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The Gamma Gauche Substituent Effect in ^{13}C NMR[1]

George B. Clemans*[2] and Mesfin Alemayehu

Department of Chemistry, Bowling Green State University,
Bowling Green, Ohio 43403 USA

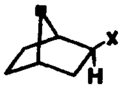
and

Department of Chemistry, Duke University,
Durham, North Carolina 27706 USA

Abstract: *Gamma gauche substituent effects are often used as stereochemical probes in ^{13}C NMR, but empirical force field calculations suggest that such applications must be made with caution.*

The gamma gauche substituent effect (γ_g) in ^{13}C NMR is generally observed as an upfield shift of the resonating carbon.[3] Because of the relatively short internuclear distances between a substituent and a gamma carbon at dihedral angles near 60°, this effect is usually thought to be primarily steric in origin,[4] although an electronic component has also been suggested.[5] Beierbeck and Saunders,[6] on the other hand, have presented evidence that the γ_g effect arises from the removal of the hydrogen that is replaced on introduction of the gamma substituent and that the previously postulated steric effects play no role at all. The mechanism of this effect thus remains obscure.[7]

We have noted a striking difference in the γ_g effects at carbon 7 in 2-substituted trimethylenenorbornyl (**1**)[8] and norbornyl derivatives (**2**). In spite of the obvious close similarity in geometry (the calculated[9] dihedral angles ω are given in Table 1), the correlation[9] of the γ_g



1

2

effects at carbon 7 in the two systems for the substituents F, Cl, Br, OH, and NH_2 was remarkably poor ($R^2 = 0.779$). This lack of correlation amply illustrates the vagaries of the γ_g effect. A plot (Figure 1) of the observed values, however, reveals some interesting patterns. Second period substituents fall on a line with a negative slope, while those in higher periods fall on a different line with a positive slope. It is thus apparent that the two systems are, for some reason, responding in opposite ways to these two types of substituents.

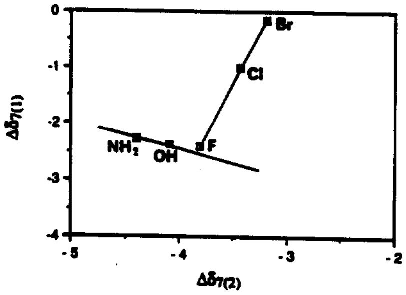


Figure 1. Plot of C_7 Substituent Effects in **1** and **2**

The reason for this is evident from the excellent correlation ($R^2 = 0.998$) for **1** between the γ_g effect and the calculated van der Waals interaction energy between the substituent and the syn hydrogen on carbon 7 (E_{XHS}, Table 1) given by Equation 1.

$$\Delta\delta_{7(1)} = -3.21 + 6.47 \times E_{XHS} \qquad (1)$$

Here the intercept ($E_{XHS} = 0$) is the upfield shift, independent of the nature of X, associated with the removal of the 2-exo hydrogen as noted by Beierbeck and Saunders.[6] The substituent is not, however, without its secondary influence which is seen as a downfield shift that increases with increasing steric repulsion partially cancelling the initial upfield shift. The norbornyl system **2** shows a similar, albeit somewhat poorer correlation ($R^2 = 0.929$), possibly because of its greater conformational mobility. Here, then, is a ready explanation for the opposing responses of **1** and **2** noted above. For the halogens, the magnitude of E_{XHS} increases in both systems, and hence they respond similarly. For the second period substituents, however, they increase for **1** but decrease and even become negative for **2** thus causing them to respond in opposite directions.

Table 1. Chemical Shift and Stereochemical Paramters for **1** and **2**.

X	$\Delta\delta_7$ (ppm)		ω(deg)[a]		E_{XHS} (kcal)[b]	
	1[c]	**2**[d]	**1**	**2**	**1**	**2**
H	0	0	80	82	0.053	0.003
F	-2.41	-3.82	79	79	0.117	0.050
Cl	-1.01	-3.43	82	82	0.345	0.096
Br	-0.16	-3.18	82	82	0.468	0.166
OH	-2.38	-4.10	80	80	0.125	0.002
NH_2	-2.27	-4.40	81	81	0.155	-0.002

a) Calculated C_7-X dihedral angle. b) Calculated van der Waals energy between X and the syn C_7 hydrogen. c) This study. d) Taken from refs. 4b and 4c.

These results strongly support the presence of a steric component in the γ_g effect. That polar effects play little role here is indicated by the striking insensitivity of $\Delta\delta_7$ to the electronegativity of X. More importantly, however, it can now be be seen why γ_g effects are often quite variable. The typical internuclear distance between a substituent and its gamma gauche carbon fall in that region of the van der Waals potential curve where the interaction changes from attractive to repulsive. As a result, even subtle changes in molecular geometry can cause significant changes in the γ_g effect, and comparisons of even closely related systems such as those in the present study must always be hazardous.

References and Notes

1. a) Presented in part at the 22nd Central Regional Meeting of the American Chemical Society, June, 1990. b) Taken in part from the MS thesis of MA, Bowling Green State University, August, 1988.

2. Visiting Professor, Duke University, Durham, North Carolina, 1988-1989. We are indebted to the Department of Chemistry, Duke University, for use of molecular modeling and statistical facilities.

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8. Compounds were prepared by standard methods, and sample purity was monitored by GC-MS analysis. Signal assigments were made on the basis of a combination of off-resonance decoupling, deuterium exchange, lanthanide shift, and long-range deuteriumn coupling studies.

9. Empirical force field calculations were made using the MM2 program of N. L. Allinger, available as program 395 from QCPE, Department of Chemistry, Indiana University, Bloomington, IN 47450 USA. Statistical analyses were made using the program SAS, SAS Institute, Inc., Box 8000, Cary NC 27511 USA.

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