

Carbon-13 Nuclear Magnetic Resonance Spectra

I—Monosubstituted Adamantanes and Adamantanones

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Abstract—The chemical shifts of 4_{ax} and 4_{eq} substituted adamantanones are compared with those calculated with the aid of a given additivity rule. It is found that both δ carbons are shielded with respect to the substituent. In contrast to the situation for the γ -atoms, however, the δ_{syn} atom is less shielded than the δ_{anti} atom. In most cases the additivity rule predicts the chemical shifts with an accuracy of approximately 1 ppm. Exceptions are carbon atoms 4 and 9 of the 4_{eq} substituted adamantanones. In both cases the measured values are 4 to 6 ppm upfield. This can possibly be explained by an electronic interaction between the carbonyl group and the substituent.

INTRODUCTION

PEHK and LIPPMAN¹ found that in *n*-amyl derivatives the chemical shifts of the δ carbon atoms are hardly affected by the substituent X, whereas in substituted cyclohexanes a high field δ effect is operative. For 2-substituted adamantanes they demonstrated² that the signals of γ_{syn} atoms are strongly shifted upfield because of their interaction with the substituent, whereas the influence of the substituent upon the γ_{anti} atoms is essentially less effective.³ In contrast, the high field effect for the δ atoms is smaller. Recently Maciel and co-workers⁴ reported for the same system that the through-space interaction of the substituent on the δ atoms is different, which causes a distinct difference in the chemical shifts of the two δ carbon atoms. By analogy with the behaviour of the γ atoms, they assumed that the δ_{syn} atom can be assigned to the signal with the larger upfield effect. This study demonstrates that there are indications for the reverse assignment.

EXPERIMENTAL

The ¹³C NMR spectra were obtained at natural abundance in the pulsed Fourier transform mode at 22.63 MHz using a Bruker WH-90 spectrometer. The samples were run at a concentration of about 1.5 molar in deuterated chloroform with tetramethylsilane as internal standard. The accuracy of the signals is about ± 0.05 ppm. Compounds **2a** and **3a** were kindly supplied by Dr Harald Klein, Ruhr-Universität, Bochum. Compounds **1b**, **1e** and **2e** were obtained from EGA-Chemie KG, Steinheim, West Germany.

1a was prepared from **1b** with 48% hydrobromic acid in carbon tetrachloride. **1c** and **1d** were obtained by the reaction of **1b** with acetyl chloride and methanesulphonyl chloride, respectively, in dry pyridine; **2b** and **3b** were prepared by rearrangement of 4-oxa-homoadamantane-5-one in 50% sulphuric acid,^{5,6} and **3d** by the reaction of sodium azide with **2e** in methanesulphonic acid.⁷ **2c**, **2d** and **3c** were obtained from **2b** and **3b** by analogy with **1c** and **1d**.

RESULTS

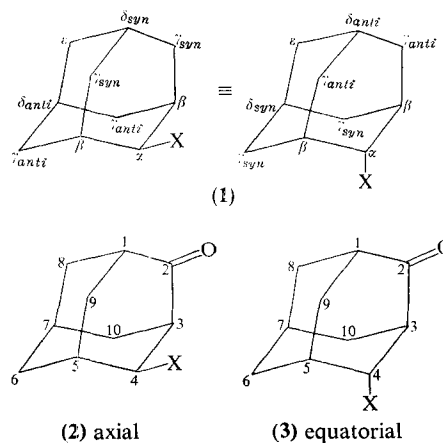
In order to determine the means by which the ¹³C NMR signals can be assigned to the two δ carbon atoms (δ_{syn} and δ_{anti}), the spectra of 4-substituted adamantanones **2a** to **2d** (substituent X axial in the ring carrying

both substituents) and **3a** to **3d** (X equatorial) were recorded. C-1 and C-7 are the two carbon atoms placed in the δ position with respect to the substituent X. Since the configuration of the substituent X in compounds **2a** to **2d** and **3a** to **3d** is known, it is also well known which of the δ atoms C-1 and C-7 is δ_{syn} or δ_{anti} .

Therefore, two pairs of values for the two atoms C-1 and C-7 are obtained from the spectra of the individual pairs of compounds (e.g. **2a** and **3a**). The assignment of these two pairs of values to the corresponding δ_{syn} and δ_{anti} atoms can be made by comparison with pairs of calculated values obtained from a new additivity rule expressed as follows:

$$\delta_{calc} = \delta_{ad} + \Delta$$

The differences between the chemical shifts of the carbon atoms of the 2-substituted adamantanes **1a** to **1d** and those of the corresponding atoms of the parent compound adamantane **1e** are taken as increments, Δ , (see Table 1, values in italics). For a 4-mono-substituted adamantanone (**2**) the calculated chemical shifts, δ_{calc} , are obtained by adding the respective increment, Δ , (Table 1) to the chemical shift of the carbon atom in question of adamantanone **2e**, δ_{ad} , (see Table 2; values in italics are the chemical shifts thus calculated). In this Table the increment α refers to that carbon atom substituted by X (C-4), increment β to the next atoms C-3 and C-5, and so on. By this method calculated values for the chemical shifts of all carbon atoms of compounds **2a** to **2d** and **3a** to **3d** are obtained which



	(2) axial		(3) equatorial		
X	a	b	c	d	e
	Br	OH	OCOCH ₃ (OAc)	OSO ₂ CH ₃ (OMs)	H

FIG. 1

TABLE 1. CARBON-13 NMR CHEMICAL SHIFTS^a OF 2-SUBSTITUTED ADAMANTANES AND INCREMENTS, Δ (IN ITALICS)^b

	α	β	γ_{syn}	γ_{anti}	δ_{syn}	δ_{anti}	ϵ
X = Br (1a)	63.7	36.5	31.7	38.8	27.7	27.0	38.0
	25.9	8.0	-6.1	1.0	-0.8	-1.5	0.2
X = OH (1b)	74.7	34.7	31.2	36.7	27.8	27.3	37.8
	36.9	6.2	-6.6	-1.1	-0.7	-1.2	0.0
X = OAc (1c)	77.0	32.0	31.9	36.5	27.4	27.2	37.5
	39.2	3.5	-5.9	-1.3	-1.1	-1.3	-0.3
X = OMs (1d)	85.6	33.0	31.1	36.3	26.9	26.6	37.1
	47.8	4.5	-6.7	-1.5	-1.6	-1.9	-0.7

^a Chemical shifts in ppm relative to tetramethylsilane; positive shifts correspond to deshielding. Concentration approximately 1.5 molar in deuterated chloroform with tetramethylsilane as internal standard.

^b Values in italics are increments which are the differences between observed shifts and the corresponding values of adamantane **1e** (CH₂: 37.8 ppm, CH: 28.5 ppm).

can be compared with those measured. It should be emphasised that the signals of the δ atoms have been assigned in the opposite manner to that adopted by Maciel and co-workers.⁴ By this conversion better agreements between the calculated and the measured chemical shifts are achieved, which means that the signal with the smaller upfield shift corresponds to the δ_{syn} atom.

Assignment

The assignment of the signals of the *sp*³-atoms is based on spectra obtained under off-resonance ¹H irradiation conditions, by which method the methine carbons C-1, C-3, C-4, C-5 and C-7 can be distinguished from the methylene carbons C-6, C-8, C-9 and C-10. In comparing the calculated and measured values for the chemical shifts of the unsubstituted carbon atoms, good agreements are given, with a few exceptions

which are explained below. Therefore, apart from the uncertainties given in Table 2, footnote c, the assignment can be regarded as correct.

DISCUSSION

The α and β effects of compounds **1a** and **1b** agree with those reported by Maciel *et al.*⁴ with sufficient accuracy. The same effects of compounds **1a**, **1b** and **1c** show a similar trend to those of the corresponding cyclohexane derivatives.¹

The earlier findings,^{2,3} namely that signals of γ_{syn} atoms are shifted upfield very significantly compared to γ_{anti} atoms, can be confirmed. The differences, also found by us, can be as large as 7 ppm.

In contrast to earlier opinions,^{2,8} the anisochrony of the two δ atoms indicates that a steric interaction is present between the substituent X and the δ atoms. This interaction is smaller, however, than in the case of the γ atoms, because of the greater distance between the centres concerned. For all four pairs of compounds the signals of the C-1 atoms of compounds **2a** to **2d** (substituent X axial, C-1 is δ_{syn} with respect to X) are more deshielded by comparison with the C-1 atoms of compounds **3a** to **3d** (substituent X equatorial, C-1 is δ_{anti}). On the other hand, all shifts of the C-7 atoms of compounds **2a** to **2d** (C-7 is δ_{anti}) are placed upfield as compared with those of compounds **3a** to **3d** (C-7 is δ_{syn}). This is in contrast to the tentative assignment made by Maciel and co-workers.⁴ Therefore, it is highly probable that in the case of the adamantane derivatives the sequence of the relative shifts of the δ atoms is opposite to that of the γ atoms. This fact is confirmed by carbon-13 NMR measurements of 2-adamantanol (**1b**) in the presence of the lanthanide shift reagent Eu(dpm)₃.[†] The rule put forward on the

[†] W. Dietrich, Ruhr Universität, Bochum, unpublished results.

TABLE 2. MEASURED^a AND CALCULATED^b CARBON-13 NMR CHEMICAL SHIFTS OF 4-SUBSTITUTED ADAMANTANONES (CALCULATED SHIFTS, δ_{calc} IN ITALICS)

C-Atom	1	2	3	4	5	6	7	8	9	10
(2a)	45.8	210.8	54.8	60.1	35.1	36.9	26.1	39.2	33.6	40.6
	46.1	210.5	54.9	65.1	35.6	37.3	26.1	39.4	33.1	40.2
(3a)	45.0	210.4	54.5	56.2	34.7	30.2	26.7	39.2	35.5 ^c	33.9 ^c
	45.4	217.6	54.9	65.1	35.6	30.2	26.8	39.4	40.2	33.1
(2b)	46.2	215.9	53.8	77.2	33.3	34.9	26.2	38.7	32.9	37.4
	46.2	210.0	53.1	76.1	33.8	35.2	26.4	39.2	32.6	38.1
(3b)	45.0	214.0	53.7	72.2	33.2	29.4	26.6	38.6	32.8 ^c	32.7 ^c
	45.7	215.5	53.1	76.1	33.8	29.7	26.9	39.2	38.1	32.6
(2c) ^d	46.1	213.4	50.8	79.3	31.3	35.1	26.3	38.9	33.2	37.9
	45.8	210.7	50.4	78.4	31.1	35.0	26.3	38.9	33.3	37.9
(3c) ^e	45.4	212.3	51.1	73.9	30.9	30.4	26.7	39.0	33.8 ^c	32.7 ^c
	45.6	215.3	50.4	78.4	31.1	30.4	26.5	38.9	37.9	33.3
(2d) ^f	45.7	211.5	51.3	86.5	38.9	34.8	25.7	38.5	32.4	38.0
	45.3	209.9	51.4	87.0	32.1	34.8	25.7	38.5	32.5	37.7
(3d) ^g	44.7	209.6	51.7	80.3	31.9	29.6	26.2	38.4	33.3 ^c	31.6 ^c
	45.0	215.1	51.4	87.0	32.1	29.6	26.0	38.5	37.7	32.5
(2e)	46.9	216.6	46.9	39.2	27.6	36.3	27.6	39.2	39.2	39.2

^a Chemical shifts in ppm relative to tetramethylsilane; positive shifts correspond to deshielding. Concentration approximately 1.5 molar in deuterated chloroform with tetramethylsilane as internal standard.

^b Values in italics are the chemical shifts calculated with the additivity rule given in the text.

^c These values may be interchanged (C-9 and C-10 of compounds **3a** to **3d**). They were so assigned that the deviations of both signals from the calculated values are as small as possible.

^d Acetyl-CO: 169.0 ppm; CH₃: 20.9 ppm.

^e Acetyl-CO: 169.0 ppm; CH₃: 21.0 ppm.

^f CH₃: 38.5 ppm.

^g CH₃: 38.3 ppm.

basis of some studies^{2,9-12} that a smaller distance between the atoms concerned, leading to an increase of steric overcrowding, causes a larger upfield shift therefore seems to be wrong. A similar observation was reported recently by Grover *et al.*^{8,13,14} They found in the case of 10-methyl-*trans*-decalols that steric compression of methyl and hydroxy groups produce relatively large downfield shifts for δ atoms, which is in direct contrast to the rule advanced above. In this study, although upfield shifts are observed, the δ atom which is nearer to the substituent X is shielded less than the other δ atom. This confirms the findings reported by Grover *et al.*¹⁴ that steric crowding can cause upfield shifts as well as downfield shifts. Very recently Giannini *et al.*¹⁵ reported upfield shifts of the three corresponding γ carbon atoms for the substituted cortisols (9 α -fluoro-, 9 α -chloro- and 9 α -bromo-), but they observed the largest shielding for the fluoro compound and the smallest for the bromo compound, which contradicts the rule of steric compression. Moreover, in a given compound they found appreciable differences for the upfield shifts of the three γ atoms present, which should be very similar.

The shifts of the C-9 carbon atoms of compounds **3a** to **3d** are observed to be 4 to 6 ppm to higher field than expected. In the case of compounds **2a** to **2d** (X axial), however, the C-9 shifts agree with the calculated shifts to an accuracy of at least 0.5 ppm. A similar observation can be made for the signals of the C-4 atoms carrying the substituent X. Here the agreement of the calculated C-4 shifts of compounds **2a** to **2d** with those observed is not as satisfactory as in the case of the signals of the C-9 atoms carrying no substituent. Nevertheless, for compounds **3a** to **3d** the signals of the C-4 atoms as well as those of the C-9 atoms are found to be 4 to 6 ppm at higher field than that expected by the increment rule described. Apparently, in addition to the previously described steric interaction,² another possibly electronic interaction is also operative. Both atoms, C-4 and C-9, are in the γ position with respect to the quasi-equatorial carbonyl group, and the substituent X is also attached to the C-4 atom in an equatorial position. In this configuration an electronic interaction of the orbitals of the substituent X with those of the carbonyl group is conceivable (Fig. 2a), particularly because the bonds involved are coplanar. Verhoeven *et al.*^{16,17} reported that in the case of 1-azaadamantane-4-one and analogous compounds (Fig. 2b) a charge transfer in a sigma-coupled transition takes place, as can be seen from the UV spectra. For C-4 they found an upfield shift of 3 to 4 ppm, whereas an upfield shift of about 1.5 ppm is expected from the comparison of adamantane with 1-azaadamantane,¹⁸ but this cannot be clearly explained as an interaction effect. For C-2 and C-9, also, no remarkable deviation

from the expected α effect is noticed, but here the bonds involved are not coplanar.

In the case of compound **2d** the signal of C-5 is 6.8 ppm further downfield than calculated by the additivity rule. An analogous phenomenon does not appear with compounds **2a**, **2b** and **2c**. A wrong assignment is excluded, because the shifts of the other methine carbons agree very well with those calculated. At present no explanation for this deviation can be found.

Apart from the few exceptions described above, the chemical shifts of the remaining signals correspond rather well to those calculated with the help of the additivity rule. The discrepancies are less than 1 ppm in most cases. This demonstrates once again the utility of additivity rules¹⁹⁻²¹ for the assignment of carbon-13 NMR signals, unless special interactions of 'disturbing groups' are operating.

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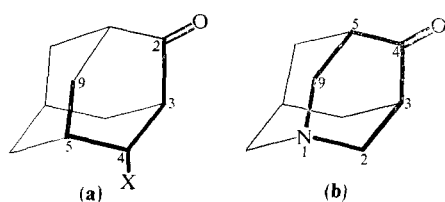


FIG. 2