^{13}C-NMR SPECTRA OF HYDROXY ADAMANTANES
ADDITIVITY IN ^{13}C-NMR SPECTRA OF DIHYDROXYADAMANTANES

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The ^{13}C-NMR spectra of all monohydroxy and ditopic dihydroxy adamantane isomers were measured and the lines assigned. The numbers of the isomers and of the non-equivalent carbon atoms permitted a verification of the simple additivity of the shielding contributions of two hydroxyl groups on the rigid adamantane skeleton in the isomers without a possibility of a direct OH—OH interaction. If such interactions occur, deviations are found. The direction and magnitude of the deviations is in agreement with the current interpretation of ^{13}C chemical shifts in other classes of cyclic compounds. It is concluded that the deviations are not caused by intramolecular hydrogen bonds. The deviations and the values of substituent chemical shifts offer some limited information about the origin of the shielding effects, especially of those dependent on stereochemistry and degree of substitution (γ_{anti} effect).

NMR spectra of various adamantane derivatives are being intensively studied because the number of different atoms in these molecules with a relatively rigid framework and a small ring strain allow testing of various hypotheses of shielding mechanisms and contributions. Only sporadically, however, such studies have involved more than one isomer[1,2] or disubstituted derivatives[1,3] on which further tests are possible. This is in particular true for the hydroxy substituted adamantanes; though ^{13}C-NMR spectra of 1-hydroxy- and 2-hydroxydamantane were measured in a few laboratories[1,2,4,5], only 1,3-dihydroxyadamantane[1], in which nonbonding interactions between the two hydroxyl groups are unlikely, was studied*. We have succeeded in preparing and isolating all the isomeric ditopic dihydroxyadamantanes (*i.e.* all the isomers except 2,2-dihydroxyadamantane). A study of their ^{13}C-NMR spectra would be interesting not only for the above reasons but also in a connection

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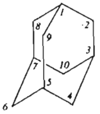
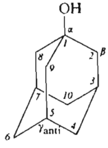
* *Note added in proof*: Duddeck H.: Tetrahedron *34*, 247 (1978), measured recently also 2,4-dihydroxyadamantanes, the results being in agreement with ours. The interactions were attributed to overlapping of free-electron pairs and bond orbitals.

with our preceding study of bis(trimethylsiloxy)adamantanes[6] as it should help to separate the shielding contributions of $Si(CH_3)_3$ from those of $OSi(CH_3)_3$ group. The results of such a study are reported here.

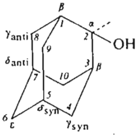
In the following discussion the adamantane carbon atoms and the shielding effects are numbered and labeled according to the following scheme:



adamantane



1-substituted adamantane



2-substituted

RESULTS AND DISCUSSION

Adamantane and Monohydroxyadamantane. Substituent Chemical Shifts of Hydroxyl Group

The chemical shifts of adamantane carbon atoms (Table I) determined here agree quite well with those found by other authors[1–4] (the internal shift is in all cases 9·4 ± 0·1 ppm) though our values are the lowest yet reported. The observed chemical shifts also agree satisfactorily with those calculated[1] according to the direct additivity scheme from the parameters of Grant and Paul[7] using a correction for cyclohexane ring[1].

The chemical shifts in monohydroxyadamantanes can be calculated from the shifts in the corresponding methyladamantanes according to the equations derived by Roberts and coworkers[8]. The calculated shifts agree with the experimental ones within the standard error except for γ_{anti} carbons in 1-hydroxyadamantane and for γ_{syn} carbons in 2-hydroxyadamantane. These deviations are due to the neglect of the spatial dependence of the γ effect in the equations of Roberts and coworkers[8].

All our chemical shift values (Table I) in monohydroxyadamantanes are also smaller than those reported in literature[1,2,4], but, because of compensation of errors, the substituent chemical shift (SCS) values (Table II) which will be subsequently used in the calculation of the chemical shifts in dihydroxyadamantanes, agree with those of refs[1,2]. Since various aspects of these SCS values have been discussed by a number of earlier authors[1–6,9,10] we shall comment only from the point of view of some more recent findings.

Larger low-field α and β shifts for C–1 than for C–2 carbon substituents were found also for other substituents[1,2,6] of adamantane which were not magnetically

TABLE I

^{13}C-NMR Chemical Shifts δ in Hydroxy Adamantanes^a

Substitution	C−1	C−2	C−3	C−4	C−5	C−6	C−7	C−8	C−9	C−10	RMS
—	28·07	37·59									
1-OH	67·27	44·81	30·48	36·13	30·48	36·13	30·48	44·81	44·81	36·13	
2-OH	34·08	73·73	34·08	30·78	27·38	37·62	26·97	36·42	30·78	36·42	
1,2-(OH)$_2$	69·78^b	77·30^b	36·27^b	29·52^c	30·22	35·81^b	29·72^c	43·14	38·00	35·81^b	
	(−3·50	−3·65	−0·22	0·20	0·43	−0·35	0·34	−0·50	0·00	0·85)	0·52
1,3-(OH)$_2$	69·52^b	51·92	69·52^b	43·38^b	31·07^b	34·72	31·07^b	43·38^b	43·38^b	43·38^b	
	(−0·16	−0·11	−0·16	0·03	−1·82	0·05	−1·82	0·03	0·03	0·03)	0·26
1,4^E (OH)$_2$	66·86^b	43·00	35·83^b	72·73^b	35·83^b	29·49	29·78^b	44·90^b	43·00	29·49	
	(0·69	−0·64	−0·66	0·46	−0.66	0·17	−0·03	0·06	−0·64	0·17)	0·16
1,4^A-(OH)$_2$	66·89^b	38·26	36·71^b	72·03^b	36·71^b	34·96	29·31^b	44·46^b	38·26	34·96	
	(0·29	0·26	0·22	−0·24	0·22	−0·03	−0·07	−0·38	0·26	−0·03)	0·07
2^E,4^E-(OH)$_2$	33·17^b	72·27^b	40·66	72·27^b	33·03^b	30·92	26·89	30·92	33·20	24·49^b	
	(0·05	−0·29	−0·55	−0·29	0·05	0·11	0·16	0·11	−2·05	0·52)	0·24
2^A,4^E-(OH)$_2$	33·26	75·16	40·42	68·52	33·76	30·81^b	26·39	36·24	30·28^b	29·84^b	
	(0·28	2·60	0·33	1·60	0·37	0·00	0·09	−0·21	0·67	0·23)	0·32
2^A,4^A-(OH)$_2$	34·19^b	75·45^b	38·27	75·45^b	34·19	36·13^b	25·70	36·13^b	25·12	34·97	
	(0·78	8·53	−1·82	8·53	0·80	−0·32	−0·17	−0·32	1·15	−0·28)	1·23
2,6-(OH)$_2$	33·55	73·55^b	32·97	29·69^b	33·55	73·55^b	32·97	29·69^b	24·11^b	34·96	
	(0·14	−0·21	−0·01	0·08	0·16	−0·21	−0·01	0·08	0·14	−0·29)	0·04

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[a] The chemical shifts are in δ-scale (ppm units, relative to $(CH_3)_4Si$). The adamantane carbon atoms are numbered as shown in the text. The lines in parentheses are the deviations from additivity, a positive deviation indicates that the experimental chemical shift is larger than that calculated. [b] The line assigned without any recourse to the additivity rule. [c] The assignment of the labeled lines in the same row can be interchanged. [d] The assignment of the labeled lines in the rame row can be interchanged.

anisotropic. This trend is in agreement with more general observations[8,1-13] that various authors described in somewhat different terms: the α and β effects decrease with increasing total number of hydrogen atoms replaced at the α and β carbons[13] or that all the carbons of a γ-fragment are more shielded in the conformation having smaller dihedral angles, or more γ-gauche interactions and less skew pentane interactions[12]. (In adamantane, the 1-substituent has all dihedral angles with γ carbon atoms 180° while there are two carbon atoms, C—4, and C—9, which are γ to the 2-substituent and have the dihedral angle 60°.) Also the relative magnitude of the δ effects in the hydroxyadamantanes is in accord with the recently made observation[14] that the carbons closely neighbouring δ nuclei other that hydrogen are deshielded relatively to those in less crowded orientations. In general, the SCS values of hydroxyl groups on adamantane carbons are similar to the SCS values for other cyclohexane systems as discussed by Eggert and coworkers[12] and collated recently by Stothers and Tan[15].

Notable differences are, however, found for γ_{anti} effects of substituents bound to quaternary carbon atoms. These $\gamma_{\mathrm{anti}}^{(t)}$ effects of OR groups in adamantane and steroid derivatives are, in agreement with the now established rule[12,16,17], in all cases paramagnetic but, while their magnitude depends on the type of the carbon skeleton (*e.g.* it is 2·4, 3·9, and 4·3 ppm in adamantanes, androstane-5α-ol[12], and cholestan-3-one-5α-ol[16], resp.) the effect is virtually independent of the nature of the group R (*e.g.* the $\gamma_{\mathrm{anti}}^{(t)}$ effect is 2·4 and 2·0 ppm for R = H and $Si(CH_3)_3$, resp., in adamantanes and 4·3 and 4·6 for R = H and CH_3, resp., in cholestenan-3-one-5α-ol[16]). These two observations suggest that the mechanism causing the deshielding $\gamma_{\mathrm{anti}}^{(t)}$ effect might be different from the mechanism dominating the more usual diamagnetic γ_{anti} effect observed when the substituent is attached to a carbon atom bearing a hydrogen atom. The deviations from additivity (see below) observed

TABLE II

^{13}C Substituent Chemical Shifts (SCS) of Hydroxyl Group in Adamantanes[a]

Position[b]	α	β	γ_{syn}	γ_{anti}	δ_{syn}	δ_{anti}	ε
(t)	39·20	7·22	—	2·41	—	−1·46	—
(s)	36·14	6·01	−6·81	−1·17	−0·67	−1·10	0·03

[a] SCS values calculated as the difference between the observed ^{13}C chemical shifts of the corresponding atoms in hydroxyadamantane and adamantane. A positive value indicates a paramagnetic shift due to the hydroxyl group. [b] Hydroxyl group position on tertiary (C—1) and secondary (C—2) adamantane carbon atoms indicated by (t) and (s), resp.

on the carbon influenced by two deshielding $\gamma_{anti}^{(t)}$ interactions suggest electric field origin of this effect (discussed *e.g.* in ref.[12]).

Duddeck and Dietrich[5] found the $\delta_{anti}^{(s)}$ effect of 2-OH group to be larger than $\delta_{syn}^{(s)}$ effect of the same group. Our results confirm their assignment which is in line with the δ effects recently observed in other systems[12,14,16]. The difference between the $\delta_{anti}^{(s)}$ and $\delta_{anti}^{(t)}$ (the δ_{anti} effect of the 1-OH group in adamantane) indicates that the gauche-*trans* δ effect depends on the type (tertiary or quaternary) of the substituted carbon atom similarly as does the γ_{anti} effect.

Dihydroxyadamantanes. Additivity of the Substituent Effects

The chemical shifts of carbon atoms in dihydroxyadamantane isomers are given in Table I together with their deviations (the lines in parentheses) from the shifts calculated according to the direct additivity rule from the SCS values of Table II. Similarly as in the study of bis(trimethylsiloxy)adamantanes[6] the agreement between the experimental and calculated chemical shifts which is observed for the most of the carbons proves the correctness of the SCS values (*i.e.* the correctness of the assignments in the spectra of the monohydroxyadamantanes) and the validity of the direct additivity rule for the disubstituted adamantanes (with sufficiently separated substituents). If the two hydroxyl groups are, however, close enough for nonbonding interactions between them to take place, deviations are observed.

Considerable deviations (larger than 1 ppm) occur only for the substituted carbon atoms in the 1,2- and 2,4-isomers, for the carbon atoms which are subject to two β (C−3) or two $\gamma_{syn}^{(s)}$ (C−9) effects in the $2^A,4^A$-isomers, and, finally, for those subject at two $\gamma_{anti}^{(t)}$ effects (C−5 and C−7 carbons in the 1,3-isomer). It should be noted that the same pattern of the signs and magnitudes of the deviations was observed in the spectra of bis(trimethylsiloxy)adamantanes[6] (except for a minor difference in the case of the C−9 carbon in the $2^A,4^A$-isomers).

Only a few tests of applicability of additivity rule to disubstituted all-sp^3-carbon-skeletons have been reported, in a few instances they included hydroxyl and methyl groups as the substituents. Since these groups have similar SCS values[8] the results of such tests might be illustrating especially as it has been recently shown[18] that in many cases the effects of OH—OH interactions can be approximated by the magnitude and direction of analogous OH—C interactions. (Indeed, in some bicyclic systems[11] large positive deviations were observed for the substituent bearing carbon atoms in spatial arrangement analogous to that in 2,4-disubstituted adamantanes and large negative deviations in those resembling 1,2-disubstituted adamantanes.) Since such approximations are likely to fail if a strong intramolecular hydrogen bond can be formed[18] (which would be the case of 1,2-, $2^A,4^E$-, or $2^A,4^A$-dihydroxyadamantanes) the only sound comparison which can be made is with the study of dihydroxysteroids[18] in which the deviations were interpreted along similar lines as the deviations in the study of CH_3—OH interactions in bicyclic systems[11].

In dihydroxysteroids, similarly as in dihydroxy- or bis(trimethylsiloxy)substituted adamantanes, sizable deviations occur only if the two oxygen atoms are separated by three or four bonds[18]. In agreement with the generally accepted interpretations[11,16,17], the negative deviations (*i.e.* those with the predicted shielding smaller than observed) in 1,2-diols are explained by upfield shifts of all carbons in γ-fragments with small dihedral angles. The additional γ-gauche interaction (with the other OH group) not accounted for by the additivity, causes the additional upfield shift of 6 ppm in the case of axial-equatorial substituents and 4 ppm in the equatorial-equatorial case with a larger dihedral angle. The data of ref.[18], however, also indicate that the deviations are smaller if the substituted carbon atom is quaternary. Hence, deviation of −4 ppm or less should be expected for 1,2-dihydroxyadamantane which is in accord with the deviation found (−3·5 ppm). Deviations found for the substituted carbon atoms in steroids with the substituents in relative 1,3-*syn* diaxial or 1,3-*trans* positions (+8 and +3 ppm, resp.[18]) are similar to those in $2^A,4^A$- and $2^A,4^E$-dihydroxyadamantanes which have analogous geometry. Apparently, the interpretation[18] based on a replacement of a γ-gauche interaction of one hydroxyl group with a γ-carbon atom by a skew pentane OH—OH interaction with the other hydroxyl group applies also to the $2^A,4^A$-isomer. Additional supporting evidence for this interpretation can be derived from the spectra of α,ω-dihydroxyalkanes[19] in which the deviations[14,20] are of the signs expected according to this interpretation but their magnitudes are smaller due to the conformational mobility.

The authors of the above interpretation[18] could not discern any trend or pattern in the deviations of β carbon atoms. Four examples of carbon atoms subject to two β effects had the deviations in the range −1·7 ppm to +1·2 ppm. The deviation observed for the C−3 carbon in $2^A,4^A$-dihydroxyadamantane is not far from this range.

The deviations found in the case of C−9 carbon which is subject to two $\gamma^{(s)}_{syn}$ effects in the $2^A,4^A$-dihydroxyadamantane and not in its trimethylsiloxy analogue has its counterpart in the +1·2 ppm deviation[19] of C−5 carbon in 5α-cholestane-1α-,3α-diol in which the spatial relationships are similar and the substituent bearing carbons are also not quaternary; but no interpretation of the deviations of β carbon shifts in 1,3-diols was offered[18]. Since there are other carbon atoms in the studied dihydroxyadamantanes which are also subject to two $\gamma^{(s)}_{syn}$ effects (C−9 in the 2,6-isomer and C−10 in the $2^E,4^E$-isomer) of well separated hydroxyl groups but with small deviations, the deviation observed on the C−9 carbon of the $2^A,4^A$-isomer must be due to some interaction between the two hydroxyl groups and the axial hydrogen atom on the C−9 carbon which does not take place in $2^A,4^A$-bis(trimethylsiloxy)adamantane.

The C−5 and C−7 carbon atoms in the 1,3-substituted adamantane are the only carbon atoms among all the adamantane carbons which are subject to two $\gamma^{(t)}_{anti}$

effects. The magnitude of the combined effect is such as if each of the two effects were attenuated by a factor of about two. Such an attenuation (1·7) would also result if the effects had to be added as vectors (in the C—O directions) which would be necessary if they had their origin in electric field contribution. This suggestion is in accord with the noted[1] dependence of $\gamma_{\text{anti}}^{(t)}$ effects on the inductive σ^* constant of the substituent. In agreement with such suggestion negligible deviations were observed[1] for C-5 and C-7 carbons in 1,3-disubstituted adamantanes in which only one substituent had a sizable (larger than 1 ppm) $\gamma_{\text{anti}}^{(t)}$ contribution. Of 1,3-dihaloadamantanes (in which deviations also occur for these carbons) only the shifts in the difluoro derivative support this suggestion, in others the deviations are less than 50% of their $\gamma_{\text{anti}}^{(t)}$ effects[3] but heavy halogen substituents are often found exceptional. On the other hand, attenuation of the effects of two γ-substituents by a factor of 1·6 was also observed in some isomeric octanes[21,22] and different transmission of inductive effects through the carbon chains containing secondary and tertiary atoms was suggested as an explanation[6,21,22].

It should be mentioned, however, that the above interpretation of the deviations, though it can be of diagnostic value, is only phenomenological. Till we know more about the origin of the observed shifts, the interpretation cannot go much further. Though, from the same pattern of deviations in dihydroxy as in bis(trimethylsiloxy)-adamantanes follows that the intramolecular hydrogen bond cannot be the cause of the deviations.

Summarising, our results, which confirm the earlier determined values of hydroxy group substituent chemical shifts and prove their additivity in dihydroxyadamantanes lend further support to the generality of the found exceptionality of γ effects of bridgehead substituents, to the steric dependence of δ effects and to the assignment of the larger δ upfield effect to the *anti* arrangement. The deviations observed in dihydroxyadamantanes with proximate hydroxyl groups are in accord with the trends found in other systems and are not due to intramolecular hydrogen bonding. It is suggested that the $\gamma_{\text{anti}}^{(t)}$ effects add vectorially since they are likely to be of electric field origin.

EXPERIMENTAL

Synthesis and preparation of the studied hydroxy- and dihydroxyadamantanes are outlined in other communications[6,23]. The spectra were measured as described earlier[6] except that a few drops of methanol were added to the samples in order to increase the solubility of the adamantane derivatives in tetrachloromethane. Assignment of the lines in the spectra to individual carbon atoms was carried out exactly as described in detail earlier[6] for the trimethylsiloxy substituted adamantanes.

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