Tetrahedron Vol. 34, pp. 247 to 251. Pergamon Press 1978. Printed in Great Britain

^{13}C NUCLEAR MAGNETIC RESONANCE SPECTRA—VII[1]

THROUGH-BOND INTERACTIONS AND HYPERCONJUGATIVE SUBSTITUENT EFFECTS AT 2,4-DISUBSTITUTED ADAMANTANES

HELMUT DUDDECK
Ruhr-Universität Bochum, Abteilung für Chemie, Postfach 10 21 48, D-4630 Bochum 1, West Germany

(*Received in UK 5 July 1977; Accepted for publication 1 August 1977*)

Abstract—The ^{13}C NMR spectra of a series of 2,4-disubstituted adamantanes with the substituents in various configurations are reported and discussed in terms of through-bond and through-space interactions of the substituents. Through-bond interactions in equatorially disubstituted adamantanes and equatorially substituted adamantanones are attributed to overlapping of free-electron pairs and bond orbitals in symmetrically favoured orientations.

Although ^{13}C NMR spectroscopy has become a routine method for organic chemists during the last few years, the ^{13}C chemical shift is not yet well understood. Thus the prediction of ^{13}C chemical shifts and the signal assignments can still be difficult for larger molecules.

In general, substituent effects on ^{13}C chemical shifts (SCS) are additive within a limit of about ± 1 ppm so that the chemical shifts of polyfunctional molecules can be calculated with good accuracy, when the SCS of the single substituents at the same molecular skeleton are known. However, this additivity may no longer be valid if there is a through-space or through-bond interaction between the substituents. For example, in 1,3-disubstituted compounds with steric interaction between the substituents it is often found that the signals of the substituent-bearing carbons appear at lower field than expected[2] (see also below). Very recently, we reported ^{13}C NMR spectra of β substituted adamantanones[3] which reveal SCS-non-additivities at certain carbons which are caused obviously by through-bond interactions between carbonyl groups and heterosubstituents (OR, Hal). These interaction even affect unsubstituted carbons.

RESULTS

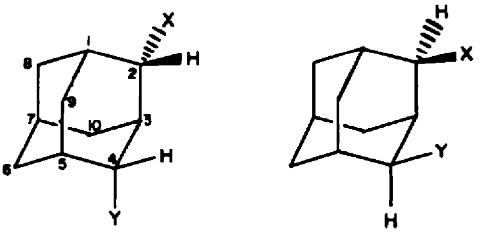
In Table 1 the ^{13}C chemical shifts of a series of 2,4-disubstituted adamantanes are reported. For two different substituents X and Y four epimers are possible which are depicted in Scheme 1. The abbreviations ee, aa, ea and ae represent the substituents' orientation at C-2 and C-4 relative to the highest substituted ring which is formed by the carbons 1, 2, 3, 4, 5 and 9, e standing for equatorial and a for axial.

The values in parentheses in Table 1 are deviations of the experimental chemical shifts from those calculated by a simple rule which implies that the SCS obtained from the spectra of the monosubstituted adamantanes (Table 2) are additive.[3] Deviations smaller than 1 ppm upfield or downfield will not be discussed and are considered to be negligible.

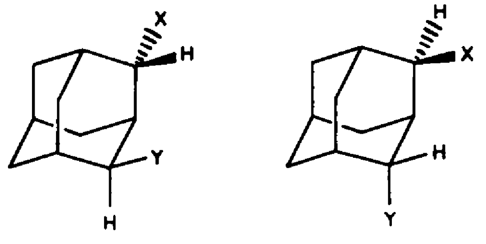
Additivity of the SCS is found for the signals of most carbons with remarkable accuracy except some of them which are in a distinguished position:

Type A (*diequatorial*). Non-additivities occur at the two substituted carbons C-2 and C-4 and, additionally, at the unsubstituted C-9, due to through-bond interactions of the two substituents. All deviations are negative, i.e. the signals appear at higher field than expected. These effects will be discussed in the next section.

Type B (*diaxial*). Non-additivities of SCS are also observed for the signals of the substituted carbons. But in contrast to the Type A adamantanes the deviations are positive. Similar observations were published recently by Djerassi *et al.*[2] who interpreted these deviations by assuming a direct throughspace interaction of the substituents and, additionally, by the lack of a γ-*gauche* interaction with a hydrogen for each substituent which occurred in the corresponding monosubstituted compounds. Likewise, we reported positive deviations from



Type A (ee) Type B (aa)



Type C (ea) Type D (ae)

	1	2	3	4	5	6	7	8	9
X	OH	OH	OH	OH	NHAc	NHAc	Cl	Br	I
Y	OH	Cl	Br	I	Cl	Br	Cl	Br	I

Scheme 1.

Table 1. ^{13}C chemical shifts of 2,4-disubstituted adamantanes and deviations between the experimental and calculated shifts (in parentheses), in ppm[a]

	1	2	3	4	5	6	7	8	9	10	others
1A[b]	33.3	71.4	41.2	71.4	33.3	31.1	27.0	31.1	33.1	24.8	
	(−0.1)	(−0.1)	(+0.4)	(−0.1)	(−0.1)	(0.0)	(0.0)	(0.0)	(−2.2)	(+0.3)	
2A	33.2	73.6	42.4	64.7	34.6	31.0[c]	26.9	31.2[c]	34.9	24.9	
	(0.0)	(−1.6)	(+0.2)	(−2.3)	(−0.2)	(−0.1)	(0.0)	(−0.1)	(−2.3)	(+0.4)	
3A	33.3	73.8	42.9	58.9	35.1	31.8	26.9	31.4	35.5	25.6	
	(+0.1)	(−1.9)	(+0.2)	(−3.7)	(−0.2)	(+0.1)	(−0.1)	(0.0)	(−2.2)	(+0.5)	
4A	33.6	73.4	44.1	40.2	36.3	33.3	27.2	32.0	35.9	27.0	
	(+0.3)	(−2.3)	(+0.3)	(−5.1)	(−0.1)	(+0.3)	(+0.1)	(+0.4)	(−1.8)	(+0.6)	
5A	30.6	52.9	39.3	64.8	34.6	30.9	26.5	32.0	36.0	25.7	168.4 (C=O)
	(0.0)	(−1.1)	(−0.3)	(−2.8)	(−0.2)	(−0.1)	(0.0)	(−0.1)	(−1.8)	(+0.4)	23.5 (CH_3)
6A	30.8	53.3	40.0	59.4	35.2	31.8[c]	26.7	32.4[c]	36.7	26.4	169.2 (C=O)
	(+0.2)	(−1.2)	(−0.1)	(−3.7)	(−0.1)	(+0.2)	(+0.1)	(+0.2)	(−1.6)	(+0.5)	23.5 (CH_3)
7A	34.3	64.6	42.8	64.6	34.3	31.1	26.7	31.1	36.6	24.8	
	(−0.2)	(−4.0)	(−0.7)	(−4.0)	(−0.2)	(−0.1)	(0.0)	(−0.1)	(−2.2)	(+0.4)	
8A	34.8	58.0	43.5	58.0	34.8	32.1	26.9	32.1	38.0	26.1	
	(−0.2)	(−6.7)	(−1.0)	(−6.7)	(−0.2)	(+0.2)	(0.0)	(+0.2)	(−1.8)	(+0.5)	
9A	36.2	38.1	45.3	38.1	36.2	33.9	27.4	33.9	39.0	28.6	
	(0.0)	(−9.3)	(−1.4)	(−9.3)	(0.0)	(+0.5)	(+0.3)	(+0.5)	(−0.8)	(+0.4)	
1B	34.6	76.0	33.7	76.0	34.6	36.3	25.8	36.3	25.3	35.2	
	(+0.6)	(+7.9)	(−2.2)	(+7.9)	(+0.6)	(−0.4)	(−0.3)	(−0.4)	(+0.7)	(−0.4)	
2B	34.5	75.7	40.5	67.1	35.8	39.4	25.8	36.6	24.8	38.0	
	(+0.7)	(+7.7)	(−1.7)	(+5.6)	(+0.5)	(+0.1)	(0.0)	(−0.2)	(+0.3)	(+0.8)	
3B	34.4	75.8	41.0	60.1	36.6	39.2	26.0	36.8	25.6	39.2	
	(+0.5)	(+7.2)	(−1.7)	(+3.0)	(+0.8)	(+0.4)	(+0.2)	(−0.1)	(+0.5)	(+1.5)	
1C[b]	34.0	67.3	40.9	74.0	33.5	36.1	26.3	30.9	29.9[c]	30.2[c]	
	(+0.1)	(+1.2)	(+0.1)	(+2.5)	(+0.1)	(−0.4)	(−0.2)	(−0.2)	(0.0)	(+0.3)	
2C	34.3	68.9[c]	41.9	68.0[c]	35.1	38.1	26.2	31.0	30.6	32.1	
	(+0.5)	(+0.9)	(−0.3)	(+1.0)	(+0.3)	(−0.2)	(−0.1)	(−0.3)	(+0.6)	(+0.4)	
3C	34.4	69.5	42.4	62.3	35.8	38.9	26.3	31.4[c]	31.2[c]	33.0	
	(+0.5)	(+0.9)	(−0.3)	(+0.3)	(+0.5)	(+0.1)	(0.0)	(0.0)	(+0.6)	(+0.8)	
7C	35.2[c]	62.0	42.8	67.9	34.8[c]	38.2	26.1	30.9	31.9	31.9	
	(+0.1)	(+0.6)	(−0.7)	(−0.7)	(+0.3)	(−0.2)	(0.0)	(−0.3)	(+0.3)	(+0.3)	
8C	35.8[c]	57.2	43.7	62.3	35.5[c]	39.1	26.2	31.8	33.2[c]	33.4[c]	
	(+0.1)	(+0.4)	(−0.8)	(−2.4)	(+0.5)	(+0.1)	(0.0)	(−0.1)	(−0.5)	(+0.7)	
2D	33.7	76.0	42.5	63.3	35.5	31.0	26.5	36.5	32.0	30.2	
	(+0.5)	(+0.8)	(+0.3)	(+1.8)	(+0.2)	(−0.1)	(+0.1)	(−0.3)	(+0.3)	(+0.2)	
3D	33.7	76.2	43.0	58.6	36.0	31.7	26.5	36.7	32.5	31.0	
	(+0.5)	(+0.5)	(+0.3)	(+1.5)	(+0.2)	(0.0)	(0.0)	(−0.2)	(+0.3)	(+0.4)	
4D	33.8	75.7	44.2	40.6	37.1	33.1	26.7	37.1	32.5	32.5	
	(+0.5)	(0.0)	(+0.4)	(+0.8)	(+0.2)	(+0.1)	(+0.1)	(0.0)	(+0.3)	(+0.6)	

[a] Recorded in deuterochloroform with tetramethylsilane as internal standard unless otherwise noted.
[b] Recorded in dimethylsulphoxide-d_6.
[c] Signals may be interchanged.

additivity for some 4-substituted adamantanones with the substituent in axial position. The C-9 signals of the Type B adamantanes are not affected here. The deviations at C-3 in these compounds may be due to non-additive changes in the geometrical arrangement of those carbons caused by the substituents' through-space interaction.

Type C and D (*equatorial + axial*). No obvious trends of deviations can be seen. Whereas calculated and experimental chemical shifts agree excellently for all unsubstituted carbons there are positive and negative deviations as well for the signals of C-2 and C-4. When the compounds are arranged according to the sub-

Table 2. ^{13}C chemical shifts and substituent effects (in parentheses) of 2-substituted adamantanes, in ppm[a,b]

	1/3	2	4/9	5	6	7	8/10	others
H	28.5	37.8	37.8	28.5	37.8	28.5	37.8	
OH	34.7 (6.2)	74.7 (36.9)	31.2 (-6.6)	27.8 (-0.7)	37.8 (0.0)	27.3 (-1.2)	36.7 (-1.1)	
OH[c]	34.2 (6.6)	72.4 (35.3)	30.8 (-6.3)	27.3 (-0.3)	37.4 (+0.3)	26.8 (-0.8)	36.2 (-0.9)	
NHAc	32.1 (3.6)	53.5 (15.7)	32.0 (-5.8)	27.4 (-1.1)	37.7 (-0.1)	27.3 (-1.2)	37.3 (-0.5)	169.2 (C=O) 23.6 (CH_3)
Cl	36.0 (7.5)	68.1 (30.3)	31.1 (-6.7)	27.6 (-0.9)	37.9 (+0.1)	27.0 (-1.5)	38.3 (+0.5)	
Br	36.5 (8.0)	63.7 (25.9)	31.7 (-6.1)	27.7 (-0.8)	38.0 (+0.2)	27.0 (-1.5)	38.8 (+1.0)	
I	37.6 (9.1)	46.4 (8.6)	33.0 (-4.9)	27.8 (-0.7)	38.2 (+0.4)	27.1 (-1.4)	38.8 (+1.0)	

[a] Recorded in deuterochloroform with tetramethylsilane as internal standard unless otherwise noted.

[b] Taken in part from Ref. 3.

[c] Recorded in dimethylsulphoxide-d_6; SCS obtained by comparison with adamantane chemical shifts in the same solvent: CH_2 37.1 ppm, CH 27.6 ppm).

stituents' polarizabilities, as they are in the series **1C**, **2C**, **3C**, **7C** and **8C**, a monotonous sequence can be found for the C-4 signals ranging from +2.5 ppm to −2.4 ppm. However, this trend can not yet be correlated with the substituents' nature, their configuration or any other substituent property. More experimental data are necessary.

DISCUSSION

The substituent effect on chemical shifts of *γ-gauche* situated carbons, the so-called "steric γ effect", has been investigated thoroughly during the last few years[4] and is a valuable aid in peak assignment. However, SCS on chemical shifts on γ carbons in antiperiplanar configuration attracted much less attention. Eliel *et al.*[5] suggested that the γ_{anti} SCS may be originated by hyperconjugative interaction of the substituents' free-electron pair with the C^{α}–$C^{\beta}\delta$ bond orbitals involving the δ bond orbital between the γ carbon and the δ positioned atom (Fig. 1).

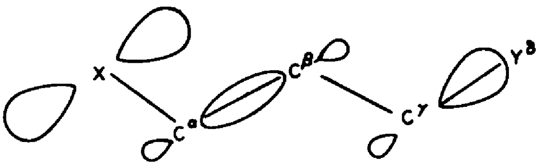


Fig. 1. Hyperconjugative interaction of a substituent X on a γ carbon in antiperiplanar configuration.

The nature of the bond between the γ carbon and the δ positioned atom plays an important part could recently be shown by inspecting the spectra of some bridgehead-substituted triamantanes.[6] While the γ_{anti} SCS on carbons with coplanar C^{γ}–*Hδ* bond orbitals show the "regular" values and are similar to those obtained from the corresponding adamantanes and diamantanes, those on the quarternay C-1 carbons are about 5 ppm smaller (in the δ scale) for all substituents OH, Br and Me.

The effectiveness of this mechanism should be enhanced by coplanarity of the participating atoms. This could be confirmed by us, at least for bridgehead-substituted compounds in a recent publication.[1] The non-additivities of the SCS at C-2, C-4 and C-9 of the 2^e, 4^e-disubstituted adamantanes (Type A) can be explained using the same through-bond interaction mechanism:

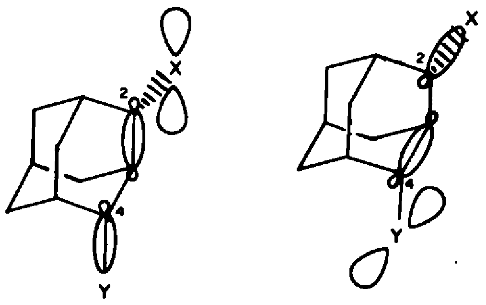


Fig. 2.

In the disubstituted compounds the interactions of the free-electron pairs at X with the C^4-Y bond orbital via the C^2–C^3 bond orbital of course are not identical with those with the C^4-H bond orbital in the monosubstituted adamantanes. Thus the substituent effect of X must also be different in the two cases. The same is valid for Y, leading to chemical shifts at C-2 and C-4 which cannot be predicted by simply adding the individual SCS to the chemical shift value of a methylene carbon in adamantane itself.

The value of the deviation at a given carbon, C-2 or C-4, strongly depends on the characters of both substituents, the directly bonded and the γ positioned one. Generally it can be stated that the effect increases in the series NHAc ≈ OH < Cl < Br < I. Whereas for example in the adamantanediol the deviation is zero, it will be enhanced at both carbons by replacing one OH group by a halogen atom, more at the halogen substituted atom

C-4 and less at the OH substituted C-2. If also the second OH group is replaced by the same halogen, the deviation is nearly doubled compared with that at C-4 in the former compound.

Apparently, the interaction mechanism is supported by increasing the substituents' polarizabilities. On the other hand, electronegativity seems not to play an important part. The non-additivity at C-9 can be explained by the following considerations: The introduction of Y at C-4 causes a perturbation in the electronic environment of C-2. Thereby the interaction of the p orbital at X with the coplanar C^9-H δ bond orbital will be changed. Analogously, the effect of Y on C-9 is altered by the introduction of X. Both perturbations are reflected in the non-additivity of the two SCS of X and Y at C-9 (Fig. 3).

In contrast to the substituted carbons the deviations at C-9 are astonishingly uniform (about − 2 ppm); only for the diiodoadamantane it is only − 0.8 ppm.

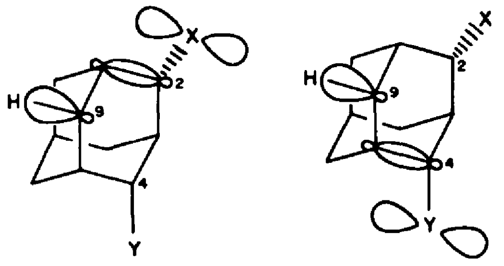


Fig. 3.

All these observations correspond to those made by us earlier[3] for 4^e-substituted adamantanones, although the magnitude of the non-additive effects is somewhat smaller than that for the adamantanones.

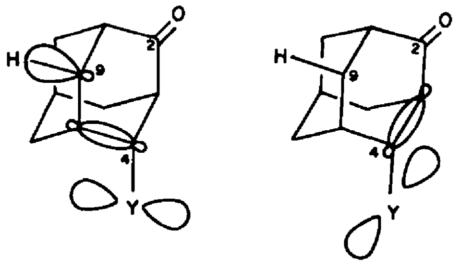


Fig. 4.

Recent investigations[7] led us to the conclusion that indeed free-electron pairs at Y are necessary to observe non-additivities. So these effects appear to be very weak for 4^e-substituted adamantanones with Y = CH_2OH and CH_2OTs (Ts ≡ *p*-toluenesulphonyl). Furthermore, no effect could be detected at C-5 of 3-methylcyclohexanone. This cannot be due to the conformational flexibility of that system, since the signal for C-5 of 3-methoxycyclohexanone appears about 3.5 ppm at higher field than predicted assuming additivity.

For an effective interaction at an unsubstituted carbon in β position to the CO and γ_{anti} to the substituent X these two substituents must be in β position to each other also, just as they are in the adamantanones or cyclohexanones. This can be deduced from the fact that in the case of 3β-substituted 5α-cholestan-7-ones (Fig. 5) perfect additivity at C-5 and only minor deviations at C-3 and C-7 are found.

In 4-substituted bicyclo[2.2.2]octanones the carbons C-6 and C-7 are enantiotopic and correspond to C-9 in the adamantanones (Fig. 6). Already in an earlier study[3] we reported that there are no significant deviations from SCS additivity at these carbons. This becomes clear, if one considers that none of the adjacent $C^{6/7}$-H bond orbitals is coplanar with the Y-C^4-C^5-C^6-moiety (or the Y-C^4-C^8-C^7-moiety respectively). However, the equatorial hydrogen at C-9 in the adamantanones in coplanar and can be affected by the through-bond mechanism (see above and Figs. 3 and 4). Morris[8] recently investigated SCS in 4-substituted camphors and related compounds. He also observed that the SCS on the γ_{anti} positioned C-6 carbons are very small and mostly negative, whereas introduction of a 4^e-substituent in the adamantanone skeleton causes a strong upfield shift of the C-9 signal (corresponding to C-6 in the camphors). Therefore Morris' findings seem to indicate that just as in the case of the bicyclo[2.2.2]octanones there are no significant non-additive substituent effects at the C-6 carbons again.

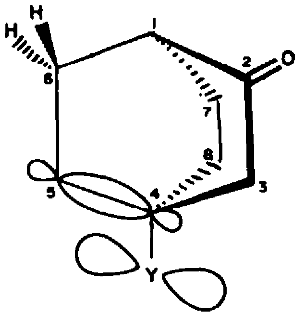


Fig. 6.

It is generally agreed that among all contributions to the total nuclear shielding the paramagnetic contribution is the decisive one:[9,10]

$$\delta_p = -\frac{e^2\hbar^2}{2m^2c^2}(\Delta E)^{-1}\left\langle\frac{1}{r^3}\right\rangle_{2p}\left(q_{AA} - \sum_{B\neq A} q_{AB}\right)$$

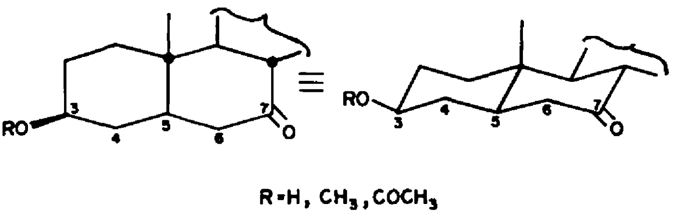


Fig. 5.

In this equation ΔE represents the mean excitation energy, r the distance between 2p electrons and nucleus and q_{AA} and q_{AB} are terms describing the bond order and the charge density. Morris[8] pointed out that apparently it is not the ΔE^{-1} term which is responsible for the chemical shift dependence of the carbonyl carbons in the camphor series, since no significant differences appeared in the UV spectra of these compounds with various substituents. Likewise, we found that the λ_{max} of all 4^{e}-substituted adamantanones are similar.[7] Even if the CO group is replaced by a 1,1-dicyanovinylen group their UV spectra show no essential dependence on the substituents' nature.[7] That means that the interaction involved must be of another type than the σ coupled transition discussed by Verhoeven *et al.*[11] On the other hand, in the ^{13}C NMR spectra of their compounds they found no remarkable evidence for such an interaction.

Further investigations in this field, expecially with different π electron chromophors are in progress in this laboratory.

EXPERIMENTAL

Chemical. The adamantanediols and the haloadamantanols (substituent code numbers 1 to 4) were obtained by reduction of the corresponding hydroxy- and haloadamantanones,[3] respectively, with zinc borohydride.[12] Both isomeric adamantanediols or haloadamantanols resulted from the reduction experiments in various ratios with good overall yields. They were separated by column chromatography (silicagel with ligroin/acetone mixtures) and characterized by ^{1}H NMR, IR and mass spectra. In all cases the derivatives with the newly generated OH group in axial position were eluated first followed by the isomer with the equatorial OH. Reduction of the axial iodoadamantanone gave several compounds, some of them in traces. Among them the two epimers with the I atom in equatorial position could be detected. One more iodoadamantanol was isolated which, however, did not fit the sets of calculated chemical shifts for **4B** and **4C**. This reaction is still to be investigated in this laboratory.

The configuration of the OH group was determined by 90 MHz ^{1}H NMR spectra: The chemical shifts of the protons at C-2 and C-4 were calculated using the SCS of the monosubstituted compounds assuming additivity.[13] The deviations between calculated and observed chemical shifts are small. **3A** could also be identified by comparison with the spectrum of an authentic sample. This as well as compounds **5A** and **6A** were kindly supplied by Prof. H. Wynberg, Groningen, The Netherlands. **7A**, **7C**, **8A**, **8C** and **9A** were prepared according to known procedures.[14]

Measurements. The ^{13}C NMR spectra were recorded at natural abundance in the PFT mode at 22.64 MHz using a Bruker WH-90 spectrometer with internal deuterium lock. The samples were run in deuterated chloroform with 5% TMS as internal standard if not otherwise noted. Positive values of chemical shifts correspond to deshielding. Accuracy of chemical shifts is about ± 0.05 ppm. The signal assignment is based on spectra obtained under ^{1}H off-resonance irradiation conditions, by which the number of adjacent hydrogens could be determined for the carbons unambiguously, even for superimposing signals. ^{1}H NMR spectra were recorded using a Bruker HFX-90 spectrometer in the CW mode.

Acknowledgements—The author thanks Prof. G. Snatzke, Bochum, West Germany, for many helpful discussions and Prof. H. Wynberg, Groningen, The Netherlands, who made available some compounds. This work was supported by the Deutsche Forschungsgemeinschaft.

REFERENCES

[1] For Part VI: H. Duddeck and H. Klein, *Tetrahedron* **33**, 1971 (1977).

[2] C. L. VanAntwerp, H. Eggert, G. D. Meakins, J. O. Miners and C. Djerassi, *J. Org. Chem.* **42**, 789 (1977).

[3] H. Duddeck, *Org. Magn. Resonance* **7**, 151 (1975); H. Duddeck and P. Wolff, *Org. Magn. Resonance* **9**, 528 (1977).

[4] D. M. Grant and B. V. Cheney, *J. Am. Chem. Soc.* **89**, 5315 (1967); H. Beierbeck and J. K. Saunders, *Can. J. Chem.* **54**, 2985 (1976); K. Seidman and G. E. Maciel, *J. Am. Chem. Soc.* **99**, 659 (1977) and many others; see also Ref. 10.

[5] E. L. Eliel, W. F. Bailey, L. D. Kopp, R. L. Willer, D. M. Grant, R. Bertrand, K. A. Christensen, D. K. Dalling, M. W. Duch, E. Wenkert, F. M. Schell and D. W. Cochran, *J. Am. Chem. Soc.* **97**, 322 (1975).

[6] H. Duddeck and M. A. McKervey, to be published.

[7] H. Duddeck, preliminary results.

[8] D. G. Morris and A. M. Murray, *J. Chem. Soc., Perkin Trans.* II 1579 (1976).

[9] J. A. Pople, *J. Chem. Phys.* **37**, 53, 60 (1962); M. Karplus and J. A. Pople, *Ibid.* **38**, 2803 (1963).

[10] J. B. Stothers, *Carbon-13 NMR Spectroscopy*. Academic Press, New York (1972).

[11] A. W. J. D. Dekkers, J. W. Verhoeven and W. N. Speckamp, *Tetrahedron* **29**, 1691 (1973); C. Worrell, J. W. Verhoeven and W. N. Speckamp, *Tetrahedron* **30**, 3525 (1974); P. Pasman, J. W. Verhoeven and Th. J. DeBoer, *Tetrahedron* **32**, 2827 (1976); *Tetrahedron Letters* 207 (1977).

[12] W. J. Gensler, F. Johnson and A. D. B. Sloan, *J. Am. Chem. Soc.* **82**, 6074 (1960); E. R. H. Walker, *Chem. Soc. Rev.* **5**, 23 (1976).

[13] F. W. van Deursen and P. K. Korver, *Tetrahedron Letters* 3923 (1967); F. W. van Deursen and A. C. Udding, *Rec. Trav. Chim.* **87**, 1243 (1968); F. W. van Deursen and J. Bakker, *Tetrahedron* **27**, 4593 (1971); see also R. C. Fort, Jr., *Adamantane*, Marcel Dekker, New York (1976).

[14] A. C. Udding, Thesis, Rijksuniversiteit Groningen, The Netherlands (1968).