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Nuclear Spin-Spin Coupling via Nonbonded Interactions. 2. γ-Substituent Effects for Vicinal Coupling Constants Involving ^{13}C

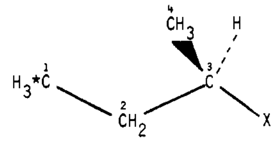
M. Barfield,*[1a] J. L. Marshall,*[1b] and E. D. Canada, Jr.[1b]

Contribution from the Department of Chemistry, University of Arizona, Tucson, Arizona 85721, and the Department of Chemistry, North Texas State University, Denton, Texas 76203. *Received May 7, 1979*

Abstract: The well-known γ effect on ^{13}C chemical shielding is shown to have a counterpart in vicinal coupling constants $^3J_{CX}$ involving a ^{13}C nuclear spin and a trans-oriented nuclear spin X. Experimental and theoretical results for vicinal ^{13}C1-C2-C3-^{1}H and ^{13}C1-C2-C3-^{13}C coupling constants in a number of C3-substituted aliphatic compounds in the trans arrangement and alicyclic compounds show a substantial decrease relative to the parent compound. By means of modified INDO-FPT molecular orbital procedures, which permit investigation of the importance of nonbonded interactions, it is shown that the γ-substituent effects arise in a complex way from the nonbonded interactions associated with groups bonded to the C3 or γ-carbon atom. A major factor is the *positive* contribution to $^3J_{CX}(180°)$ from the hydrogen atoms on the γ-carbon atom of the parent compound. Methyl groups on C3 make negative contributions; a major factor is the interaction between the hydrogen atoms of the C1 methyl and the hydrogen atoms of the methyl groups on the C3 carbon atom. It is further shown that other substituents also make *negative* contributions, and that hydrogen atoms on the γ substituents are not essential for the observation of a negative γ effect on vicinal coupling constants. The γ-substituent effects on vicinal ^{13}C-X coupling constants appear to be general phenomena of substantial magnitude; their recognition is important for conformational and other coupling-constant studies as they lead to results which appear to be anomalous.

Introduction

The γ effect on ^{13}C chemical shielding, which arises from gauche 1,4 carbon atoms,[3] has been used extensively in ^{13}C chemical shift assignments. The interpretation[3] in terms of a steric interaction model involving the hydrogens on the C1 and C4 carbon atoms in **1** has been questioned in some recent experimental[4] and theoretical studies.[5,6] In the present study experimental and theoretical results are used to demonstrate that substituents on the C3 or γ-carbon atom in **1** lead to a decrease in the magnitude of the vicinal coupling constants in the trans arrangement [$^3J_{CX}(180°)$] between the C1 and X nuclei. This appears to be a general result for vicinal coupling as well as shielding for cases in which hydrogens on the γ-carbon atom are replaced by other functional groups.[7,8]



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By means of a modified molecular orbital procedure, described in the first paper in this series,[9] it is shown that the γ-substituent effect for vicinal coupling arises from the nonbonded interactions associated with the atoms on the γ-carbon atom; hydrogen atoms at the γ carbon make positive contributions to the vicinal ^{13}C-H coupling constants, whereas other substituents give negative contributions. There are also some indications of δ-methyl substituent effects on vicinal coupling constants, and these are of opposite sign to the γ-methyl effects, in complete analogy with the situation suggested for chemical shifts.[10]

Results and Discussion

1. γ-Methyl and Methylene Substituent Effects on Vicinal ^{13}C-^{1}H and ^{13}C-^{13}C Coupling Constants. Entered in Table I are the calculated INDO (intermediate neglect of differential overlap) finite perturbation theory[11] (FPT) molecular orbital (MO) results for for the Fermi contact (FC) contributions to vicinal ^{13}C-^{1}H and ^{13}C-^{13}C coupling constants (X = ^{1}H and $^{13}CH_3$ in Table I) for the trans (180°) arrangements of a number of aliphatic and alicyclic hydrocarbons. In all cases the standard geometrical model[12] (SGM) was used in the calculations. The similar patterns for vicinal ^{13}C-^{19}F coupling constants, which were noted in the preliminary results,[8] would be expected to follow throughout, but were not included in these more extensive tables. Experimental data from this study and available literature values are given in parentheses in Table I. In addition to the calculated results for propane and butane (**2**, X = H and $^{13}CH_3$, respectively), calculated results are given for molecules having one to four methyl groups in the C1, C2, and C3 positions (**3-16**) and for several cyclic molecules (**17-20**).

The calculated results for vicinal ^{13}C-H coupling in Table I clearly show that the effects of methyl substitution at the α (C1) and β carbon (C2) are small; the values for **3-6** differ from the propane coupling constant by less than 0.2 Hz. However, results discussed in part 1[9] suggest that there may be a decrease in $^3J_{CH}$ on C2 methyl substitution. It is interesting to note that successive methyl substitution at the γ- (C3) carbon atom (entries **7** and **8**, X = H) leads to a decrease in $^3J_{CH}$ of about 0.8 Hz per methyl group. In part 1[9] it was

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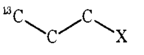
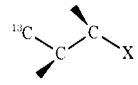
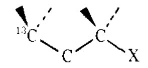
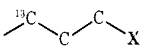
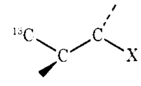
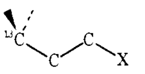
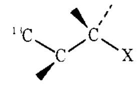
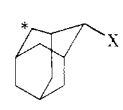
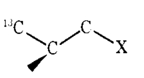
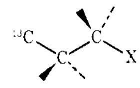
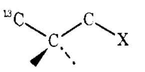
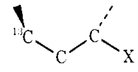
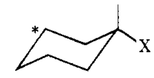
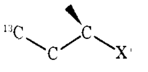
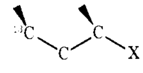
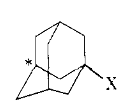
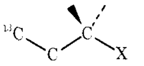
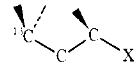
Table I. Calculated INDO-FPT MO Results for Vicinal Coupling Constants $^3J_{CH}(180°)$ and $^3J_{CC'}(180°)$ in Propane (X = H), Butane (X = $^{13}CH_3$), Methyl-Substituted Derivatives, and Cyclic Compounds (Experimental Values in Parentheses)[a]

molecule	$^3J_{CX}$, Hz		molecule	$^3J_{CX}$, Hz		molecule	$^3J_{CX}$, Hz	
	X = H	X = $^{13}CH_3$		X = H	X = $^{13}CH_3$		X = H	X = $^{13}CH_3$
2 	8.78 (13 ± 1)[b]	4.27	**9** 	7.76	3.37	**16** 	9.24[c]	4.47[c]
3 	8.74	4.26	**10** 	7.78	3.40	**17** 	7.63 (8.12)[d]	3.72 (4.3)[e]
4 	8.62	4.11	**11** 	7.03	3.06	**18** 	7.57 (7.17)[f]	3.32 (3.44)[g]
5 	8.72	3.81	**12** 	7.08	2.76			
6 	8.74	3.44	**13** 	7.76	3.75	**19** 	6.96	3.39
7 	7.82	3.81	**14** 	8.85[c]	4.30[c]	**20** 	6.82 (5.33)[g]	3.32 (3.2)[h]
8 	7.07	3.44	**15** 	8.87[c]	4.27[c]			

[a] All values are in hertz. [b] This is an estimated value for the trans coupling constant from the experimental value of 5.7 ± 0.2 Hz for propane reported by Wasylishen, R. E.; Schaefer, T. *Can. J. Chem.* **1974**, *52*, 3247. [c] Pairs of methyl hydrogens on C1 and C3 are separated by 0.735 Å in the geometry based on the standard geometrical model.[12] [d] A low-temperature experimental value from the work of Chertkov, V. A.; Sergeyev, N. M. *J. Am. Chem. Soc.* **1977**, *99*, 6750. [e] Unpublished results of Hansen, P. E.; Poulson, O. K.; Berg, A. Cited by Hansen, P. E. *Org. Magn. Reson.* **1978**, *11*, 215. [f] Ayadin, R.; Günther, H. *Z. Naturforsch. B*, in press. [g] This work; see Experimental Section. [h] Reference 15.

demonstrated that this decrease in the calculated values assumes its largest magnitude for the ϕ = 180° arrangements in which the γ methyls are gauche to the C1 carbon atom. Furthermore, for the series of cyclic molecules having single γ-methylene substituents in Table I (**17** and **18**, X = H), $^3J_{CH}$ is decreased by 1.2-1.4 Hz from the propane value, and in those molecules with two γ methyls or methylenes (**19** and **20**, X = H) the calculated vicinal ^{13}C-H coupling constants are decreased by 1.8 and 2.0 Hz, respectively, relative to the propane value. It is important to note that the experimental results in this series of compounds are ~13 Hz for propane[9] (**2**, X = H), 8.1 Hz for low-temperature cyclohexane (**17**, X = H), and 7.2 and 5.3 Hz for the two possible trans arrangements of adamantane (**18** and **20**, respectively, X = H). As a consequence, it appears that the actual effects of γ methyls (methylenes and methines) are at least twice as large as suggested by the calculated results in Table I.

Some additional substituent patterns are also apparent from the calculated values for $^3J_{CH}$ in Table I; a third or fourth methyl substituent at the C2 carbon (**11** and **12**, X = H) changes the coupling-constant value from that in **8** by less than 0.05 Hz. However, methyl substituents at the C1 *and* C3 carbons increase $^3J_{CH}$ above the propane value provided that they are on the same side such that there are substantial interactions due to the close proximity of the methyl groups. For example, note that the calculated values for **9** and **13** are identical (X = H), but in the case in which the two methyls are on the same side the calculated $^3J_{CH}$ is increased by about 1.1 Hz. With two methyls at both the C1 and C3 positions (**16**, X = H) the calculated value is increased by an additional 1.1 Hz. In these cases hydrogen atoms are separated by only 0.74 Å in the SGM; it seems likely that actual molecules would be substantially distorted from these arrangements.

In the case of vicinal ^{13}C-^{13}C coupling constants (X = $^{13}CH_3$ in Table I) the effects of methyl and methylene substitution are similar to those for $^3J_{CH}(180°)$; methyl substitution at the C1 carbon (or C4, by symmetry) produces a slight decrease in $^3J_{CC'}(180°)$. Also, methyl substitution at the C2 and C3 positions (**5** and **7** or **6** and **8**, X = $^{13}CH_3$) gives identical results by symmetry. However, progressive methyl substitutions decrease the coupling constants from the butane value (**2**, X = $^{13}CH_3$) by 0.5 (**5**, X = $^{13}CH_3$), 0.8 (**6**, X = $^{13}CH_3$), 1.2 (**11**, X = $^{13}CH_3$), and 1.5 Hz (**12**, X = $^{13}CH_3$). In contrast, the calculated value for $^3J_{CH}$ in the tetramethylpropane (**12**, X = H) differs negligibly from the dimethylpropane (**8**, X = H). This provides further evidence for the importance of the gauche γ-methyl substituent effects.

The calculated and experimental results for vicinal ^{13}C-^{13}C coupling in the cyclic compounds (**17-20**, X = $^{13}CH_3$ in Table I) are also consistent with the interpretation of the γ-substituent effect. The calculated and experimental values for $^3J_{CC'}$ in methylcyclohexane (**17**, X = $^{13}CH_3$) with one γ-methylene are greater that the values for 2-methyladamantane (**18**), dimethylcyclohexane (**19**), and 1-methyladamantane (**20**), each of which have two γ-methylenes (methyls or methines). The equality of the calculated results for $^3J_{CC'}(180°)$ in 1-methyl- and 2-methyladamantanes in Table I is reasonably consistent with the experimental values.

2. Effects of Other γ Substituents on $^3J_{CH}(180°)$ and $^3J_{CC'}(180°)$. Calculated INDO-FPT MO results for the Fermi contact contributions to the vicinal ^{13}C-H and ^{13}C-^{13}C coupling constants of a number of C3 disubstituted propanes and butanes are entered in Table II. In addition to the reference values for the parent compounds (**2**, X = H and $^{13}CH_3$) and the 3,3-dimethyl compounds **8** from Table I, results are included for the diethyl- (**21**), difluoro- (**22**), di(trifluoromethyl)- (**23**), and three symmetrical orientations of the 3,3-dihydroxypropanes **24a-c**. In the latter cases these correspond to the following: **24a**, the OH hydrogen atoms are trans to C2; **24b**, the OH hydrogens are gauche to C2 and X; **24c**, the OH hydrogens are trans to H. The total calculated energy in the INDO approximations is slightly less for the arrangement in **24b.** Detailed discussions of the conformational and substituent dependencies for compounds **2**, **8**, and **22** are given in part 1.[9]

In all cases the calculated values for the disubstituted compounds are smaller than the values for the parent compounds in Table II. In the cases of F and OH, the decrease is due in part to the effects of electronegative substituents as discussed in part 1;[9] the calculated values for 3,3-difluoropropane drop below the values for 2,2-difluoropropane at angles near 180°. It should be noted that the calculated values of $^3J_{CH}(180°)$ decrease in the series **24a–c** as the hydrogens are rotated toward the C1 methyl group with about a 1.1-Hz decrease in going from **24b** to **24c**.

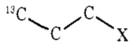
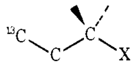
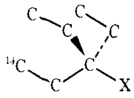
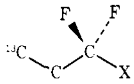
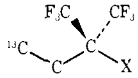
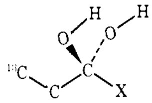
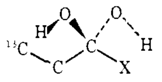
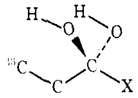
It is quite interesting to note that replacing the two proximate hydrogens of the γ-methyl groups of **8** by methyl groups to obtain 3,3-diethylpropane and diethylbutane (**21**) in the arrangement shown *increases* the coupling constants to values greater than the dimethyl values. In this case there are pairs of hydrogen atoms involving the C1 or α carbon and the C5 or δ carbons which are separated by only 0.735 Å in the SGM.[12] This result is suggestive of a δ effect on vicinal ^{13}C coupling constants analogous to the δ effects on chemical shielding.[10] This behavior also parallels that noted for those cases in which there are methyls on both the α and γ carbons as in **14–16** in Table I.

3. Contributions to Vicinal Coupling Constants Provided by the γ Substituents. To determine the importance of the many nonbonded electronic interactions on the calculated vicinal coupling constants, a modified INDO–FPT MO procedure was adopted. Elements of the Fock matrices associated with orbitals centered on various atom pairs were set equal to zero in each SCF cycle, thereby eliminating the transmission of coupling along the path provided by that nonbonded interaction.[9] A series of calculations was carried out for the Fermi contact contributions to the vicinal ^{13}C–H coupling in propane (**2**), 3,3-dimethylpropane (**8**), 3,3-difluoropropane (**22**), and the dihydroxypropanes **24a–c.** Entered in Table III are the differences $\Delta J_{CH}(180°)$ in the calculated results obtained on setting to zero the interaction between the pairs of underscored atoms, all of which involve the atoms R on the γ carbons (or the atoms comprising R). Subtraction of the recalculated results from those for the corresponding molecules in Table II gives $\Delta J_{CH}(180°)$, which provides a measure of the coupling contributions associated with the various paths involving the groups on the γ-carbon atom.

From the ΔJ_{CH} data for propane in Table III it can be noted that the coupling paths associated with the two γ-gauche hydrogen atoms give positive or negative contributions depending on whether the other atoms in the path are separated from the ^{13}C by an odd or even number of bonds, respectively. One consequence of this is that the various contributions cancel so that it is not possible to identify those specific interactions which lead to the total value of +1.14 Hz at the bottom of Table III. It is significant to note that only hydrogen atoms at the γ carbon give a total ΔJ_{CH} of *positive* sign so that replacement of the γ-gauche hydrogens of propane by any other group will *decrease* the vicinal ^{13}C–H coupling constant by at least this amount.

The data for 3,3-dimethylpropane (R = CH_3) in Table III exhibit a similar pattern of sign alternation (this is likely to be a major factor in the occurrence of γ and δ effects on magnetic resonance parameters). Clearly, the most important nonbonded coupling contribution is the −2.65-Hz value associated with the proximate hydrogens of the two γ-methyl groups and the hydrogens centered on the C1 carbon atom. This is partially offset by a value of +1.24 Hz for the path involving the valence atomic orbitals of C1 and the hydrogens of the two γ-methyl groups and other contributing coupling paths. The total provided by all of the the ΔJ_{CH} contributions, which is given at the bottom of Table III, is −1.4 Hz. As a consequence replacement of the two γ-gauche hydrogen atoms by two methyl groups should decrease $^3J_{CH}(180°)$ by about 2.5 Hz, a value in qualitative conformity with the 1.7-Hz decrease noted in the data of Table I. Similarly, replacement of the two γ hydrogens of propane with fluorines is predicted to produce a decrease of 1.6 Hz (1.4 Hz if the results are based on calculated data in which all interactions involving the groups on the γ carbon are eliminated in the same calculations). In comparing the calculated data as a function of dihedral angle in part 1, it was noted that the trans value of $^3J_{CH}$ in 3,3-difluoropropane was 1.2 Hz less than the value in 2,2-difluoropropane, and this was thought to be due to a γ-substituent effect.

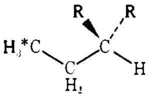
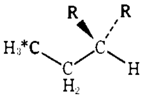
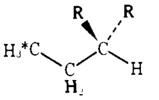
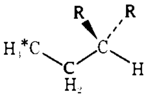
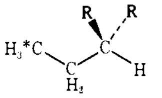
Table II. Calculated INDO–FPT Results for Trans Coupling Constants $^3J_{CH}(180°)$ and $^3J_{CC'}(180°)$ in a Number of γ-Disubstituted Compounds

molecule	$^3J_{CX}$, Hz	
	X = H	X = $^{13}CH_3$
2 	8.78	4.27
8 	7.07	3.44
21 	8.12[a]	4.10[a]
22 	5.64	2.69
23 	7.84	*b*
24a 	6.55[c]	*b*
24b 	6.44[d]	*e*
24c 	5.30[f]	*b*

[a] Internuclear separations between pairs of hydrogens on the C1 or α carbon and the C5 or δ carbons are only 0.735 Å in the SGM. [b] Not calculated. [c] The hydroxyl hydrogen atoms are trans to the C2 carbon atom. [d] The hydroxyl hydrogen atoms are gauche to C2 and X. [e] Calculations of $^3J_{CC'}(\phi)$ for a single OH group in this orientation are given by Barfield, M.; Burfitt, I.; Doddrell, D. *J. Am. Chem. Soc.* **1975**, *97*, 2631. [f] The hydroxyl hydrogens are trans to X.

Also included in Table III are the calculated ΔJ_{CH} for the three conformations **24a–c** of the 3,3-dihydroxypropanes. The total values become more negative as the hydrogens are moved closer to the C1 methyl group in this series. In fact, the difference of 1.1 Hz between the values of ΔJ_{CH} for **24b** and **24c** is almost exactly the difference between the calculated values of $J_{CH}(180°)$ for these two compounds in Table II. A very interesting feature of the calculated results for R = OH occurs in the first two rows of the table; the total contributions associated with the paths involving the hydrogens of the C1 methyl and the orbitals of the OH groups range from −0.9 to −1.1 Hz. However, the contributions associated with the oxygen and with the hydrogen atoms change sign as the OH is rotated toward C1! The important consequence of these results is that *hydrogen atoms on the γ substituent are not essential for the*

Table III. Calculated Changes $\Delta J_{CH}(180°)$ Due to Nonbonded Interactions Associated with Orbitals of Atoms on the γ Carbon of Propane and Derivatives

molecule	$\Delta J_{CH}(180°)$, Hz R = H (**2**)	 R = CH$_3$ (**8**)	 R = F (**22**)	 R = OH (**24a**)	 R = OH (**24b**)	 R = OH (**24c**)
	0.79	0.26 (C) −2.65 (H$_3$)	−0.58	−0.98 (O) 0.09 (H)	−1.10 (O) 0.13 (H)	0.12 (O) −2.23 (H)
	−0.44	0.08 (C) 1.24 (H)	0.48	0.70 (O) −0.10 (H)	0.81 (O) −0.12 (H)	0.05 (O) 1.35 (H)
	−0.27	−0.27 (C) 0.00 (H$_3$)	−0.12	−0.14 (O) 0.00 (H)	−0.13 (O) −0.02 (H)	−0.17 (O) 0.07 (H)
	0.56	0.28 (C) −0.98 (H$_3$)	−0.85	−0.95 (O) 0.09 (H)	−1.23 (O) 0.12 (H)	−0.18 (O) −1.18 (H)
	0.50	0.77 (C) −0.12 (H$_3$)	0.54	0.71 (O) 0.13 (H)	0.73 (O) 0.05 (H)	0.59 (O) −0.27 (H)
sum of $\Delta J_{CH}(180°)$	1.14[a]	−1.39	−0.53[b]	−0.45	−0.76	−1.85

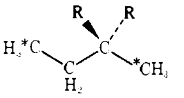
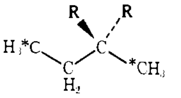
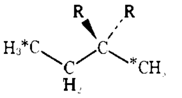
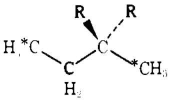
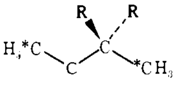
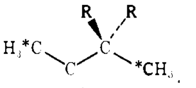
[a] A value of 1.10 Hz was obtained in a single calculation with all of these interactions set equal to zero. [b] A value of −0.39 Hz was obtained in a single calculation with all of these interactions set equal to zero.

occurrence of the γ-substituent effect on vicinal coupling constants.

In Table IV are the calculated changes $\Delta J_{CC'}(180°)$ in the vicinal $^{13}C-^{13}C$ coupling constants due to nonbonded interactions involving the atoms or groups in the γ-gauche positions of butane. Except for the reduction in the magnitudes of the contributions along the various coupling paths, the pattern for changes in the $^{13}C-^{13}C$ coupling constants is very similar to that noted for vicinal $^{13}C-H$ coupling in Table III. In butane the γ-gauche hydrogen atoms provide about 0.7 Hz to the total value of 4.3 Hz in Table I (**2**, X = $^{13}CH_3$). The most important nonbonded interactions on replacement of the two γ hydrogens by methyl groups involve the hydrogens of the γ methyls and the hydrogens of the C1 carbon. Again, the total value of $\Delta J_{CC'}$ for R = CH$_3$ is negative (−0.6 Hz), so that replacement of the two hydrogens by two methyl groups should lead to a decrease of about 1.3 Hz in the vicinal $^{13}C-^{13}C$ coupling constant. This is somewhat larger than the difference of 0.9 Hz between **2** and **8** (X = $^{13}CH_3$) in Table II. Also, note that replacement of the γ hydrogens by fluorines should lead to a decrease of about 0.8 Hz in the coupling, and would account for about 50% of the difference between the calculated $^3J_{CC'}(180°)$ for butane (**2**, X = $^{13}CH_3$) and 3,3-difluorobutane (**22**, X = $^{13}CH_3$) in Table II.

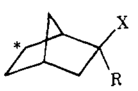
4. γ-Substituent Effects Involving Coupling to Groups Other Than H and $^{13}CH_3$. In Table V are given the calculated and experimental coupling constants $^3J_{CX}$ in the series of cyclic molecules **25–27** and **20**. The dihedral angles in **25** and **26** are usually taken to be 170 and 175°, respectively.[13] However, the calculated values for the substituted cyclohexanes **26** are based on the SGM with ϕ = 180°. With the exception of the results for $^3J_{CF}$ in Table V, all of the experimental coupling constants follow the same trends toward decreased values in these series of compounds. The results for **25** and **26** with X = $^{13}CH_3$ are not exceptional because there are additional substituents (R = OH) on the γ carbons, and these would be expected to decrease these coupling constants below the values in **27**. The calculated and experimental results in Table V indicate that the maxima in the plots of $^3J_{CX}$ as a function of dihedral angle will be shifted away from the expected 180° value, and raise questions[14] of the adequacy of an angular dependence of the Karplus type.

Table IV. Calculated Changes $\Delta J_{CC'}(180°)$ Due to Nonbonded Interactions Associated with Orbitals of Atoms on the γ Carbon of Butane and Derivatives

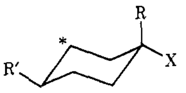
molecule	$\Delta J_{CC'}$ (180°), Hz R = H (**2**)	 R = CH$_3$ (**8**)	 R = F (**22**)
	0.36	0.08 (C) −1.28 (H$_3$)	−0.25
	−0.18	0.07 (C) 0.58 (H$_3$)	0.22
	−0.13	−0.14 (C) −0.01 (H$_3$)	−0.06
	0.29	0.14 (C) −0.49 (H$_3$)	−0.39
	0.47	0.35 (C) −0.05 (H$_3$)	0.22
	−0.12	0.19 (C) 0.01 (H$_3$)	0.17
sum of $\Delta J_{CC'}(180°)$	0.69	−0.55	−0.09

5. Importance of Multiple Impinging Rear Lobes on $^3J_{CH}(180°)$ and $^3J_{CC'}(180°)$. Prior to the recognition of the importance of the γ-substituent effects on $^3J_{CX}(180°)$, the decrease calculated for $^3J_{CC'}(180°)$ in the series *trans*-butane, equatorial methylcyclohexane, and 1-methyladamantane was attributed[15] to the effects of multiple impinging rear lobes. Based on these few INDO-FPT MO calculations, it was proposed that all of the apparently anomalous experimental results[13,15] for vicinal $^{13}C-^{13}C$ coupling constants could be ra-

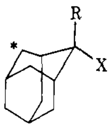
Table V. Comparisons of Calculated and Experimental Vicinal Coupling Constants $^3J_{CX}$ (Hz) for a Series of Cyclic Molecules at or near the Trans Arrangement



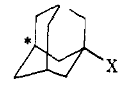
25



26



27



20

	25		**26**		**27**		**20**	
X	calcd[a]	exptl[b]	calcd	exptl[b]	calcd	exptl[b]	calcd	exptl
^1H	7.35	8.75[c]	7.63	8.12[d]	7.57	7.17[e]	6.82	5.33[f]
^{19}F	16.29[g]	9.8[h]	17.38[g]	11.5[i]	15.39[g]	8.5[j]	13.08[g]	9.61[f]
$^{13}CH_3$		3.6 (R = OH)[k]	3.72	3.2 (R = OH)[k]	3.32	3.44[f,l]	3.32	3.2[m]
$^{13}CH_2OH$				4.2[n]		3.54[f,o]		3.27[n]
$^{13}CO_2H$		4.9[p]		4.0[p]	5.54[q]	4.2[p]	4.59[q]	3.6[p]
$^{31}PO(OCH_3)_2$		18.4[r]		12.6[r] (R = OH; R′ = *t*-Bu)		11.8 (R = OH)[r]		
$^{119}Sn(CH_3)_3$		69[s]				60.0[s]		51.1[s]

[a] Calculations for norbornane were based on a geometry from the electron diffraction data of Yokozeki, A.; Kutchitsu, K. *Bull. Chem. Soc. Jpn.* **1971,** *44,* 2356. [b] R = H and R′ = H unless indicated otherwise. [c] This value was obtained from the ^{13}C–^2H coupling constant: Günther, H., private communication, 1978. [d] Chertkov, V. A.; Sergeyev, N. M. *J. Am. Chem. Soc.* **1977,** *99,* 6750. [e] Ayadin, R.; Günther, H. *Z. Naturforsch. B,* in press. Obtained from the ^{13}C–^2H coupling constant. [f] This work. [g] Reference 8. [h] Grutzner, J. B.; Jautelat, M.; Dence, J. B.; Smith, R. A.; Roberts, J. D. *J. Am. Chem. Soc.* **1970,** *92,* 7107. [i] Subbotin, O. A.; Sergeyev, N. M. *Ibid.* **1975,** *97,* 1080. [j] Maciel, G. E.; Dorne, H. C.; Greene, R. L.; Kleshick, W. A.; Peterson, Jr., M. R.; Wahl, Jr., G. H. *Org. Magn. Reson.* **1974,** *6,* 178. [k] Barfield, M.; Burfitt, I.; Doddrell, D. *J. Am. Chem. Soc.* **1975,** *97,* 2631. [l] Chemical shifts and other $J_{CC'}$ values (numbering system is that in ref 13) follow. δ_C (Me_4Si): 1, 31.5; 2, 39.3; 3, 31.5; 4, 34.0; 5, 28.4; 6, 38.8; 7, 28.7; 8, 39.6; 9, 34.0; 10, 39.6; 11, 19.0. $J_{CC'}$: 1,11, 1.1; 2,11, 35.7; 3,11, 1.1; 4,11, 0.4; 9,11, 0.4. Chemical shifts were verified by off-resonance decoupling and are secure, except for 5 and 7, which may be reversed. [m] Barfield, M.; Della, E., unpublished work cited in ref 15. [n] Reference 20. [o] Comments for footnote *l* apply. δ_C (Me_4Si): 1, 29.3; 2, 47.2; 3, 29.3; 4, 32.0; 5, 28.1; 6, 38.3; 7, 28.5; 8, 39.0; 9, 32.0; 10, 39.0; 11, 65.1. J_{CC} : 2,11, 38.2; 3,11, broadened, <0.5. [p] Reference 13. [q] Reference 16. [r] Reference 14. [s] Doddrell, D.; Burfitt, I.; Kitching, W.; Bullpitt, M.; Lee, C.; Mynott, R. J.; Considine, J. L.; Kuivila, H. G.; Sarma, R. H. *J. Am. Chem. Soc.* **1974,** *96,* 1640.

tionalized in terms of a model involving the increase in the number of impinging rear lobes in this series of compounds. This situation is depicted in Figure 1; there are two, three, and four carbon rear lobes in a hybrid orbital description as one proceeds in the series of compounds **2**, **17**, and **20** (X = H, $^{13}CH_3$). Subsequently, it was proposed that the decrease in the series was due to the increase in the number of β-methylene substituents, and that the effects of multiple impinging rear lobes were negligible.[16]

To investigate the importance of the additional indirectly bonded coupling paths in **17** and **20**, associated with the C5 and C7 carbon orbitals, modified INDO-FPT MO calculations were performed for **20**; interactions between the pairs of atoms C1-C5, C1-C7, C3-C5, C3-C7, and C5-C7 were set equal to zero (but not the interaction between C1 and C3[9]). The calculated changes in the vicinal coupling constants are $\Delta J_{CH}(180°) = 0.82$ Hz in adamantane and $\Delta J_{CC'}(180°) = 0.38$ Hz in methyladamantane. Thus, the calculated contributions from these types of nonbonded interactions are not only too small to account for the observed decrease in the vicinal coupling constants, they are of the wrong sign.

Conclusions

On the basis of experimental and theoretical results it has been shown that trans vicinal ^{13}C-^1H and ^{13}C-^{13}C coupling constants are decreased in magnitude relative to the parent hydrocarbon by the presence of substituents on the C3 or γ-carbon atom. By means of a large number of modified INDO-FPT MO calculations it is shown that these effects are due to the nonbonded interactions associated with the γ substituents. Although there are a great many possible interactions, coupling paths involving the hydrogen of the C1 methyl and the hydrogens of γ-methyl groups lead to substantial negative contributions, and these are only partially offset by the positive contributions associated with the orbitals of the C1 carbon atom and the γ-methyl hydrogens. It is important to note that the calculations indicate that nonbonded H-H interactions are not a necessary criterion for a negative γ-substituent effect. A major factor is the nonbonded contribution of *positive* sign arising from the two γ-gauche hydrogen atoms of the parent compound; these are replaced by methyl or other substituents which give *negative* nonbonded contributions. Replacement of atoms which make positive contributions with those that make negative contributions further enhances the magnitude of the γ-substituent effects. It is quite

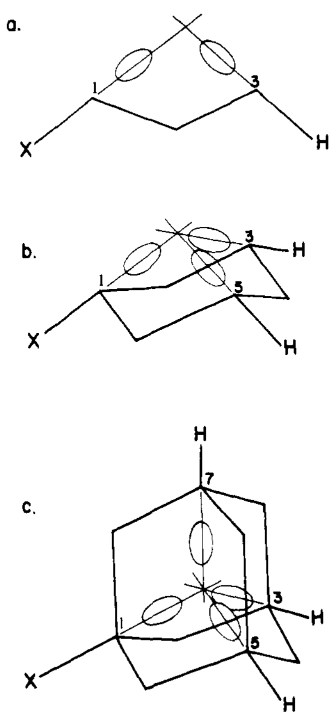


Figure 1. Schematic representation of the increase in the number of impinging multiple rear lobes in the series (a) propane, (b) cyclohexane, and (c) adamantane (X = H); (a) butane, (b) equatorial methylcyclohexane, and (c) 1-methyladamantane (X = CH_3).

important to recognize these substituent effects involving vicinal coupling to ^{13}C and possibly other first-row atoms as they lead to results which would appear to be anomalous, or could lead to incorrect conclusions about conformations of molecules based on coupling-constant data.

Experimental Section

^{13}C NMR spectra were recorded on a Bruker Instruments WH-90 Fourier transform NMR spectrometer[1a] operating at a frequency of 22.63 MHz (2-methyladamantane) and a JEOL PFT-100 Fourier transform NMR spectrometer[1b] operating at a frequency of 25.14 MHz (2-hydroxymethyladamantane and 1-fluoroadamantane). Spectra were recorded in solutions of chloroform-*d*, which served as the internal ^2H lock. The $J_{CC'}$ values were obtained using 8K/4K data points over a 600-Hz spectral width, and were reproducible to ±0.1 Hz. The ^{13}C NMR spectra for 1-hydridoadamantane-d_{15} were obtained on a Varian XL-100 Fourier transform NMR spectrometer in the ^2H-decoupled mode to obtain the J_{CH} coupling constants to ±0.1 Hz.[17]

Syntheses of ^{13}C-labeled compounds with an isotopic enrichment of >90% utilized carbon-^{13}C dioxide (Monsanto Corp., Miamisburg, Ohio) with vacuum line techniques previously reported.[13]

1-Bromoadamantane. A mixture of 25 mL of reagent-grade bromine and 10 g of adamantane was heated under reflux for 3 h, cooled, diluted with 100 mL of carbon tetrachloride, and washed with 50-mL portions of saturated sodium bisulfite solution until the color of bromine was discharged. The resulting solution was washed twice with water, dried (anhydrous magnesium sulfate), and concentrated in vacuo. The crude product was recrystallized (methanol, −78 °C) and sublimed to give a white solid.

This same procedure for adamantane-d_{16} (Aldrich Chemical Co., Milwaukee, Wis.), 0.500 g, gave 0.628 g of 1-bromoadamantane-d_{15} (83%), mp 110-112 °C (lit.[18] 118 °C).

1-Hydridoadamantane-d_{15}. 1-Bromoadamantane-d_{15} (0.628 g) in 20 mL of ether was added dropwise, over a 30-min period, to a rapidly stirred suspension of 0.484 g of lithium aluminum hydride in 50 mL of dry ether under nitrogen at 5 °C. The mixture was then heated under reflux for 18 h, cooled, quenched with wet ether, and filtered. The resulting solution was washed, dried (anhydrous magnesium sulfate), and concentrated in vacuo to give after recrystallization (methanol, −78 °C) and sublimation 0.403 g (98%), mp 265-267 °C (sealed) (lit.[19] 268 °C, sealed). The ^1H NMR consisted of a singlet, and the mass spectrum showed a parent peak at m/e 151.

1-Fluoroadamantane. 1-Bromoadamantane was reacted with mercuric fluoride in chloroform using the procedure utilized before[15] to give a 61% yield of 1-fluoroadamantane.

2-Adamantanecarboxylic acid-*carboxyl*-^{13}C was prepared from 2-bromoadamantane (Aldrich Chemical Co.) in the manner previously described[13] to give 8.8 g (42% based on the bromide), mp 140-142 °C.[13]

2-Adamantanemethanol-*C11*-^{13}C was prepared by the lithium aluminum hydride reduction of the corresponding carboxylic acid in the manner previously described[20] to give 6.8 g (90%), mp 88.0-90.0 °C (lit.[21] mp 94.9-95.8 °C).

2-Methyladamantane-*methyl*-^{13}C. A mixture of 2-adamantylmethanol-*C11*-^{13}C (5.08 g), thionyl chloride (4.5 mL, distilled from calcium chloride), and pyridine (100 mL, distilled from BaO) was heated under reflux overnight, quenched with 100 mL of water, mixed with 100 mL of 12 N hydrochloric acid, and extracted with three 25-mL portions of ether. The combined ethereal extracts were dried (anhydrous magnesium sulfate), concentrated in vacuo, and distilled trap to trap to give 1.9 g (26%) of 2-adamantylmethyl-*C11*-^{13}C chloride, a pale yellow liquid. The Grignard reagent of this chloride was prepared by its addition to a mixture of "activated magnesium"[22] prepared by reacting 1.19 g of dry magnesium chloride (Alfa Inorganics), potassium iodide (1.66 g, oven dried), freshly cut potassium (1.56 g), and 150 mL of dry tetrahydrofuran. The Grignard mixture was quenched with water and the product was extracted with ether. The ethereal extracts were dried over anhydrous magnesium sulfate and purified by liquid chromatography on F-20 alumina with hexane to give a white solid, 1.3 g (87%), mp 142-146 °C.

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References and Notes

(1) (a) University of Arizona. (b) North Texas State University.
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