Experimental and Theoretical Studies of $^{13}C-^{13}C$ Coupling Constants. 2. Conformational and Substituent Dependencies of Geminal Coupling Constants $^{2}J(^{13}C-^{13}C)$

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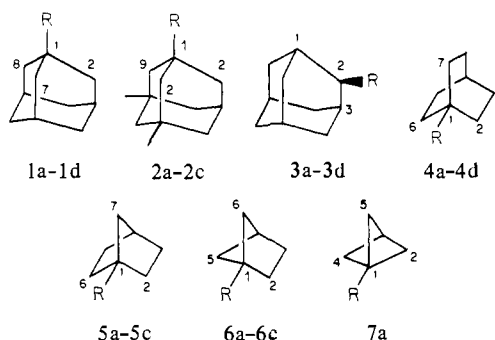
Abstract: To investigate the importance of conformational and substituent factors on geminal $^{13}C-^{13}C$ coupling constants $^{2}J_{CC'}$, use is made of both molecular orbital (MO) and valence-bond (VB) techniques. The MO results qualitatively reproduce certain trends due to hybridization, substituents, and bond angle effects, but even these trends appear to be lost in highly strained systems. By means of a VB bond-order formulation for coupling constants, it is demonstrated that $^{2}J_{CC'}$ is proportional to differences of geminal and vicinal $^{1}H-^{1}H$ or $^{13}C-^{1}H$ coupling constants. In the case of geminal $^{13}C-^{13}C$ coupling involving a methyl group, the dihedral angle dependence disappears, and the relatively small observed magnitudes indicate that the geminal term is effectively cancelled by the several vicinal terms. Substituents at C2 affect $^{2}J_{CC'}$ in a manner completely analogous to $^{2}J_{CH}$ and $^{2}J_{HH'}$. However, the VB formulation shows that substituents at C1 (or C3) should lead to an angular dependence of the vicinal type. In the case of OH substituents the equation $^{2}J_{CC'}(\phi') = 1.7 \cos^{2} \phi' - 0.9 \cos \phi' - 1.9$ provides an excellent correlation of the available experimental data.

Experimental studies of geminal $^{13}C-^{13}C$ coupling constants $^{2}J_{CC'}$ have shown that the magnitudes and signs are dependent on hybridization[2,3] and substituents[3] at the intervening (C2) atom, the C1–C2–C3 angle,[4,5] and the substituent orientation[6-9] and hybridization[3,5] at the C1 or C3 carbon atoms. Some attempts have been made[6,9] to relate $^{2}J_{CC'}$ to geminal $^{13}C-^{1}H$ coupling constants $^{2}J_{CH}$ for which stereochemical dependencies have been established and a number of signs determined.[9-11]

With few exceptions molecular orbital results[5,12] for $^{2}J_{CC'}$ do not always reproduce the experimental trends. Some cases in which MO results are qualitatively consistent with the data are the prediction of more positive values for electronegative substituents at C2,[12] and for sp² hybridization at C2,[12] and for substituted cyclobutanes for which large, presumably negative, values of $^{2}J_{CC'}$ are observed.[5] A lack of understanding of the factors that determine the geminal $^{13}C-^{13}C$ coupling constants has limited their usefulness in structural and conformational studies.

The present study makes use of a variety of $^{2}J_{CC'}$ data which have been obtained in these[13-16] and other[7,8,17] laboratories. Calculated results, which were based on the FPT formulation with INDO MO wave functions,[18] are compared with experimental

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Chart I

1a–1d   2a–2c   3a–3d   4a–4d

5a–5c   6a–6c   7a

a, R = $^{13}CH_3$; b, R = $^{13}CH_2$; c, R = $^{13}CO_2$; d, R = ^{1}H

data for several series of multicyclic compounds. Certain trends in the experimental data are shown to be consistent with the MO results, but others are not reproduced at all. A semiempirical valence-bond description permits the separation of various coupling paths and interrelates geminal $^{13}C-^{13}C$, $^{13}C-^{1}H$, and $^{1}H-^{1}H$ coupling constants. From these relationships it is shown that substituents (X) at the C1 or C3 carbon atom lead to geminal $^{13}C-^{13}C$ coupling constants which follow an angular dependence of the vicinal type,

$$^{2}J_{CC'}(\phi') = A \cos^{2} \phi' + B \cos \phi' + C \qquad (1)$$

where ϕ' is the dihedral angle associated with C1 and X, which is measured about the C2–C3 bond as depicted in Figure 1a. For the case in which the substituent is a hydroxyl group, eq 1 provides an excellent correlation of the available experimental data.

Results and Discussion

Molecular Orbital Results for $^{2}J_{CC'}$ in Cyclic Compounds. Entered in Table I are geminal $^{13}C-^{13}C$ coupling constants from several series of relatively rigid molecules 1–7 with ^{13}C-labeled methyl, hydroxymethyl, and carboxyl.[16,17] Also included are the calculated results for the Fermi contact contributions based on the INDO-FPT MO method.[18] The molecular geometries which were used in the calculations are discussed in ref 14 and 16. Calculations were performed on a Control Data Corp. CYBER 175 computer.

In the 1-substituted adamantanes 1 and 2 with R = $^{13}CH_3$ and $^{13}CH_2OH$ all $|^{2}J_{CC'}| < 0.2$ Hz, whereas in the corresponding

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Table I. Experimental Results for Geminal ^{13}C-^{13}C Coupling Constants in Several Series of Cyclic Compounds and Calculated INDO-FPT Results[a]

		a, R = ^{13}CH$_3$		b, R = ^{13}CH$_2$OH		c, R = ^{13}CO$_2$H	
		exptl	calcd	exptl	calcd	exptl	calcd
1	^2J(C11,C2)[b]	<0.2[c]	-5.03	<0.17[c]	-5.24	(-)1.39[c]	-7.06
2	^2J(C11,C2)[d]	e	f	<0.08[c]		(-)1.40[c]	-7.29
	^2J(C11,C8)	e	f	<0.07[c]		(-)1.37[c]	-6.38
3	^2J(C11,C1)[g]	(+)0.60[c]	-4.64	(+)0.27[c]	-4.85	(-)1.09[c]	-6.60
4	^2J(C9,C2)[h]	(+)0.34[i]	-4.76	(+)0.58[i]	-4.95	(-)0.88[i]	-6.80
5	^2J(C8,C2)[k]	(+)1.56[i]	-3.65	<0.9[i]	-3.85	(+)1.71[i]	-4.81
	^2J(C8,C7)	(+)1.07[i]	-3.94	<0.9[i]	-3.73	(±)1.02[i]	-6.66
6	^2J(C7,C2)	(+)2.44[i]	-3.88	(+)1.87[j]	-3.05	(+)3.03[j]	-5.77
	^2J(C7,C5)[l]	<0.27[i]	-5.76	(-)0.52[j]	-6.17	<0.12[j]	-7.35
7	^2J(C6,C2)[m]	<0.27[i]	-2.36	e	f	e	f

[a] All values in hertz. [b] C2, C7, and C8 are equivalent. [c] Reference 13; for R = ^{13}CH$_2$I and ^{13}CH$_2$CN ^2J(C11,C2) were <0.2 and <0.07 Hz, respectively. [d] C2 and C9 are equivalent. [e] Not measured. [f] Not calculated. [g] C1 and C3 are equivalent. [h] C2, C6, and C7 are equivalent. [i] Reference 17. [j] Reference 16. [k] C2 and C6 are equivalent. [l] C5 and C6 are equivalent. [m] C2, C4, and C5 are equivalent.
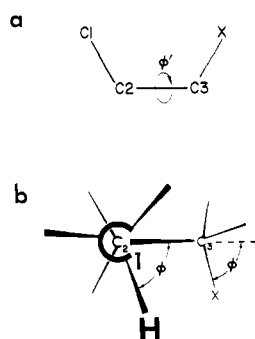

Figure 1. (a) Specification of the C1-C2-C3-X dihedral angle ϕ'. (b) Specification of the dihedral angles ϕ and ϕ' in a substituted propane.

2-substituted adamantanes **3** and bicyclo[2.2.2]octanes **4** the magnitudes range from 0.27 to 0.60 Hz. In the strained bicyclic compounds **5–7** the magnitudes of $^2J_{CC'}$ increase and then become too small to measure in **7a**. Possibly, this is associated with the varying s character in the orbitals centered on the β-carbon. In all cases in which R = ^{13}CO$_2$H (an exception is a value <0.12 Hz in **6c**) the geminal coupling constants are in the range 0.88–3.03 Hz.

The signs of the experimental $^2J_{CC'}$ in Table I are assumed on the basis of the trends in the calculated results and other correlations (vide infra). As a consequence, even though there is internal consistency for most of the entries, these signs are speculative. The calculated MO results in Table I are consistently more negative than the experimental data. The signs assumed for the experimental data are consistent with the addition of about 5.1 Hz to the calculated results for molecules with R = ^{13}CH$_3$ and ^{13}CH$_2$OH. Exceptions are the data for the highly strained ring systems **6** and **7**. The calculated results for R = ^{13}CO$_2$H are consistently more negative than those for R = ^{13}CH$_3$ and ^{13}CH$_2$OH in Table I. Thus, the experimental values for compounds **1c–4c** are assumed to be negative, which is in conformity with other criteria for signs.[3]

Valence-Bond Bond-Order Formulation for Geminal ^{13}C-^{13}C Coupling Constants. The Relationship to ^{13}C-^{1}H and ^{1}H-^{1}H Coupling Constants. The complexity of substituent and conformational factors for $^2J_{CC'}$ can be studied by relating them to ^{13}C-^{1}H and ^{1}H-^{1}H coupling constants for which there is more experimental and theoretical information. For this purpose use is made of a semiempirical valence-bond description,[19] which makes use of the relationship of Fermi contact coupling to Penney–Dirac bond orders.[19] This formulation provides a conceptual basis for discussing mechanisms of spin–spin coupling, and it is useful for interrelating different types of coupling constants[20] without explicit calculations of molecular wave functions. For
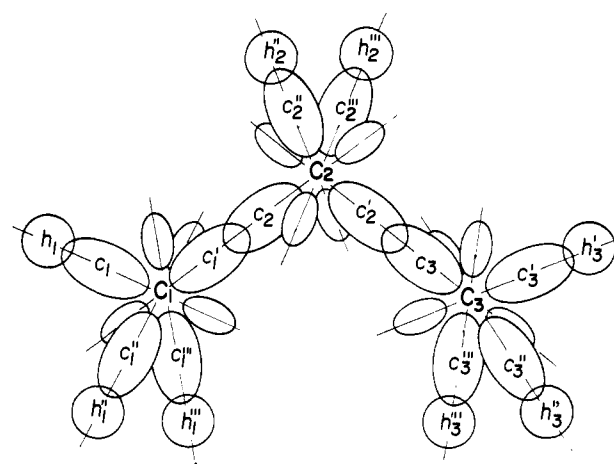

Figure 2. Designation of the orbitals in propane.

example, it has been used to interrelate ^{13}C-^{19}F and ^{1}H-^{19}F coupling constants[21] and to relate $^3J_{CC'}$ to $J_{HH'}$.[22]

The derivation of the relevant equations was given previously[21] and will not be reproduced here. Intercarbon coupling constants $J_{CC'}$ are related to interproton coupling constants $J(H_i,H_k)$ by an explicit sum over all of the bonds i on C and all of the bonds k on C',

$$J_{CC'} = (K/K')^2 \sum_{i,k}(-1)^{n_i + n_k}J(H_i,H_k) \qquad (2)$$

where n_i is equal to zero if the hydrogenic orbital h_i replaces c_i (a hybrid orbital on C) and equal to one if the orbital c_i is directed toward h_i; n_k is defined in the same way for bond k. The ratio of the coefficients in eq 2 is given by

$$K/K' = [\gamma_C\alpha^2\phi^2_{2s}(C)/\gamma_H\phi^2_{1s}(H)] \qquad (3)$$

where α^2 denotes the s character of the hybrid orbitals, γ_C and γ_H are the magnetogyric ratios, and $\phi^2_{2s}(C)$ and $\phi^2_{1s}(H)$ are theoretical values of the densities at carbon and hydrogen, respectively. For sp^3 and sp^2 hybrids K/K' are 0.316 and 0.422, respectively. Carrying out an explicit sum over k in eq 3 leads to an expression relating $J_{CC'}$ to J_{CH},

$$J_{CC'} = (K/K')\sum_{i}(-1)^{n_i}J(H_i,C) \qquad (4)$$

Consider the application of eq 4 to the geminal ^{13}C-^{13}C coupling in propane for which the relevant orbitals are depicted in Figure 2. Since there are four bonds on C'(C$_3$) there will be four terms in the summation in eq 4,

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$$^2J_{CC'}(\phi') = (K/K') \times$$
$$[^2J'_{CH} - ^3J_{CH}(\phi') - ^3J_{CH}(\phi' + 120°) - ^3J_{CH}(\phi' - 120°)] \quad (5)$$

where ϕ' is the C1–C2–C3–H3' dihedral angle. A prime is placed on the first term in brackets in eq 5 because it is obtained by the artificial procedure of replacing a carbon atom by a hydrogen atom; this would modify the integrals which lead to the expression for $^2J_{CH}$. In terms of the exchange integrals for the propanic fragment in Figure 2

$$^2J'_{CH} \propto \left\{ \frac{K(c'_1,c_3) + K(c_2,c'_2) - K(c_2,c_3) - K(c'_1,c'_2)}{2K(c'_1,c_2) + 2K(c'_2,c_3)} \right\} \quad (6)$$

where $K(c_i,c_j)$ denotes the two-center VB exchange integrals. It is interesting to note that the substitution of reasonable values for the integrals[23] into eq 6 leads to a positive value for $^2J'_{CH}$; therefore, vanishing of $^2J_{CC}$ in some of the cyclic compounds in Table I can be understood to arise from the cancellation of a positive $^2J'_{CH}$ and positive values of the three $^3J_{CH}$ terms in eq 5.

Since the vicinal $^{13}C-^1H$ coupling constants have an angular dependence of the form of eq 1, eq 5 for propane yields

$$\langle ^2J_{CC}\rangle = (K/K')[^2J'_{CH} - (3/2)A - 3C] \quad (7)$$

which is independent of dihedral angle.

In eq 5 any dependence on the second dihedral angle ϕ in Figure 1b enters by considering the relationship to H–H coupling constants,

$$^2J'_{CH}(\phi) = (K/K') \times$$
$$[^2J'_{HH'} - ^3J_{HH'}(\phi) - ^3J_{HH'}(\phi + 120°) - ^3J_{HH'}(\phi - 120°)] \quad (8)$$

and

$$^3J_{CH}(\phi,\phi') = (K/K')[^3J_{HH'}(\phi') - ^4J_{HH'}(\phi,\phi') - ^4J_{HH'}(\phi +$$
$$120°,\phi') - ^4J_{HH'}(\phi - 120°,\phi')] \quad (9)$$

with analogous expressions for $^3J_{CH}(\phi' + 120°)$ and $^3J_{CH}(\phi' - 120°)$. Substituting these into eq 5 leads to an expression for $^2J_{CC'}(\phi,\phi')$ which contains the following 16 H–H coupling constants in the sum: $^2J'_{HH'}$, six vicinal terms $^3J_{HH'}$, and nine long range coupling terms $^4J_{HH'}$. Since the latter have magnitudes less than 2 Hz in typical systems,[24] and in propane $^4J_{HH'}$ is less than 0.18 Hz in magnitude,[25] it is safe to ignore these in unstrained molecules. Equations 8 and 9 should also prove to be useful in studies of $^2J_{CH}$ and $^3J_{CH}$.

Correlations among $^2J_{CC'}$, $^2J_{CH}$, and $^2J_{HH'}$. Geminal $^{13}C-^1H$ coupling constants were correlated with $^1H-^1H$ coupling constants in methyl-substituted five- and six-membered rings,[26]

$$^2J_{CH} = 0.55^2J_{HH'} + 4.93 \quad (10)$$

Even though this relationship is only numerically correct for a small class of compounds, it illustrates some important features of $^{13}C-^1H$ and $^1H-^1H$ coupling constants. The slope of 0.55 indicates that the magnitude of geometric or substituent-induced changes in $^1H-^1H$ coupling constants will only be about half as large for similar $^{13}C-^1H$ coupling constants. Almost all aliphatic $^2J_{HH}$ values are large and negative (about –12 Hz), and there is rarely any doubt about their sign values. Geminal aliphatic $^2J_{CH}$ values are usually negative, but the large 4.93-Hz intercept is indicative of the observation that many more $^2J_{CH}$ values are positive than $^2J_{HH}$ values. Moreover, the change in going from $^2J_{HH'}$ to $^2J'_{HH'}$ in eq 8 must more than offset the negative influence of the vicinal terms in this equation.

Table II contains a collection of $^2J_{CC'}$ and $^2J_{CH}$ data for some structurally similar compounds in which the coupled hydrogen

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Table II. Correlation of Experimental Values of $^2J_{CC'}$ with $^2J_{CH}$ in a Compound in which an Alkyl Group Replaces a Hydrogen Atom[a]

compound	$^2J_{CC'}$	compound	$^2J_{CH}$
$CH_3CH_2{}^{13}CH_2CH_2 - {}^{13}\overset{\overset{O}{\|}}{C} - OH$	(–)1.73[b]	$^1H - CH_2 - {}^{13}\overset{\overset{O}{\|}}{C} - OH$	–6.7[c]
$CH_3 - {}^{13}CH_2 - CH_2 - {}^{13}CH_2^-$	(–)0.73[d]	$H - CH_2 - {}^{13}CH_2^-$	–4.58[e]
1a	<0.2[f]	1d	(–)3.32[g]
3a	(+)0.60[f]	3d	(–)3.34[g]
4a	(+)0.34[h]	4d	–2.9[i]
$^{13}CH_3 - \overset{\overset{OH}{\|}}{\underset{\underset{CH_3}{\|}}{C}} - {}^{13}CH_2CH_3$	(+)2.4[j]	$^{13}CH_3 - \overset{\overset{OH}{\|}}{\underset{\underset{CH_3}{\|}}{C}} - {}^1H$	(–)0.76[k]
$\overset{\overset{O}{\|}}{\underset{{}^{13}CH_3}{C}}{}^{13}CH_3$	+16.1[l]	$\overset{\overset{O}{\|}}{\underset{{}^{13}CH_3}{C}}{}^1H$	+26.7[m]

[a] All values in hertz. [b] A value of ±1.7 Hz was reported by Marshall and Ihrig: Marshall, J. L.; Ihrig, A. M. *Tetrahedron Lett.* **1972**, *21*, 2139. More accurate coupling constants were obtained in these laboratories.[15] [c] Gray, G. A.; Ellis, P. D.; Traficante, D. D.; Maciel, G. E., *J. Magn. Reson.* **1969**, *1*, 41. The sign is taken to be negative in analogy to the -6.6 Hz value for CH_3COH, which was reported by Dreeskamp and Sackmann: Dreeskamp, H.; Sackmann, E. "Nuclear Magnetic Resonance in Chemistry"; Pesce, B., Ed., **1965**, p 143. [d] This value was not reported in a previous study.[22] The ^{13}C-labeled compound was reexamined on the Bruker WM-250 in these laboratories (Barfield, M. unpublished results, 1982). The sign is taken to be negative on the basis of a large number of studies of geminal $^{13}C-^1H$ coupling constants which show that for sp^3-sp^3 systems the *magnitudes* increase with increasing substituent electronegativity [Miyazima, G.; Utsumi, Y.; Takahashi, K. *J. Phys. Chem.* **1969**, *73*, 1370] and the values are only positive in heavily substituted situations [Freeman, R.; Anderson, W. A. *J. Chem. Phys.* **1963**, *39*, 806; Schaefer, T.; Chum, K.; McKinnon, D.; Chauham, M. S. *Can. J. Chem.* **1975**, *53*, 2734]. [e] Spoormaker, T.; de Bie, M. J. A. *Recl. Trav. Chim. Pays-Bas*, **1978**, *97*, 135. [f] Reference 14. [g] Aydin, R.; Günther, M. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1979**, *34B*, 528. [h] Reference 17. [i] Reference 16; the $^2J(^1H-^2H)$ value in Table I of ref 16 was multiplied by $\gamma(^1H)/\gamma(^2H)$. [j] Reference 12. [k] Wasylishen, R. E.; Chum, K.; Bukata, J. *Org. Magn. Reson.* **1977**, *9*, 473. [l] Schumann, C.; Dreeskamp, H.; Hildenbrand, K. *J. Magn. Reson.* **1975**, *18*, 97. [m] Yamamoto, O.; Watabe, M.; Kikuchi, O. *Mol. Phys.* **1969**, *17*, 249.

is replaced by an alkyl group. Again, it is emphasized that the signs of all coupling constants in parentheses are assumptions based on trends within the series with use of such criteria as the known influence of β-substituents, carboxyl groups, etc. A linear least-square fit of the tabulated data gives
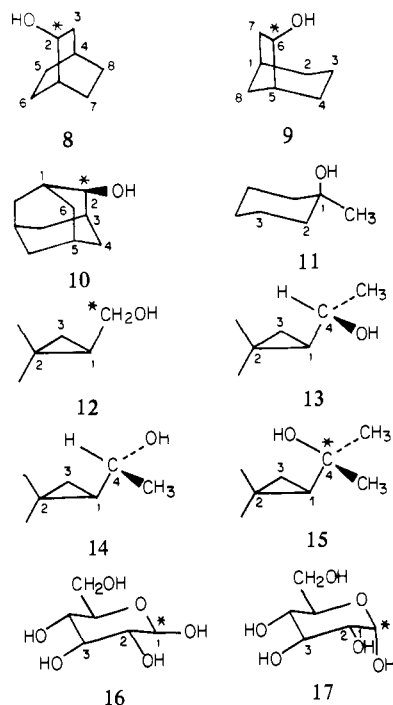
$$^2J_{CC'} = 0.53^2J_{CH} + 2.0 \quad (11)$$

with correlation coefficient $r^2 = 0.996$. The 2.0-Hz intercept places the average aliphatic $^2J_{CC}$ value so near zero that nearly as many $^2J_{CC}$ values will be positive as negative. The intercept in the $^2J_{CH}$ correlation is dependent on the type of carbon that replaces the coupled $^2J_{CH}$ hydrogen. When the hydrogen is replaced by a carboxylic acid group a similar least-squares fit gives an intercept of only 0.4 Hz.

The Influence of β- (or C2) Substituents on $^2J_{CC'}$. Substituents at the β- (or C2) carbon atom of propane will affect $^2J_{CC'}$ via the two-bond and three-bond terms that enter the expressions for $^2J_{CC'}$. The symmetry arguments for the effects of various types of substituents on $^2J_{HH}$[27] can be carried over to $^2J_{CH}$ and $^2J_{CC'}$. These effects can be seen for several of the entries in Table II. Moreover, substituent effects for *vicinal* $^1H-^1H$ coupling or $^{13}C-^1H$ coupling constants will also enter the expression for $^2J_{CC'}$ in eq 5, 8, and 9. As a consequence, all of the complexities associated with the

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

Chart II

effects of substituents on vicinal H–H coupling constants[28] will (to a smaller degree) affect $^2J_{CC'}$. As an example, electronegative substituents that decrease the magnitude of $^3J_{HH'}$ will give more positive values of $^2J_{CC'}$.

There is a substantial amount of experimental data for $^2J_{CC'}$ in which there are OH groups at the β- (or C2) carbon.[12-15] In contrast to the $^2J_{CC'}$ values which are <0.5 Hz in those cases in which the hydroxy group is at the C1 carbon,[29] the magnitudes of compounds with OH groups at C2 are in the range 1–3 Hz. In view of the well-documented effects of electronegative substituents on $^2J_{HH'}$[27] and $^3J_{CH}$,[11] it is probably safe to assume that the values are positive. In subsequent discussions it will be assumed on empirical grounds that an OH group at a β-carbon atom contributes +3 Hz to $^2J_{CC'}$.

Orientational Dependence of α- (or C1/C3) Substituents on $^2J_{CC'}$. If one of the hydrogen atoms (say H'3) on carbon C3 of propane in Figure 2 is replaced by a substituent X, the corresponding vicinal term $^3J_{CH}(\phi')$ in eq 5 will be changed to $^3J_{CX}(\phi')$. It is reasonable to assume that the form of the angular dependence will be the same as in eq 1; however, the coefficients will be changed by the electronic perturbation,[30]

$$^3J_{CX}(\phi') = A' \cos^2 \phi' + B' \cos \phi' + C' \quad (12)$$

and the other two vicinal terms in eq 5 are given by

$$^3J_{CH}(\phi' \pm 120°) =$$
$$A'' \cos^2 (\phi' \pm 120°) + B'' \cos (\phi' \pm 120°) + C'' \quad (13)$$

where A'', B'', and C'' can be taken from any of the studies of the angular dependencies of $^3J_{CH}$.[10,11,31-34] Substituting eq 12

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(30) For convenience, it is assumed that X has the magnetic properties of a proton but the electronic properties of the heteroatom.

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Table III. Angular Dependence of $^2J_{CC'}$ in Compounds with Hydroxyl Groups at the C1 and/or C3 Position Compared with Semiempirical Results Based on the Equation $^3J_{CC'}(\phi') = 1.7 \cos^2 \phi' - 0.9 \cos \phi' - 1.9$ Hz

compd	coupled nuclei C, C	$^2J_{CC'}$, Hz	dihedral angle, ϕ',[a] deg	calcd,[b] Hz
8[c]	C2, C4	(−)1.0	~120	(−1.02)
	C2, C6	(−)1.9	~60	(−1.92)
	C2, C7	(+)0.7	~180	(+0.70)
9[c]	C1, C6	(−)1.7	~120	−1.02
	C4, C6	(−)2.2	~30	−1.40
	C8, C6	(+)6.1	~150	0.15 + $^3J_{CC'}$[d]
10[c]	C2, C6	(−)1.8	60	−1.92
	C2, C7	(+)0.7	180	0.70
11[f]	C1, C3	(−)1.7	~60	−1.92
12[g]	C2, C4	(−)1.19	130, 250	−1.00
	C3, C4	(−)0.61	162, 42	−0.56
13[h]	C2, C4	(−)1.69	80	−2.26
	C3, C4	<0.2	212	0.04
14[h]	C2, C4	<0.4	195	0.54
	C3, C4	(−)1.83	97	−1.99
15[i]	C2, C4	(−)1.44	30 (300)	−1.40 (−1.92)
	C3, C4	(−)1.71	262 (−8)	−1.74 (−1.12)
16[i]	C1, C3	(+)3.5	60, 180, 180	+2.5[k]
17[j]	C1, C3	<1.5	60, 60, 180	−0.1[k]

[a] The dihedral angle ϕ' is measured about the C–C bond as depicted in Figure 1. For compounds 8–11, 16, and 17 these are estimated from Dreiding models; for 12–15 the angles were based on coupling constant data. [b] Calculated from eq 15. Values in parentheses were used to determine the coefficients in this equation. [c] Reference 8. [d] A vicinal path is involved. [e] Reference 7. [f] Marshall, J. L.; Müller, D. E. *J. Am. Chem. Soc.* **1973**, 95, 8305. [g] Reference 13; coupling constants are taken to be the average of two rotamers with the indicated dihedral angle. [h] Reference 13. [i] Reference 13; the experimental vicinal coupling constant data are consistent with dihedral angles of either 30 or 300°. [j] Reference 6. [k] It is assumed that the OH on C2 makes a contribution of +3 Hz to the total.
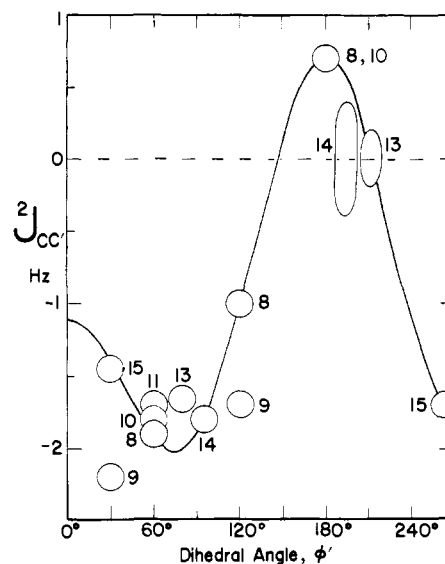

Figure 3. Geminal $^{13}C-^1H$ coupling constants (circles and ellipses) plotted as a function of the dihedral angles ϕ'. The circles and ellipses are crudely indicative of the uncertainties in the experimental values and the estimates of the dihedral angles from Dreiding stereomodels. The solid curve is a plot of the semiempirically determined eq 15.

and 13 into eq 5, the geminal $^{13}C-^{13}C$ coupling constant is dependent on the dihedral angle ϕ'

$$^2J_{CC'}(\phi') = (K/K')[^2J'_{CH} - (A' - A'') \cos^2 \phi' - (B' - B'') \cos \phi' - (3/2)A'' - 2C'' - C'] \quad (14)$$

Since $^2J'_{CH}$ in eq 14 is independent of dihedral angle, it can be combined with the constant terms so that eq 14 has an angular

dependence of the form of eq 1.

Entered in Table III are the experimental values for $^2J_{CC'}$ in a series of more or less rigid molecules **8–17**. Since no sign determinations were performed, the signs in parentheses are assumed values. Dihedral angles in Table III are crude estimates based on Dreiding stereomodels. In the case of the dimethylcyclopropanes **12–15** dihedral angles are estimates based on vicinal $^1H-^1H$ and/or $^{13}C-^{13}C$ coupling constant data.[13] The experimental values of the geminal coupling constants for all molecules except **12, 16**, and **17** are plotted in Figure 3 as a function of the estimated dihedral angles ϕ' in the range 0–270°. The data points are represented by circles and ellipses to give a crude indication of the uncertainties in the experimental values and the estimated dihedral angles. A very good fit (solid line in Figure 3) to the experimental data is obtained by assuming an angular dependence of the form of eq 1 and the first three data points in Table III

$$^2J_{CC'}(\phi') = 1.7 \cos^2 \phi' - 0.9 \cos \phi' - 1.9 \text{ Hz} \qquad (15)$$

All of the other calculated values, which are entered in the last column of Table III, were obtained from eq 15 and the estimated dihedral angles. The reasonable agreement with the experimental data strongly suggests that the vicinal-type interactions dominate the substituent orientational dependencies.

In the case of the 1-(hydroxymethyl)-2,2-dimethylcyclopropane (**12**) the $^3J_{HH'}$ and $^3J_{CC'}$ are reproduced if it is assumed that the dihedral angles ϕ' ($\angle C2–C1–C4–O$) of 130° and 250° correspond to equal rotamer populations.[13] Substitution of a methyl group to give **13** and **14** seems to produce enough steric hindrance to substantially favor single rotamers with $\phi' = 80°$ and 195°, respectively. The correspondence between the calculated and experimental geminal coupling constants $^2J(C2,C4)$ and $^2J(C3,C4)$ is consistent with this proposal. For the tertiary alcohol **15** dihedral angles of 30° or 300° were completely consistent with the experimental vicinal coupling constant data. However, it is interesting to note that the 30° value for $\angle C2–C1–C4–O$ ($\angle C3–C1–C4–O = 262°$) gives calculated geminal $^{13}C-^{13}C$ results in Table III which are within experimental error of the measurements.

The application of eq 15 to the $^2J_{CC'}$ in β-[D]glucose **16** and α-[D]Glucose **17** gives results in good conformity with the experimental data if we assume that the OH group at the C2 carbon contributes +3 Hz to the total (vide supra) and that the contributions from eq 15 for each of the three oxygen substituents at C1 and C3 are additive. The total of the four contributions are +2.5 Hz and –0.1 Hz, which are in good conformity with the experimental values of 3.5 Hz and <1.5 Hz, respectively.

Conclusions

Geminal $^{13}C-^{13}C$ coupling constants exhibit dependencies on substituent orientation, hybridization, and C1–C2–C3 bond angle effects. Some of the trends are qualitatively reproduced by means of the INDO-FPT MO method, but the calculated magnitudes are often 5–6 Hz too negative.

By means of a valence-bond bond-order formulation, $^2J_{CC'}$ in a propanic fragment are related to geminal, vicinal, and long range $^1H-^1H$ or to geminal and vicinal $^{13}C-^1H$ coupling constants. The long range terms make relatively small contributions, but the small magnitudes of $^2J_{CC'}$ in saturated hydrocarbons must be due to a cancellation between the geminal and vicinal terms. In freely rotating systems a good linear correlation is observed between the experimental data for $^2J_{CC'}$ and $^2J_{CH}$.

Substituent effects at the C2 carbon follow the same trends observed for geminal $^1H-^1H$ and $^{13}C-^1H$ coupling constants wherein electronegative substituents lead to more positive values of $^2J_{CC'}$. By means of VB formulation it is shown that substituents at C1 or C3 should lead to an angular dependence of the vicinal type. A single equation of this type is found to provide a good correlation of the experimental data.

Side-Chain vs. Main-Chain Conformational Flexibility in Aromatic Dipeptides

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Abstract: The ^1H NMR and CD spectra of Ac-Trp-Trp-NHMe, Ac-Phe-Phe-NHMe, and Ac-Tyr-Tyr-NHMe in either 2,2,2-trifluoroethanol (TFE) or tetrahydrofuran (THF) have been recorded down to subzero temperatures. The results indicate a preferentially folded structure in TFE and an extended one in THF solutions as a common feature for the main chain of the three dipeptides, the evidence being strongest for the case of Ac-Trp-Trp-NHMe. An analysis of the conformational space of this latter molecule helps in delineating four low-energy structures for the peptide backbone, which include three extended conformers and one folded conformer (β-turn, type III). For each of these low-energy structures (only two in the case of Ac-Phe-Phe-NHMe and Ac-Tyr-Tyr-NHMe), ensembles of conformers have been generated comprising many different possible geometries of the side chains. Populations of side-chain rotamers, ring-current effects, coupling constants ($J_{C\alpha HNH}$), and CD spectra have been calculated for each ensemble at 200 K and then compared with experimental results obtained at the lowest possible temperature. The results of such a comparison are consistent with the conformational model above and indicate that conformational preferences of side chains can be predicted without including an explicit solvation term in the conformational energy calculation, at least when the main-chain conformation can be represented with one single conformer type, as is the case of Ac-Trp-Trp-NHMe in TFE.

Introduction

Thermodynamic flexibility[1] is a major obstacle for the conformational study and characterization of short linear peptides dissolved in protic solvents. This obstacle can be circumvented

only by a combination of theoretical and experimental methods:[2–6]
(i) the investigated peptides are represented with a computed

(1) In this paper, the expression "thermodynamic flexibility" indicates the presence of comparable amounts of many conformers at equilibrium.

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