Communication

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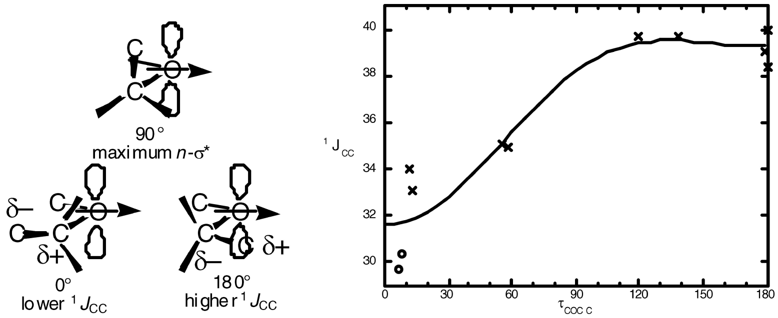

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One-Bond C−C Coupling Constants in Ethers Are Not Primarily Determined by *n*−*σ** Delocalization

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One-bond C−H coupling constants ($^1J_{CH}$) have been studied extensively. A major determinant is the hybridization of the carbon, since only an s orbital has electron density at the nucleus.[1] Another feature is the lower $^1J_{CH}$ value for an axial C−H bond adjacent to O or N in a six-membered ring, compared to equatorial. This is called the Perlin effect,[2] and it is often used for stereochemical assignment in sugars and related substances. It is invariably attributed to an $n-\sigma^*$ (anomeric) interaction, whereby a lone pair is delocalized into the antiperiplanar C−H bond,[3] as suggested in Figure 1.

Nevertheless, $^1J_{CH}$ values in three ethers were recently calculated to follow a cosine dependence on the HCOC dihedral angle τ.[4] This reproduces the Perlin effect, with a lower $^1J_{CH}$ at $\tau = 60°$ than that at 180°. Yet it diverges from the $\cos(2\tau)$ dependence of $n-\sigma^*$ delocalization, which was therefore rejected as accounting for $^1J_{CH}$. Those results are astounding, but they are exclusively computational and demand experimental verification.

We here demonstrate a cosine dependence of $^1J_{CC}$ on dihedral angle τ_{COCC}. Fourier analysis is crucial for this investigation, since a lower value at 60° than at 180° can be consistent with both $\cos(\tau)$ and $\cos(2\tau)$. To distinguish these, it is necessary to probe near 0°, which is not accessible experimentally for $^1J_{CH}$. We therefore turn to $^1J_{CC}$, which has also been studied extensively and used for stereochemical assignment.[5] Among the determinants are the hybridizations of the carbon orbitals (since J is proportional to s character), the inductive effect of substituents (which operates largely by hybridization changes), steric effects (which may also operate via hybridization), and antiperiplanarity to a heteroatom lone pair. Evidence for a C−C analogue to the Perlin effect is that $^1J_{CC}$ in 4,4,5-trimethyl-1,3-dioxane is 42.5 Hz to the equatorial methyl but only 39.0 Hz to the axial.[6] We here investigate whether antiperiplanar lone pairs are responsible for reducing $^1J_{CC}$. Rather than parametrize according to the dihedral angle between lone pair and C−C bond, we focus on the COCC dihedral angle τ.

We now report that the dominant contribution to $^1J_{CC}$ in a series of ethers is the $\cos(\tau)$ term, rather than the $\cos(2\tau)$ expected from $n-\sigma^*$ delocalization. Results are shown in Table 1 and Figure 2.[7] The data appear to show a monotonic increase from a minimum at 0° toward a maximum at 180°. This is consistent with the calculated $^1J_{CH}$ values in ethers[4] and confirms those calculations. The results also agree with calculated $^1J_{CC}$ in ethanol and ethylene glycol,[8] and it confirms that calculation too. However, it should be noted that no explanation was proposed for this behavior, which was not even recognized as unusual and which was later misstated as "minimal and maximal when the HOCC torsion angle is ~60° and ~180°" (perhaps because the reduction of $^1J_{CC}$ was attributed to an antiperiplanar lone pair).[9]

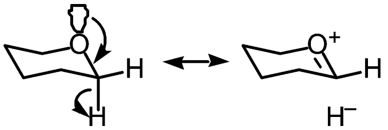

Figure 1. Delocalization of lone pair into antiperiplanar C−H bond, proposed to reduce $^1J_{CH}$.

Table 1. MM2-Calculated COCC Dihedral Angles and Observed Coupling Constants in Ethers

ether	τ (°)	$^1J_{CC}$ (Hz)
oxetane	6	29.8
3,3-dimethyloxetane	8	30.4
tetrahydrofuran	13[a]	33, 32.5[b]
7-oxabicyclo[2.2.1]heptane	56	35.1
tetrahydropyran	58	34.9
exo-2,3-epoxynorbornane	88	40.3[c]
1,1-dimethyloxirane	110	45.2[c]
2,2,5,5-tetramethyltetrahydrofuran	12[a], 120[a,c]	34, 39.7[c]
2-methyltetrahydrofuran	139[a]	39.6[c]
ethyl ether	179	39.1, 39.0[b]
butyl ether	180	38.4
tert-butyl ethyl ether	80[d]	40.0[d]

[a] Average. [b] At −85 °C in 1:1 $CDCl_3$:$CFCl_3$. [c] Exocyclic. [d] Ethyl.

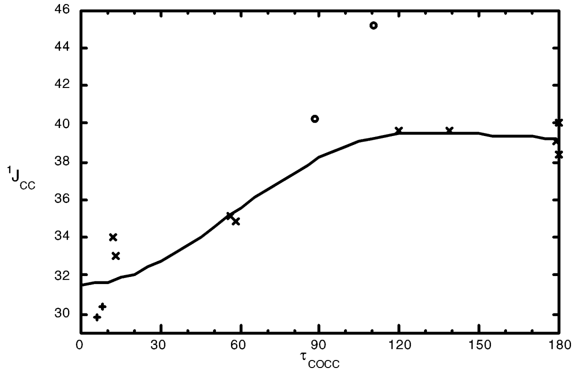

Figure 2. Dependence of $^1J_{CC}$ on COCC dihedral angle in ethers: (×) experimental, (+) oxetanes, (−) fit to eq 1, omitting epoxides (○).

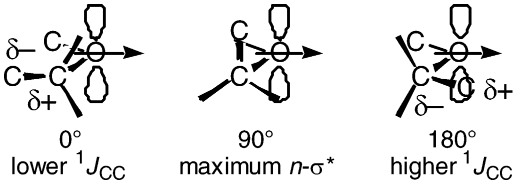

Figure 3. Variations with COCC dihedral angle of overlap between n_p and CC bond and of polarization of electron density by oxygen dipole.

The key finding is that J shows no minimum at a dihedral angle τ of 90°. This is where interaction between the σ^* orbital and the p lone pair (of highest energy and strongest delocalization, rather than any sp^3 hybrid) ought to reduce J the most. Figure 3 illustrates how $n_p-\sigma^*_{CC}$ delocalization is maximum at a COCC dihedral angle of 90°, not at the 60° characteristic of an antiperiplanar sp^3 lone pair. Yet the minimum J is clearly at 0°, when the C−C is

10.1021/ja0504284 CCC: $30.25

orthogonal to the p lone pair. Therefore, we must conclude that $^1J_{CC}$ is not determined by $n-\sigma^*$ delocalization!

Some of the scatter in Figure 2 is due to uncertainty about angles, owing to the flatness of the potential-energy surface. Some is due to averaging in flexible molecules. However, minor modifications of angle make little difference to the quality of Figure 2. Besides, a multiplicity of conformers cannot be a major source of error, since ^1J in tetrahydrofuran or ethyl ether is temperature-independent. The major source of scatter is variation with ring size. Epoxides deviate because the carbon of a three-membered ring devotes more s character to the exocyclic bond, thus increasing $^1J_{CC}$. If the two epoxides are excluded, three-term Fourier analysis of the data gives eq 1 (correlation coefficient $r = 0.95$), which is the solid curve in Figure 2. Oxetanes too deviate slightly, since there is more p character in the endocyclic bond, thus reducing $^1J_{CC}$, but correcting for all such variations was not successful. Regardless, 34 Hz at 0° is definitely lower than 39 Hz at 180°.

$$^1J_{CC} = 36.8 - 3.85\cos(\tau) - 1.4\cos(2\tau) \qquad (1)$$

The message of the Fourier analysis is that the magnitude of the coefficient of $\cos(\tau)$ is significantly larger than that of $\cos(2\tau)$. The latter represents the $n-\sigma^*$ delocalization, which is maximum at 90° and minimum at both 0 and 180°. Therefore, we must conclude that this does not determine $^1J_{CC}$! We also reject the claimed involvement of the hybridized σ lone pair on O,[10] since its delocalization into syn and anti C−C bonds should be nearly equal and thus show a $\cos(2\tau)$ dependence. It should be noted that the dominance of the $\cos(\tau)$ term and the appearance of Figure 2 are quite different from the familiar $\cos(2\tau)$ or $\cos^2(\tau)$ dependence (Karplus curve) of many ^3J. However, this is not a good model for the ^1J here.

We cannot exclude a small contribution to $^1J_{CC}$ from $n-\sigma^*$ delocalization. The $\cos(2\tau)$ term in eq 1 is not negligible. However, it is uncertain, since its coefficient is -1.4 ± 0.6. Besides, it arises largely from methyltetrahydrofuran and tetramethyltetrahydrofuran, where $^1J_{CC}$ is augmented by more s character in a bond exocyclic to a five-membered ring. Despite this uncertainty in whether there is any contribution to $^1J_{CC}$ from $n-\sigma^*$ delocalization, there is no question about the importance of $n-\sigma^*$ delocalization for anomeric stabilization, conformational preferences, and bond lengths.[11]

If $n-\sigma^*$ delocalization is not primarily responsible for the torsional dependence of $^1J_{CC}$, what is? A $\cos(\tau)$ dependence reverses between 0 and 180°. It was noted that the electrostatic field of the oxygen dipole exhibits just such a reversal.[4] Figure 3 illustrates this reversal, as the C−C bond goes from anti to syn relative to the dipole.

It was further proposed that this dipolar interaction acts through changes in electron density, as also suggested in Figure 3. At 0° the electrostatic field of the oxygen polarizes electron density onto the alkyl C (though polarization at the ether C may be transferred to O), whereas at 180° this reverses. Indeed, these polarizations are confirmed by calculated electron densities at the α-H of ethers.[4] Other analogies are α-haloketones, where the C−X dipole increases the C=O frequency when $\tau_{XCCO} = 0°$, and the conformations of α-diketones, which prefer $\tau_{OCCO} = 180°$.[12]

Exactly how this polarization of the electron density affects ^1J is as yet uncertain. It definitely operates by modulating the Fermi contact term, according to calculations on $^1J_{CH}$.[4] One possibility is that at $\tau = 0°$ the greater electron density on the alkyl C means that this C has become effectively more electronegative. The ether C must then direct more p character into the C−C bond,[13] thereby reducing ^1J, to which only s character contributes. Regardless of the details, it is known that an electrostatic field does affect both electron density and coupling constants.[14]

How general is this dipolar influence on ^1J? A nitrogen lone pair is of higher energy, so $n-\sigma^*$ delocalization may be more likely than for O. Indeed, oximes show a lower $^1J_{CC}$ when the C−C bond is antiperiplanar to the nitrogen lone pair,[15] and in two tricyclic orthoamides $^1J_{CH}$ at the bridgehead is 141 Hz when the C−H is antiperiplanar to the nitrogen lone pairs but 184 Hz when it is syn.[16] However, these variations may arise from the N dipole, which polarizes the C−C or C−H bond and reduces ^1J when it is anti, as in Figure 3. Because N has only one lone pair, these two examples display a $\cos(\tau)$ dependence, which cannot distinguish between dipolar interaction and delocalization of sp^2 N lone pairs.

In summary, these results are the first experimental evidence for a cosine dependence of $^1J_{CC}$ on the COCC dihedral angle. This is inconsistent with the customary interpretation of coupling constants in terms of $n-\sigma^*$ delocalization, but it is consistent with a dipolar interaction. The $\cos(\tau)$ dependence provides a more reliable guide to stereochemical assignment in ethers and related molecules than one based on the assumption of $n-\sigma^*$ delocalization.

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(7) Coupling constants were determined at natural abundance by standard ^{1}H-decoupled ^{13}C NMR at 25 °C. Typical conditions were acquisition time 1.3 s, relaxation delay 2 s, pulse angle 25°, spectral window 25 kHz, zero-fill, and Gaussian weighting. The $^1J_{CC}$ could be read easily from the satellite spectra. Where only one pair of satellites was seen, the spin rate was varied to distinguish spinning sidebands. Dihedral angles were obtained from MM2 energy minimization in Chem3DPro version 4.0. Angles were averaged for flexible molecules with more than one minimum or for those lacking symmetry.
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