ${}^3J_{H,H} = +13.7$ Hz was obtained. If these two couplings are calculated using the Karplus-like relationship obtained by Hu and Bax[48] for vicinal couplings through an H−C−N−H fragment, then the values of 7.22 and 10.06 Hz were obtained for cis and trans ${}^3J_{HH}$ SSCCs, respectively; that is, the strong hyperconjugative interactions that take place in formamide, $LP(O_p) \rightarrow (\sigma^*_{Cc-N})$ and $LP(O_p) \rightarrow (\sigma^*_{Cc-H})$, seem to cause a notable decrease in the former but an increase in the latter.

Conclusions

Very important differences both for ${}^2J_{HH}$ and ${}^3J_{HH}$ couplings and for negative hyperconjugative interactions, $LP_2(S) \rightarrow \sigma^*_{C-H}$ and $LP_2(O) \rightarrow \sigma^*_{C-H}$ in compounds **5** and **6**, are observed. These observed trends indicate that both types of SSCCs are very sensitive to hyperconjugative interactions, being, as a consequence, interesting probes to gauge hyperconjugative interactions in general and, in particular, those corresponding to the anomeric effect. Results presented in this work are compatible with the influence of hyperconjugative interactions on ${}^2J_{HH}$ discussed in the literature;[18] that is, hyperconjugative interactions into antibonding orbitals belonging to the coupling pathway cause a significant algebraic increase in the ${}^2J_{HH}$ coupling, and hyperconjugative interactions from the bond orbitals belonging to the coupling pathway cause an algebraic decrease in the corresponding ${}^2J_{HH}$ coupling.

The influence of hyperconjugative interactions on ${}^3J_{HH}$ couplings seem to be more complicated than the trends for ${}^2J_{HH}$ couplings. However, some simple cases can be quoted. Results discussed in this work suggest that hyperconjugative interactions into the (σ^*_{C-H}) antibonds for an H−C−X−H (X = C, N) fragment, coupling pathways that cause important reductions in vicinal ${}^3J_{HH}$ couplings, seem to be more important for a cis than for a trans configuration. However, hyperconjugative effects into the (σ^*_{C-C}) antibond seem to affect, notably, the Karplus dependence on the dihedral angle.

Results presented in this work are consistent with a slight inhibition of the anomeric effect due to the solvent dielectric effect. For this reason, ${}^{2,3}J_{HH}$ couplings whose coupling pathways are involved in very strong negative hyperconjugative interactions are expected to be solvent-dependent.

Trends discussed in this work were found to originate in the ${}^{FC}J_{HH}$ contribution to ${}^{2,3}J_{HH}$ SSCCs. This suggests that the ${}^{FC}J$ contribution to other types of SSCCs such as J_{CC} SSCCs should be similarly affected when bonding and antibonding orbitals, belonging to the coupling pathway, are involved in negative hyperconjugative interactions.

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References and Notes

(1) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; John Wiley & Sons: New York, 1994.

(2) Kirby, J. A. *Stereoelectronic Effects*; Oxford University Press: New York, 2000.

(3) Morris, D. G. *Stereochemistry*; The Royal Society of Chemistry: Exeter, U.K., 2001.

(4) Juaristi, E., Ed. *Conformational Behavior of Six-membered Rings: Analysis, Dynamics, and Stereoelectronic Effects*; VCH Publishers: New York, 1995.

(5) Perrin, C. L. *Acc. Chem. Res.* **2002**, *35*, 28.

(6) Reed, A. E.; Schleyer, P. v. R.. *J. Am. Chem. Soc.* **1990**, *112*, 1434.

(7) King, J. F.; Rathore, R.; Guo, Z.; Li, M.; Payne, N. C. *J. Am. Chem. Soc.* **2000**, *122*, 10308.

(8) Reed, A. E.; Curtis, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

(9) (a) Alabugin, I. V. *J. Org. Chem.* **2000**, *65*, 3910. (b) Hetémyi, A.; Martinek, T. A.; Lázár, L.; Zalán, Z.; Fülöp, F. *J. Org. Chem.* **2003**, *68*, 5705. (c) Alabugin, I. V.; Manoharan, M.; Zeidan, T. A. *J. Am. Chem. Soc.* **2003**, *125*, 14015.

(10) (a) Perlin, A. S.; Casu, B. *Tetrahedron Lett.* **1969**, 2921. (b) Wolfe, S.; Pinto, B. M.; Varma, V.; Leung, R. Y. N. *Can. J. Chem.* **1990**, *68*, 1051. (c) Cuevas, G.; Juaristi, E.; Vela, A. *J. Phys. Chem*. A **1999**, *103*, 932. (d) Cuevas, G.; Juaristi, E. *J. Am. Chem. Soc*. **2002**, *124*, 13088. (e) Malkina, O. L.; Hricovíni, M.; Bízik, F.; Malkin, V. G. *J. Phys. Chem. A* **2001**, *105*, 9188. (f) Cloran, F.; Carmichael, I.; Serianni, A. S. *J. Phys. Chem. A* **1999**, *103*, 3783. (g) Cloran, F.; Zhu, Y.; Osborn, J.; Carmichael, I.; Serianni, A. S. *J. Am. Chem. Soc*. **2000**, *122*, 6435. (h) Stenutz, R.; Carmichael, I.; Widmalm, G.; Serianni, A. S. *J. Org. Chem*. **2002**, *67*, 949.

(11) Sproviero, E. M.; Burton, G. *J. Phys. Chem. A* **2002**, *106*, 7834.

(12) Ramsey, N. F. *Phys. Rev.* **1953**, *91*, 303.

(13) Contreras, R. H.; Barone, V.; Peralta, J. E.; Facelli, J. C. *Annu. Rep. NMR Spectrosc.* **2003**, *51*, 167.

(14) Contreras, R. H.; Peralta, J. E.; Giribet, C. G.; Ruiz de Azúa, M. C.; Facelli, J. C. *Annu. Rep. NMR Spectrosc.* **2000**, *41*, 55.

(15) Mahaim, C.; Currupt, P. A.; Vogel, P. *Helv. Chim. Acta* **1985**, *68*, 2182.

(16) Pople, J. A.; Bothner-By, A. A. *J. Chem. Phys.* **1965**, *42*, 1339.

(17) (a) Barfield, M.; Grant, D. *J. Am. Chem. Soc.* **1963**, *85*, 1899. (b) Wong, T. C.; Clark, G. R. *J. Chem. Soc., Chem. Commun.* **1944**, 1518. (c) Williams, D. H.; Bacca, N. S. *Chem. Ind. (London)* **1965**, 506. (d) Sternhell, S. *Q. Rev.* **1969**, *23*, 236.

(18) Contreras, R. H.; Peralta, J. E. *Prog. Nucl. Magn. Reson. Spectrosc.* **2000**, *37*, 321.

(19) (a) Freitas, M. P.; Rittner, R.; Tormena, C. F.; Abraham, R. J. *J. Phys. Org. Chem.* **2001**, *14*, 317. (b) Yoshinaga, F.; Tormena, C. F.; Freitas, M. P.; Rittner, R.; Abraham, R. J. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1494. (c) Freitas, M. P.; Tormena, C. F.; Rittner, R.; Abraham, R. J. *J. Phys. Org. Chem.* **2003**, *16*, 27.

(20) Karplus, M. *J. Chem. Phys*. **1959**, *30*, 11.

(21) (a) Esteban, A. L.; Galache, M. P.; Mora, F.; Diez, E.; Casanueva, J.; Fabian, J. S.; Barone, V.; Peralta, J. E.; Contreras, R. H. *J. Phys. Chem. A* **2001**, *105*, 5298. (b) Minch, M. J. *Conc. Magn. Reson.* **1994**, *6*, 41. (c) Thomas, W. A. *Prog. NMR Spectrosc*. **1997**, *30*, 183. (d) Altona, C. In *Encyclopedia of NMR*; Grant, D. M., Harris, R. K., Eds.; Wiley: Chichester, U.K., 1996; Vol. 8, p 4909. (e) Imai, K. and Osawa, E. *Magn. Reson. Chem*. **1990**, *28*, 668.

(22) Bent, H. A. *Chem. Rev.* **1961**, *61*, 275.

(23) 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.; 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. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(24) Becke, A. D. *Phys. Rev.* **1988**, *A 38*, 3098.

(25) Lee, C.; Yang, W.; Parr, R, G. *Phys. Rev. B* **1988**, *37*, 785.

(26) Glendening, E. D.; Reed, A. E.; Carpenter, J. E.; Weinhold, F. NBO, version 3.1; Gaussian, Inc.: Pittsburgh, PA, 1998. (Included in the Gaussian98 package of programs.)

(27) Pople, J. A.; Beveridge, D. L. *Approximate Molecular Orbital Theory*; McGraw-Hill: New York, 1970.

(28) (a) Sychrovský, V.; Gräfenstein, J.; Cremer, D. *J. Chem. Phys.* **2000**, *113*, 3530. (b) Helgaker, T.; Watson, M.; Handy, N. C. *J. Chem. Phys.* **2000**, *113*, 9402.

(29) Barone, V.; Peralta, J. E.; Contreras, R. H.; Snyder, J. P. *J. Phys. Chem. A* **2002**, *106*, 5607.

(30) Helgaker, T.; Jensen, H. J. A.; Jørgensen, P.; Olsen, J.; Ruud, K.; A×c1gren, H.; Andersen, T.; Bak, K. L.; Bakken, V.; Christiansen, O.; Dahle, P.; Dalskov, E. K.; Enevoldsen, T.; Fernandez, B.; Heiberg, H.;

Hettema, H.; Jonsson, D.; Kirpekar, S.; Kobayashi, R.; Koch, H.; Mikkelsen, K. V.; Norman, P.; Packer, M. J.; Saue, T.; Taylor, P. R.; Vahtras, O. *Dalton*, version 1.1; , University of Oslo: Oslo, Norway, 1999; http://www.kjemi-.uio.no/software/dalton/dalton.html.

(31) Provasi, P. F.; Aucar, G. A.; Sauer, S. P. A. *J. Chem. Phys.* **2001**, *115*, 1981.

(32) Kendall, R. A.; Dunning, T. H.; Harrison, R. J. *J. Chem. Phys.* **1992**, *96*, 6796.

(33) Helgaker, T.; Jaszuński, M.; Rudd, K. *Chem. Rev.* **1999**, *99*, 293.

(34) Peralta, J. E.; Scuseria, G. E.; Cheeseman, J. R.; Frisch, M. J. *Chem. Phys. Lett*. **2003**, *375*, 452.

(35) (a) Mertius, S.; Scrocco, E.; Tomasi, J. *Chem. Phys.* **1981**, *55*, 117. (b) Mertius, S.; Tomasi, J. *Chem. Phys.* **1982**, *65*, 239.

(36) Elleman, D. D.; Manatt, S. L. *J. Mol. Spectrosc.* **1962**, *9*, 477.

(37) Manatt, S. L.; Elleman, D. D.; Brois, S. J. *J. Am. Chem. Soc.* **1965**, *87*, 2220.

(38) Pérez, J. E.; Ortíz, F. S.; Contreras, R. H.; Giribet, C. G.; Ruiz de Azúa, M. C. *J. Mol. Struct.: THEOCHEM* **1990**, *210*, 193.

(39) Grayson, M.; Sauer, S. P. A. *Mol. Phys*. **2000**, *98*, 1981.

(40) (a) Eliel, E. L.; Giza, G. A. *J. Org. Chem.* **1968**, *33*, 3754. (b) Lemieux R. U.; Pavia; A. A.; Marti, J. C.; Watanabe, K. A. *Can. J. Chem.* **1969**, *47*, 4427.

(41) Ando, I.; Inoue, Y.; Watanabe, S.; Sakamoto, Y.; Webb, G. A. *J. Mol. Liq.* **1984**, *27*, 179.

(42) (a) Taha, A. N.; True N. S. *J. Phys. Chem. A* **2000**, *104*, 2985. (b) Chuck, R. J.; Gilles, D. G.; Randall, E. W. *Mol. Phys.* **1969**, *16*, 121. (c) Vaara, J.; Kaski, J.; Jokisaari, J.; Diehl, P. *J. Phys. Chem. A* **1997**, *101*, 5069.

(43) Provasi, P. F.; Aucar, G. A.; Sauer, S. P. A. *Int. J. Mol. Sci.* **2003**, *4*, 231.

(44) Hansen, P. E. in *The Chemistry of Double-Bonded Functional Groups*; Patai, S., Ed.; Wiley: New York, 1989; chapter 3.

(45) Barone, V.; Peralta, J. E.; Contreras, R. H. *J. Comput. Chem*. **2001**, *22*, 1615.

(46) Gil, M. S.; von Philipsborn, W. *Magn. Reson. Chem*. **1989**, *27*, 409.

(47) Hansen, M. J.; Wendt, M. A.; Weinhold, F.; Farrar, T. C. *Mol. Phys*. **2002**, *100*, 2807.

(48) Hu, S.-J.; Bax, A. *J. Am. Chem. Soc*. **1997**, *119*, 6360.