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^{13}C NMR SPECTRA OF ADAMANTANE DERIVATIVES

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Abstract—The carbon-13 chemical shifts of mono- and 1,3-disubstituted adamantanes are reported. The effects caused by the substituents are compared with those met in aliphatic and alicyclic compounds. It is shown that the 1,4-interactions have only minor importance in 1-substituted adamantanes. The influence of polar groups on the chemical shifts of γ- and δ-carbon atoms is a typical 'through-the-bonds' interaction and correlates with inductive parameters of the substituents.

THE NONBONDED 1,4-interactions which cause very characteristic diamagnetic shifts in ^{13}C spectra, are operative in aliphatic and alicyclic compounds,[1 to 4] in norbornane derivatives[5] and also in and between the side chains of aromatic molecules.[6,7] Owing to the unique structure of adamantane, the 1,4-nonbonded interactions between the first atom of the substituent group (from the adamantane ring) and γ-carbons of the ring cannot play any significant role in 1-substituted adamantanes. In 2-substituted adamantanes a strong 1,4-interaction between the substituents and γ_{syn}-carbons of the adamantane ring could be expected. The 1,3-disubstituted adamantane derivatives provide a good check for the additivity of substituent effects.

EXPERIMENTAL

The experimental conditions and technique were reported in our earlier papers.[5,8] The substituted adamantanes were synthesized by conventional methods The sample of aminoadamantane was generously provided by J. Polis (Riga). All adamantane samples were used as concentrated solutions in CCl_4. Low solubility (in many cases less than 10%) required the use of spectral accumulation. The concentration differences did not influence the measured shift values, as was shown by dilution of a 25% 1-chloro-adamantane solution in CCl_4 to 8% concentration. In the case of some 1,3-disubstituted adamantanes methanol was added to improve solubility. Carbon chemical shifts were measured from internal CCl_4 ($\delta_{TMS} = 96{\cdot}4$ ppm; $\delta_{CS_2} = 96{\cdot}7$ ppm, compare $\delta_{CS_2} = 96{\cdot}5$[9]) and were reproducible to about $\pm 0{\cdot}1$ ppm. Off decoupled spectra were recorded for the determination of the multiplicities of carbon signals. The assignment of most spectral lines is unambiguous on the grounds of line intensities, multiplicities and regularities in the influence of polar substituents. The assignment of carbon signals of 1,3-disubstituted adamantanes was carried out on the assumption of the validity of additivity relationships, which could be expected to hold in the rigid adamantane skeleton with distant substituents.

The measured chemical shifts are given in the Tables 1, 2 and 3. No generally accepted system exists for the numbering of adamantane carbon atoms.[10 to 13] We therefore mark the carbon atoms with greek letters, starting from the substituents and depicting the adamantane skeleton in a suitable way as shown in the particular table heads.

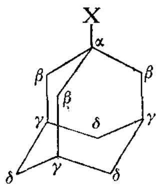
RESULTS AND DISCUSSION

Adamantane and 1-substituted adamantanes

As was pointed out in our earlier report,[8] in adamantane the methylene carbons resonate at a lower field than the methine carbons. For the calculation of ^{13}C chemical shifts from the Savitsky increments,[14] an additional parameter for the rings had to be used in analogy to the calculation of diamagnetic susceptibilities by the Pascal scheme.[15] The more sophisticated parameters of Grant and Paul[1] are even better for the calculation of ^{13}C chemical shifts in hydrocarbons, and on this basis the cyclohexane chemical shift is equal to 32·3 ppm from TMS. So the corrective term for the cyclohexyl ring turns out to be about 5 ppm. The same calculation for adamantane, including the 5 ppm corrective term and additional terms for branched hydrocarbons,[1] gives a calculated methine carbon shift equal to 29·8 ppm (exp. 28·6 ppm) and 38·9 ppm for the methylene carbon (exp. 38·0 ppm).

The good fit of the calculated shift values with experimental results shows that no large steric interactions and strain can exist between the carbon atoms in adamantane. All ^{13}C chemical shifts in adamantane derivatives can be described with the usual regularities and interactions, characteristic for the strain-free alkanes and cyclohexanes. This conclusion is in accord with the accepted strain-free structure of adamantane and at variance with the somewhat sensational recent statement about the comparatively large strain in adamantane,[16] as compared with aliphatic hydrocarbons.

TABLE 1. ^{13}C CHEMICAL SHIFTS AND SUBSTITUENT EFFECTS IN 1-SUBSTITUTED ADAMANTANES



No.	Substituent —X	Chemical shifts[a] of carbon atoms δ_{TMS}					Substituent effects[b] in ppm			
		α	β	γ	δ	Others	α	β	γ	δ
(1)	—H	28·6	38·0	28·6	38·0		0	0	0	0
(2)	—CH_3	29·9	44·6	28·9	36·9	31·1	1·3	6·6	0·3	−1·1
(3)	—NH_2	47·4	46·9	30·1	36·8		18·8	8·9	1·5	−1·2
(4)	—OH	67·5	45·8	30·9	36·5		38·9	7·8	2·3	−1·5
(5)	—Br	64·3	49·5	32·5	35·9		35·7	11·5	3·9	−2·1
(6)	—Cl	67·2	48·0	31·7	35·9		38·6	10·0	3·1	−2·1
(7)	—F[c]	90·1	43·1	31·8	36·4		61·5	5·1	3·2	−1·6
(8)	—NH_3^+	52·4	40·5	29·4	35·7		23·8	2·5	0·8	−2·3
(9)	—Ad[d]	36·4	35·5	29·1	37·7		7·8	−2·5	0·5	−0·3
(10)	—CH_2COOH	32·8	42·6	28·8	37·0	178·2[e] 48·8	4·2	4·6	0·2	−1·0
(11)	—CH_2OH	34·7	39·4	28·4	37·5	73·2	6·1	1·4	−0·2	−0·5
(12)	—CH_2Br	33·4	41·0	28·6	36·9	47·5	4·8	3·0	0	−1·1
(13)	—COOH	40·4	38·7	28·0	36·7	184·0	11·8	0·7	−0·6	−1·3
(14)	—NO_2	84·3	40·8	29·8	35·8		55·7	2·8	1·2	−2·2

[a] From external tetramethylsilane (TMS).

[b] From unsubstituted adamantane.

[c] $J_{CF} = 187$ Hz; $J_{CC.} = 18$ Hz; $J_{CCCF} = 10$ Hz.

[d] Biadamantane.

[e] Carboxyl group.

The effects of substituents on the α- and β-carbon chemical shifts depend on steric as well as on the electronic 'through-the-bonds' interactions and are not simply correlated to any single parameter characterizing the steric or inductive effects. Therefore one is usually confined to the comparative analysis and discussion of various analogously substituted compounds.[4,17]

In substituted adamantanes the α-effect correlates best with the chemical shift of the quaternary carbon atom in tertiary butyl derivatives, as can be seen from Fig. 1

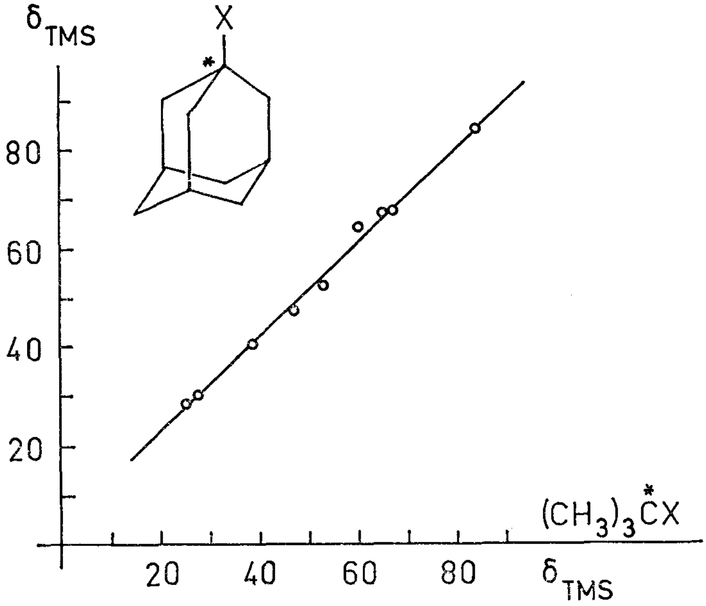


FIG. 1. Comparison of carbon ^{13}C chemical shifts of substituted atoms of 1-substituted adamantanes and *t*-butyl derivatives. Numbering is according to Table 1. ^{13}C chemical shifts of *t*-butyl derivatives are taken from [1](**1, 2**),[18] (**4, 5, 6, 13**) and measured by us (**3, 8, 14**).

(r = 0·998, standard deviation 1·4 ppm). In fact, this correlation may be even better, because chemical shifts of the *t*-butyl derivatives were taken from various sources. Although the relative stabilities of *t*-butyl and adamantyl carbonium ions and radicals may be different,[19] it appears that the behaviour of these two groups is quite similar in many ways.[20]*

Comparison of the β-carbon shifts with those in other substituted hydrocarbons leads to good correlation in a number of cases. Good correlation holds between the chemical shifts of β-carbons and methyl groups of *t*-butyl derivatives as well as with the 2,6-atoms of substituted cyclohexanes, being somewhat better in the last case. The substituents may be divided into two groups according to their effects on β-carbons. In the first group the substituents contain no more than one atom heavier than hydrogen (CH_3, OH, Br, Cl, F, NH_2) and shift the β-carbon resonances by more than 5 ppm to lower field. Within this group the more electronegative substituents as a rule give smaller paramagnetic shifts. This result is in accordance with the calculated

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* J. Polis, private communication.

alternating charges on carbon atoms owing to the polar substituents,[4] and provides a possible explanation for the unexpected β-carbon shift in protonated 1-amino-adamantane as compared to the parent compound. In the second group the 1,4-interactions play a significant role in the screening of β-carbon atoms and the shifts to lower field are less than 5 ppm. In the case of biadamantane the shift is 2·5 ppm to higher field. In the last case a strong steric perturbation takes place between the β-carbons of the two adamantyl rings. A closely similar intreaction was noted in the case of dicyclohexyl.[4] In going from methylcyclohexane to dicyclohexyl a 5·2 ppm diamagnetic shift of the carbon atoms in the 2,6-positions of the ring is observed. As a first approximation the effect on β-carbons in biadamantane must be at least 1,5 times greater than in dicyclohexyl, that is about 8 ppm, which gives an estimated shift of β-carbons in biadamantane equal to 36·6 ppm (exp. 35·5).

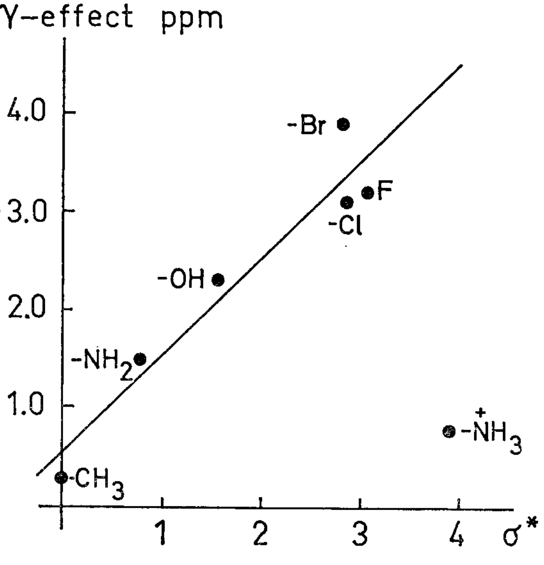


FIG. 2. Correlation between the γ-effects and inductive σ^* constants in 1-substituted adamantanes with substituents containing no more than one atom heavier than hydrogen.

There cannot be any substantial nonbonded interactions between the apical 1-substituents and γ-carbons of adamantane. Instead of the usual large diamagnetic shifts as a rule we get paramagnetic relative shifts of the γ-carbons in this case. There have been many speculations about the inductive influence between the substituents in the 1,3-positions of adamantane.[13,19] One might anticipate a correlation between the substituent effects on γ-carbons and the inductive σ^*- or σ_i-constants, but the correlation is quite poor if one takes all substituents into consideration. Yet in the case of substituents from the abovementioned I group, the correlation (see Fig. 2) is at any rate not worse than that between the chemical shifts of β-protons and the σ^*-constants in 1-substituted adamantanes,[12] which was declared to be 'as good as those observed in other cases'. The presence of an abnormal influence of the heavier halogens on the δ-carbon shifts was proved in our study of cyclohexane derivatives.[4] If one excludes Br and Cl, the correlation coefficient r improves from 0·956 to 0·974.

Also, the heavier halogen atoms that as substituents lead to diamagnetic nephelauxetic effects, may exhibit some peculiar influence in the γ- position too. Bulky substituents probably have in addition to the inductive and other effects some steric influence on the γ-carbons as well, although the mechanism is difficult to understand. It may be connected with a small change in the overall geometry of the molecule.

In aliphatic compounds usually no effect on δ-carbons is observed.[4] The C-4 atoms across the ring in cyclohexyl derivatives are shifted to high field, however, by up to about 2 ppm in the case of strongly electronegative substituents.[4] An analogous situation is observed in adamantanes. A correlation exists between the chemical shifts of δ-carbons in both series. The δ-effects are roughly correlated with the σ^* or σ_i constants of the substituents (see Fig. 3, $r = 0{\cdot}88$, $s = 0{\cdot}2$ ppm). As in the case of substituted cyclohexanes, the δ-effects of **5** and **6** are corrected, using the data for *n*-amyl derivatives.[4] A possible explanation for the high field δ-effects on the ground of alternating charges was given in our previous work.[4] It is apparent from the EHT calculations of methyl cyclohexane[21] and 1-chloroadamantane[22] that the alternation of charges on carbon atoms is inherent to cyclic compounds from both series. Therefore it is not unusual for the corresponding carbon chemical shifts to behave in a similar fashion. Moreover, the methyl group has properties of an electron-withdrawing group, both according to the results of EHT calculations and from the carbon chemical shifts. From fluorine chemical shifts of methylfluoroadamantanes the same conclusion was drawn.[23]

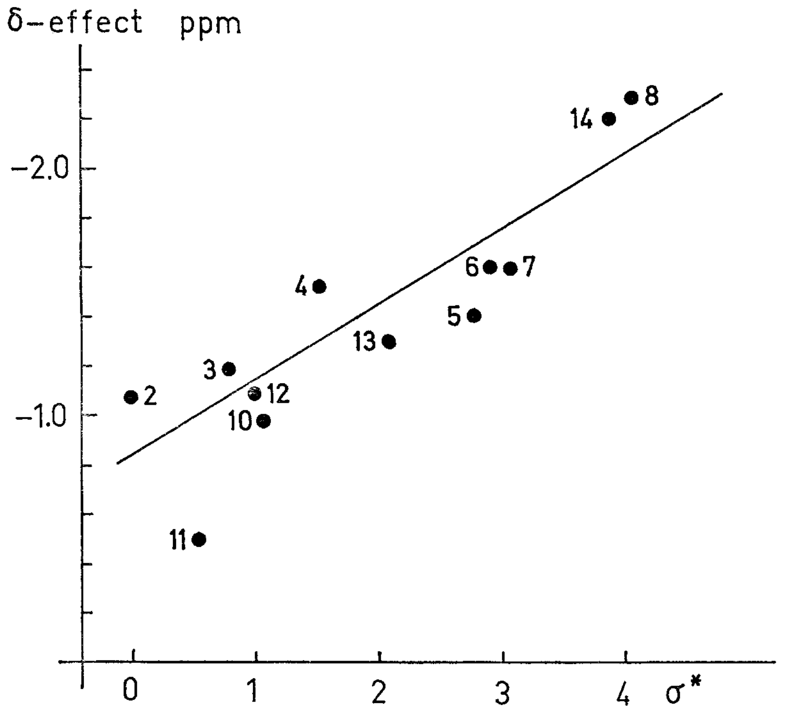


FIG. 3. Relationship between the δ-effects and σ^* constants in 1-substituted adamantanes. Numbering according to Table 1. In the case of **5** and **6** corrected δ effects are used (see text).

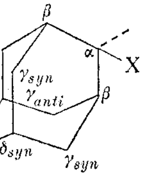
Another possibility for the explanation of the δ-effects may lie in the different geometry of substituted adamantanes as compared with adamantane itself. But the recent report on the bond lengths and bond angles of **9**[24] seems to contradict such a possibility, because only minor changes from the values of adamantane were found. The universality of high field δ-effects in 6-membered alicyclic compounds is also to some extent against the explanation of such an effect by the geometry factors.

The proton spectra of 1-substituted adamantanes are comparatively simple[12] and very useful for the structure elucidation of substituted adamantanes, but no significant correlation exists between the carbon and proton chemical shifts.

2-Substituted adamantanes

The proton spectra of methylene-substituted adamantanes are less informative than those of 1-substituted adamantanes, and higher frequencies (100 MHz or more) and double resonance techniques are necessary for the determination of all chemical shifts.[11] The ^{13}C NMR spectra, registered with proton decoupling, are universal, regardless of the substitution site. In the 2-substituted compounds (with the exception of the doubly bonded group $=X$, see Table 2) there must be a very strong interaction between the substituent and the γ_{syn}-carbon atoms.

TABLE 2. ^{13}C CHEMICAL SHIFTS IN 2-SUBSTITUTED ADAMANTANES



Compound	Chemical shifts of carbon atoms δ_{TMS}					
	α	β	γ_{syn}	γ_{anti}	$\delta_{syn} = \delta_{anti}$	ε
2-Chloroadamantane	66·7	35·7	31·0	38·1	26·9	38·1
2-Hydroxyadamantane	74·3	34·7	31·1	36·9	27·6	38·0
Adamantanone	213·1	47·1	39·1	39·1	27·7	36·6

These circumstances are illustrated by the 7 ppm high field shifts in 2-chloro- and 2-hydroxyadamantane. At the same time the γ_{anti} carbon is not influenced in 2-chloro- and shows a small diamagnetic shift in 2-hydroxyadamananc. The analogy with the behaviour of C-6 chemical shifts in borneol, isoborneol, 2-*exo*- and 2-*endo*-chlorobornane and the 2-substituted norbornanes is obvious.[5]

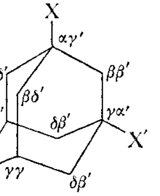
The high field δ-effect is equal for the *syn*- and *anti*-carbons, being larger in the case of the more electronegative substituent just as in 1-substituted adamantanes. The equality of δ-effects on both *syn*- and *anti*-carbons shows that the through-space interactions play no essential role on the distant δ-carbons. If one excludes the effects of minor changes in bond lengths and bond angles, caused by the introduction of substituents, then only the interaction through the bonds remains.

The most remote ε-carbon atom is not influenced in chloro- and hydroxy-derivatives. The introduction of an sp^2-hybridized carbon into the adamantane skeleton must have a more profound influence and the ε-carbon resonance in adamantanone is shifted by more than 1 ppm to high field.

1,3-Disubstituted adamantanes

The ^{13}C chemical shifts of some 1,3-disubstituted adamantanes were calculated on the basis of the substituent effects and chemical shifts of adamantane (see Table 1) and compared with the experimental results (see Table 3). As anticipated, good additivity of ^{13}C shifts holds for 1,3-disubstituted adamantanes just as in the case of proton chemical shifts of this type of compound.[12] The calculated chemical shifts as a rule fall within ±0·5 ppm from the experimental results. Larger deviations are observed on substituted carbons, especially in bromo-compounds.

TABLE 3. EXPERIMENTAL AND CALCULATED ^{13}C CHEMICAL SHIFTS δ_{TMS} IN SOME 1,3-DISUBSTITUTED ADAMANTANES[1]



Carbon atoms[a]		Substituents					
	X	Br	CH_2Br	OH	Br	C_6H_5	p-NO_2—C_6H_4
	X'	COOH	CH_2COOH	CH_2COOH	CH_2COOH	CH_2Br	CH_2Br
αγ'	exp.	61·2	34·3	68·5	60·9	37·0	37·7
	calc.	63·7	33·6	67·7	64·5		
γα'	exp.	44·7	33·2	35·8	37·3	34·7	34·7
	calc.	44·3	32·8	35·1	36·7		
ββ'	exp.	49·4	45·6	50·0[b]	53·9	46·6	46·0
	calc.	50·2	45·6	50·4	54·1		
βδ'	exp.	48·3	40·1	44·3	49·0[b]	42·6	42·1
	calc.	48·2	40·0	44·8	48·5		
δβ'	exp.	37·3	41·4	41·4	40·6	40·3	39·9
	calc.	36·6	41·5	41·1	40·5		
γγ'	exp.	31·9	28·7	30·8	32·9	29·3	29·0
	calc.	31·9	28·8	31·1	32·7		
δδ'	exp.	34·8	35·9	35·8	35·1	36·0	35·7
	calc.	34·6	35·9	35·5	34·9		
CH_2Br			46·4			47·0	46·8
C^*H_2COOH			47·9	48·2	47·7		
CH_2C^*OOH			177·8	178·0	178·0		
C_6H_5[c]							
subst. (1)						149·7	157·1
ortho (2, 6)						125·9	125·8
meta (3, 5)						128·3	123·3
para (4)						124·9	146·4

[a] The first greek letter refers to the first substituent X and the second letter to X'.

[b] This resonance coincides with the methanol (solvent) signal.

[c] Aromatic carbons, numbered from the adamantane substitution site.

The assignment of chemical shifts in the two compounds with phenyl and *p*-nitrophenyl substituents was accomplished on the basis of regularities in the influences of the various substituents. The fact that the β-, γ- and δ-effects are each operative on two ^{13}C chemical shifts with both influences approximately equal was also used. From the shifts of Table 3 the substituent effects of phenyl and *p*-nitrophenyl groups on the adamantane skeleton may be estimated. A low field chemical shift of about 0·7 ppm on the α-carbon of adamantane is observed when one introduces an NO_2 group into the *para* position of a phenyl ring. Such is the case in the methyl chemical shifts in toluene or *m*-nitrotoluene as compared with that in *p*-nitrotroluene.[25] The δ-effect of the phenyl group is about 0·8 ppm (from the shifts of the $\delta\beta'$ and $\delta\delta'$ carbons) and that of the *p*-nitrophenyl group about 1·1 ppm.

CONCLUSIONS

^{13}C NMR spectroscopy of substituted adamantanes is a useful tool for the identification of substituted adamantanes. The spectra of 1-substituted adamantanes clearly demonstrate that for an effective 1,4-interaction the spatial proximity of interaction centres is needed. The low field shifts of γ-carbons correlate with the inductive parameters of simple substituents which contain only one atom heavier than hydrogen. In other cases the γ-effects are influenced by steric and nonbonded interactions. The high field shifts of δ-carbons are widespread in 6-membered saturated rings and are roughly proportional to the substituent electronegativities. The ^{13}C spectra confirm the predicted slight alternation of atomic charges in substituted alicyclic compounds.

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