

An INDO MO Study of Substituent Effects upon  $^3J_{CC}$ 

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**Abstract:** INDO MO calculations on model systems indicate that the decrease in the calculated trans  $^3J_{CC}$  in going along the series *n*-butane, equatorial methylcyclohexane, and 1-methyladamantane arises primarily from an increase in the number of  $\beta$ -methylene groups. A numerical analysis shows that the magnitude of the effects associated with the interaction of the multiple rear lobes of carbon hybrid orbitals are much smaller than those for  $\beta$ -substituent effects in these compounds. These calculations rationalize the experimental results for a series of substituted butanes which show a larger in magnitude  $^3J_{CC}$  than those of the corresponding trans arrangement in  $\alpha$ -substituted 1-methyladamantane. Calculations of  $^3J_{CC}$  involving the carbonyl carbons of the carboxylic acid derivatives of the above systems show that  $\beta$ -substituent effects are also dependent upon which  $\beta$  carbon undergoes substitution and they are consistent with the available experimental data for these couplings.

The use of  $^{13}\text{C}$ -enriched materials incorporated into organic compounds and the NMR study of these is continuing to increase in importance for the investigation of organic and biosynthetic mechanisms. The growing ease with which  $^{13}\text{C}$  can be incorporated selectively into compounds, together with the availability of routine Fourier transform NMR spectrometers, makes the use and understanding of  $^{13}\text{C}$ - $^{13}\text{C}$  coupling constant information of immediate interest.

The recent experimental<sup>1-3</sup> and theoretical studies<sup>4-6</sup> of vicinal  $^{13}\text{C}$ - $^{13}\text{C}$  coupling constants ( $^3J_{CC}$ ) have indicated the possibility of obtaining structural information, provided that the complexities of the conformational and substituent dependencies of these are understood. A theoretical study of the conformational dependence and mechanisms for  $^3J_{CC}$  in butane by INDO-MO techniques indicated that the trans values were less in magnitude than the cis values because of a direct mechanism associated with the interactions of the rear lobes of the C1-C3 and C2-C4 orbitals, and that this impinging of the rear lobes contributed about -2.5 Hz to the C-C coupling in the trans arrangement of butane. However, the experimental findings (Table I) that  $^3J_{CC}$  values in substituted butanes are 1.2-1.4 Hz greater in magnitude than those of the similarly substituted 1-methyladamantanes were unexpected.<sup>5</sup> The former compounds show an averaged  $^3J_{CC}$  while the latter comprise only a trans orientation of nuclei which are known to give rise to a larger coupling than the corresponding gauche orientation of the same nuclei. Because of the importance of impinging rear lobes in the trans arrangement, it was suggested<sup>5</sup> that the effect has its origin in a contribution of negative sign associated with an increase in the number of interactions of the rear lobes of carbon hybrid orbitals associated with the latter. The decrease in the calculated  $^3J_{CC}$ , involving the methyl groups, on going from trans butane to methylcyclohexane to 1-methyladamantane was attributed to this effect. Further support was apparently afforded by the experimental values observed for cyclohexanecarboxylic acid and 2-adamantanecarboxylic acid of 4.0 and 4.2 Hz, respectively, which decreases to 3.6 Hz for 1-adamantanecarboxylic acid.

In these cases, however, substituted effects caused by the change of carbon atoms for hydrogen atoms have not been taken into account. In the present work these effects have been extensively investigated by the use of INDO MO theory. The above interpretation is questioned and light is shed on the importance of substituents attached to carbon atoms in the coupling pathway.

### Results and Discussion

Finite perturbation theory at the INDO level of approximation has been used, as described previously,<sup>7</sup> to calculate

Fermi-contact, orbital, and spin-dipolar contributions to the trans  $^3J_{CC}$  of the model compounds in Tables II, III, and VI. Standard geometries have been assumed throughout.<sup>8</sup> The calculations indicated that the Fermi-contact contribution was the predominant term with contributions of less than 0.01 and 0.02 Hz from the latter two terms, respectively, in all cases; hence only the former term is tabulated.

#### Methyl Derivatives of Aliphatic and Alicyclic Hydrocarbons.

The effects of alkyl substitution at the  $\alpha$  and  $\beta$  carbon atoms of the butane fragment are represented in Table II. The orientation and degree of substitution at the  $\alpha$  carbon atoms (those involved in the coupling) has only minor effects upon the magnitude of the coupling. Alkyl substitution at the intermediary  $\beta$  carbon atoms, however, produces a pronounced decrease in the magnitude of the coupling, with sequential substitution being almost additive in effect. Extension of the alkyl chain has little effect, except in those cases where proton-proton overlap occurs, thus indicating that methyl and methylene groups have similar effects.

Comparison of these results with those calculated for equatorial methylcyclohexane (3.73 Hz) and 1-methyladamantane (3.33 Hz) suggests that the primary cause of the decrease in the theoretical value of  $^3J_{CC}$  in these two compounds compared to *n*-butane arises primarily from the increase in the number of substituents on the  $\beta$  carbon atoms. Thus the primary cause of the difference in  $^3J_{CC}$  between the butyl and adamantyl systems in Table I arises from the increased  $\beta$  substitution in the latter. Similarly the experimental  $^3J_{CC}$  (3.2 Hz) to the methyl group of *cis*-4-*tert*-butyl-1-methylcyclohexanol,<sup>4,5,10</sup> which is effectively locked in the conformation with the enriched methyl group equatorial, is calculated (3.13 Hz) as arising simply from the additive effects of a  $\beta$ -methylene (-0.46 Hz) and a  $\beta$ -hydroxyl group (-0.69 Hz) on *n*-butane (4.28 Hz).

These conclusions are at variance with a previous study<sup>5</sup> in which the effects noted above were attributed to the effects of the increase in the number of impinging rear lobes of carbon hybrid orbitals in going along the series *n*-butane, methylcyclohexane, and 1-methyladamantane, while the effects of the increased number of  $\beta$ -carbon substituents were neglected.

In order to investigate the importance of multiple rear-lobe interactions,  $^3J_{CC}$  for the model compounds in the conformations shown in Table III were calculated. Three distinct effects are possible when the effects of  $\alpha$  substitution are assumed to be small. These effects arise (a) from multiple rear-lobe interactions of carbon hybrid orbitals, (b) from steric interactions of protons on the  $\alpha$  carbon atoms with protons elsewhere in the molecule, and (c) from steric interactions of protons on the  $\beta$  carbon atoms with protons elsewhere in the

**Table I.** Experimental  $^3J_{CC}$  Values in a Series of  $^{13}\text{C}$  C-1-Labeled C-1-Substituted Butanes and a Series of  $^{13}\text{C}$   $\alpha$ -Labeled  $\alpha$ -Substituted 1-Methyladamantanes<sup>a</sup>

X	$\text{CH}_3\text{CH}_2\text{CH}_2^*\text{CH}_2\text{X}$ $^3J_{CC}$ , Hz	$^3J_{CC}$ , Hz
H		3.2
OH	4.6	3.3
CN	4.7	3.4
F	4.3	
Cl	4.8	3.4
Br	5.2	
I	4.9	3.7

<sup>a</sup>From ref 5.**Table II.** The Effects of  $\alpha$ - and  $\beta$ -Alkyl Substituents upon the Fermi-Contact Contributions to Trans  $^3J_{CC}$  for Model Compounds, Related to Butane, Calculated (Hz) by INDO MO Theory<sup>7</sup> Using Standard Geometries<sup>8</sup>

$\alpha$ -substituent effects	
I	4.28
II	$\theta$ 180 4.26 60 4.23
III	$\theta_2$ 60 4.15 $\theta_2$ 180 4.12 300
IV	4.00
V	4.25
VI	$\theta$ 180 4.16 60 4.24
VII	$\theta_2$ 300 4.06 180 4.16 60 4.24
$\beta$ -substituent effects	
VIII	3.82
IX	3.45
X	3.38
XI	3.41
XII	$\theta$ 60 3.82 180 3.82 300 4.16

molecule. Assuming that  $\alpha$  substituent effects are negligible then these effects are evaluated as shown in Table IV. Numerical evaluation gives the ranges shown in Table V.

The small magnitude of effect (a) and the nonappearance of effects (b) and (c) in methylcyclohexane and 1-methyladamantane confirm the conclusions reached above and cast doubt on the validity of the concepts expounded regarding the magnitude of the effects of impinging multiple rear lobes<sup>5</sup> in the above series of compounds.

**Carboxylic Acid Derivatives of Aliphatic and Alicyclic Hydrocarbons.** It is interesting to note that the coupling calculated for both 1- and 2-methyladamantanes is of the same magni-

**Table III.** Spatial Effects upon the Fermi-Contact Contributions to Trans  $^3J_{CC}$  (Hz). All Compounds Have Staggered Conformations<sup>a</sup>

XIII	3.97	XVIII	$\theta$ 180 4.10 60 3.79
XIV	3.89	XIX	a 4.13 b 3.71
XV	a 3.54 b 3.80	XX	a 3.29 b 3.74
XVI	3.57	XXI	3.33
XVII	3.73	XXII	3.33

<sup>a</sup>In all the sterically hindered standard geometry<sup>8</sup> conformations shown the interacting protons were 0.7348 Å apart.

**Table IV.** Evaluation of the Effects Present between Pairs of Compounds Taken from Tables II and III Caused by (a) Rear-Lobe Interactions of Carbon Hybrid Orbitals, (b) Steric Interactions of Protons on the  $\alpha$  Carbon Atoms with Protons Elsewhere in the Molecule, and (c) Steric Interactions of Protons on the  $\beta$  Carbon Atoms with Protons Elsewhere in the Molecule

Set	Comps considered <sup>a</sup>	Effects present	Magnitude, Hz
(i)	XII (300)-VIII	1c + 1a	+0.34
(ii)	XVIII (60)-IX	1c + 1a	+0.34
(iii)	XIXa-XIXb	1c	+0.42
(iv)	XXb-XXa	1c	+0.45
(v)	XVIII (180)-XII (300)	1c + 1a <sup>b</sup>	+0.31
(vi)	VII (300)-II (60)	1b + 1a	-0.17
(vii)	XIII-III (300, 60)	1b + 1a	-0.15
(viii)	XVb-XVa	1c	+0.26
(ix)	XVI-XVII	1b + 1a	-0.16
(x)	XVb-XVII	1a + 1b + 1c	+0.07
(xi)	XIV-III (300, 60)	2b - 2a	-0.23

<sup>a</sup> The compounds have been numbered as shown in Table II. <sup>b</sup> The increase in the substitution of a methyl on the  $\beta$  carbon has to be taken into account (+0.37 Hz).

tude, which is consistent with the present interpretation, as both have the same number of  $\beta$  substituents but differing numbers of impinging rear lobes. At first sight this appears to be in conflict with the experimental evidence. Thus, although the experimental value of  $^3J_{CC}$  for 2-methyladamantane is not known, the corresponding carboxylic acid values for both derivatives are and these are quite different (1-adamantanecarboxylic acid, 3.6 Hz; 2-adamantanecarboxylic acid, 4.2 Hz).

In order to clarify this point calculations were performed for butanoic acid, its methyl derivatives, cyclohexanecarboxylic

**Table V.** Magnitude and Ranges of the Effects Evaluated in Table IV

Sets considered	Effect	Range, Hz	Middle of range, Hz
(i), (ii), (v)	1a	+0.08 to -0.14	-0.03 ± 0.11
(vi), (vii), (ix), (x), (xi)	1b	-0.12 to -0.26	-0.19 ± 0.07
(iii), (iv), (viii)	1c	+0.26 to +0.45	+0.36 ± 0.09

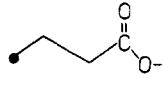
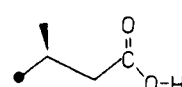
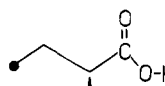

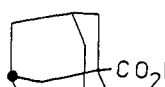

acid, and 1- and 2-adamantanecarboxylic acids (Table VI). In the latter three compounds the averaged  $^3J_{CC}$  values were calculated, by the use of Simpson's rule for numerical integration with  $30^\circ$  grids, to allow for rotation about the C-CO bond. It is immediately apparent that the calculated values for these three compounds reflect the order and relative magnitude of the experimental couplings. The results for butanoic acid and its derivatives show that *the substituent effect upon J is dependent upon which  $\beta$  carbon undergoes substitution*. These results now allow rationalization of the adamantanecarboxylic acid results. In 1-adamantanecarboxylic acid the two methylene substituents are  $\beta$  to the carboxylic acid group while in 2-adamantanecarboxylic acid one methylene substituent is  $\beta$  to the carboxylic acid group while the other is  $\beta$  to the coupled methylene carbon. From the butanoic acid calculations one expects the 1 derivative to have a lower  $^3J_{CC}$  than the 2 derivative, a result that is calculated theoretically and observed experimentally.

This effect of the dependency upon the position of  $\beta$  substitution is not without precedence for other couplings and has been observed for vicinal proton-fluorine couplings.<sup>11</sup>

Thus the difference in  $^3J_{CC}$  for the adamantanecarboxylic acids can be explained from  $\beta$ -substitution effects without the necessity of invoking effects due to the impinging of the multiple rear lobes of carbon hybrid orbitals. A similar argument probably holds for the difference in the experimental  $^3J_{CSn}$  values in 1- and 2-adamantylstannanes,<sup>12</sup> although here calculations are not possible.

From the above it can be seen that semiempirical MO results are particularly encouraging for these three-bond couplings with the trends and magnitudes of the changes in the experimental couplings being well reproduced even though the theory assumes constant values for the carbon nuclear valence shell s-electron density. It must be emphasized, however, that the extension of these methods to describe both shorter and longer range couplings must be treated with some caution as the theory is known to be inadequate for describing certain details of H-H<sup>13</sup> and C-C<sup>6</sup> couplings which may arise from approximations inherent in the theory. Contributions from the orbital and spin-dipolar terms are expected to be significant making the use of only the Fermi-contact term dubious.

**Table VI.** Calculated Fermi-Contact Contributions to  $^3J_{CC}$  Involving the Carbonyl Carbon of Various Carboxylic Acid Derivatives in the Conformations Shown<sup>a</sup>

	6.17		6.66
	5.50		5.20
	4.59		5.54

<sup>a</sup>Simpson's rule for numerical integration with  $30^\circ$  grids was used to allow for rotation about the C-CO bond in the cyclohexane and adamantanecarboxylic acids.

In conclusion we have shown that INDO MO calculations can rationalize the experimental values of  $^3J_{CC}$  for both the methyl-substituted hydrocarbons and their carboxylic acid derivatives. In particular substituents at all carbon atoms along the coupling pathway need to be considered if these couplings are to be used in the future to derive conformational information. Effects of a similar nature are to be expected for  $^3J_{CF}$  in saturated systems as these appear to be Fermi contact dominated.<sup>14</sup>

## References and Notes

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