

APPLICATION OF SHIFT REAGENTS IN THE STUDY OF DISUBSTITUTED DERIVATIVES OF ADAMANTANE BY NMR SPECTROSCOPY

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Application of the shift reagent $\text{Eu}(\text{DPM})_3$ (DPM is 2,2,6,6-tetramethyl-3,5-heptanedione) for the analysis of disubstituted hydroxy and oxo derivatives of adamantane is described. The spectra were interpreted by means of a computational method assuming the mean coordination of the shift reagent to the two functional groups of the substrate molecule.

The lanthanide NMR shift reagents were hitherto used mostly for the analysis of compounds with one functional group in the molecule, while only few papers have been concerned with compounds containing two or more functional groups¹⁻⁴. In several cases, the observed shifts for polyfunctional compounds could be expressed quantitatively by comparing their spectra with those of analogous monofunctional compounds. In some other instances the elucidation of the spectra was based on the favored coordination of the reagent to one of the functional groups in the molecule.

In this paper we present the analysis of the NMR spectra of some disubstituted oxygen-containing derivatives of adamantane, *viz.* 2,4-adamantanediol (*I*), 5-hydroxy-2-adamantanone (*II*), 4_{ax}-hydroxy-2-adamantanone (*III*), and 4_{eq}-hydroxy-2-adamantanone (*IV*) (the axial and equatorial positions refer to the ring, which is substituted to the highest degree).

EXPERIMENTAL

The reagent $\text{Eu}(\text{DPM})_3$ was prepared according to⁵ and kept in a vacuum desiccator over P_2O_5 . CDCl_3 with 1% tetramethylsilane served as the solvent. Chloroform was dried over a molecular sieve (4 Å) for 24 hours. The reagent was weighed directly in the cell, CDCl_3 was added by means of a calibrated syringe (for experimental conditions see⁷).

2_{ax},4_{ax}-Adamantanediol (*I*) was prepared from 4-hydroxy-2-adamantanone⁶. 4_{ax}-Hydroxy-2-adamantanone (*III*) as well as 4_{eq}-hydroxy-2-adamantanone (*IV*) were prepared by using the procedure by Faulkner and McKervey⁷. 5-Hydroxy-2-adamantanone (*II*) was obtained by the oxidation of adamantanone⁸.

The NMR measurements were carried out on a spectrometer Varian XL-100-15 at 37°C. The

dependences $\delta_{i,\text{obs}}$ vs R_p ($\delta_{i,\text{obs}}$ is the chemical shift in the presence of the shift reagent, R_p is the ratio of molar concentrations of the shift reagent and the substrate) in the range of R_p from 0 to 0.5 were evaluated by applying the least squares method. The best set of calculated values of bound chemical shifts $\Delta_{i,\text{cal}}$ was selected by using the nonlinear regression method⁹, with the optimization criterion of the form¹⁰

$$P = \left(\sum_i^N (\Delta_{i,\text{obs}} - \Delta_{i,\text{cal}})^2 / N \right)^{1/2},$$

where $\Delta_{i,\text{cal}}$ and $\Delta_{i,\text{obs}}$ are the calculated and observed bound chemical shifts, respectively, and N is the number of protons in the molecule. The coordinates of the protons in the molecule were either determined from Dreiding models or calculated. All calculations were performed on a computer Tesla 200.

RESULTS AND DISCUSSION

We measured the spectra of the compounds *I–IV* both without and with the shift reagent. A partial interpretation of the NMR spectra of *I–IV* without the application of shift reagents was presented by Geluk¹¹ and Faulkner⁷. We refined their interpretation (Table I) and confirmed our interpretation by the interpretation of the

TABLE I

Chemical Shifts δ_i (p.p.m.) of Protons of the Compounds *I–IV* without the Shift Reagent
Concentration of the sample 0.32M; tetramethylsilane; 37°C.

Proton	<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>
1	1.93	2.61	2.43	2.50
2 _{ax}	—	2.0	—	—
2	3.91	2.0	—	—
3	2.23	2.61	2.66	2.62
4 _{ax}	—	—	—	3.97
4 _{eq}	3.91	—	4.28	—
5	1.93	—	2.0	2.1
6 _{ax}	1.73	2.0	2.0	2.35
6 _{eq}	1.73	2.0	2.0	1.75
7	1.53	2.34	2.0	1.80
8 _{ax}	1.73	2.0	2.0	2.0
8 _{eq}	1.73	2.0	2.0	2.0
9 _{ax}	2.43	2.0	2.43	2.0
9 _{eq}	1.47	2.0	2.0	2.0
10 _{ax}	1.73	2.0	2.0	2.57
10 _{eq}	1.73	2.0	2.0	1.75

NMR spectra using the shift reagent. The dependence of $\delta_{i,obs}$ on R_p was utilized for the interpretation. The shift values obtained by extrapolating this dependence to $R_p = 0$ were almost equal to those obtained without the shift reagent. The dependence was followed up to the ratio $R_p = 1.2-1.4$; higher values of R_p could not be attained due to the low solubility of the shift reagent. The linear part of this dependence ($R_p = 0-0.5$) was used for the calculation of the experimental values of bound chemical shifts, $\Delta_{i,obs}$ (Table II).

The interpretation of NMR spectra of disubstituted derivatives with shift reagents is much more complicated than that for monosubstituted derivatives. In fact, coordination of the shift reagent depends on the nature of the functional groups as well as on their position in the molecule of the substrate. Consequently, several possibilities

TABLE II

Observed (a) and Calculated (b) Values of Bound Chemical Shifts for the Compounds I-IV
P Optimization criterion; x, y, z coordinates of the lanthanide.

Proton	I		II		III		IV	
	a	b	a	b	a	b	a	b
1	16.3	13.3	5.5	5.5	—	—	4.3	5.3
2 _{ax}	—	—	—	—	—	—	—	—
2 _{eq}	—	—	—	—	—	—	—	—
3 _{eq}	24.3	24.9	5.5	5.5	19.8	18.1	17.8	17.8
4 _{ax}	—	—	15.1	15.1	—	—	28.2	27.1
4 _{eq}	—	—	14.8	14.8	26.5	27.8	—	—
5	16.3	13.3	—	—	15.4	15.2	16.7	16.4
6 _{ax}	6.8	7.3	14.8	14.9	7.2	7.0	6.7	7.3
6 _{eq}	7.8	7.9	14.8	14.9	7.2	6.0	17.7	18.5
7	5.9	6.4	4.9	5.3	4.9	5.1	7.4	6.9
8 _{ax}	6.8	7.3	6.4	6.9	5.8	5.7	6.0	5.2
8 _{eq}	7.8	7.6	4.6	4.7	5.8	5.4	6.0	5.0
9 _{ax}	24.3	25.3	6.4	5.9	19.7	20.1	7.5	8.0
9 _{eq}	9.1	11.0	4.6	4.7	8.3	8.1	7.6	6.1
10 _{ax}	8.5	9.0	15.1	15.1	7.2	7.8	17.6	19.6
10 _{eq}	8.5	9.0	14.8	14.8	6.8	6.9	8.2	8.6
	P =	1.43	P =	0.25	P =	0.82	P =	0.97
	x =	3.4	x =	2.1	x =	1.7	x =	2.2
	y =	0.0	y =	0.0	y =	0.3	y =	-0.4
	z =	-1.5	z =	0.0	z =	1.2	z =	0.8

can occur, depending on whether the nature of the functional groups *a*) is the same *b*) or is different, and whether the functional groups are located *c*) symmetrically *d*) or unsymmetrically in the molecule. The mutual combinations of these fundamental aspects can involve several particular cases; thus, *e.g.*, for the combination of *a*) with *c*), one molecule of the shift reagent can be coordinated to one of the two functional groups or to both of them under the occurrence of an exchange reaction between the groups, or two molecules of the reagent can be coordinated to the two functional groups. In the combination of *b*) with *d*), the coordination of one molecule of the shift reagent can occur either to one of the functional groups (depending on the nature and substitution position of the groups), or to both of them (with different probabilities of coordination), or two molecules of the shift reagent can be coordinated to the functional groups. Analogous considerations could be made for all other possible combinations of the fundamental factors. An individual analysis of these possibilities must be carried out for the interpretation of a given molecule; this we applied also to the case of the derivatives I–IV.

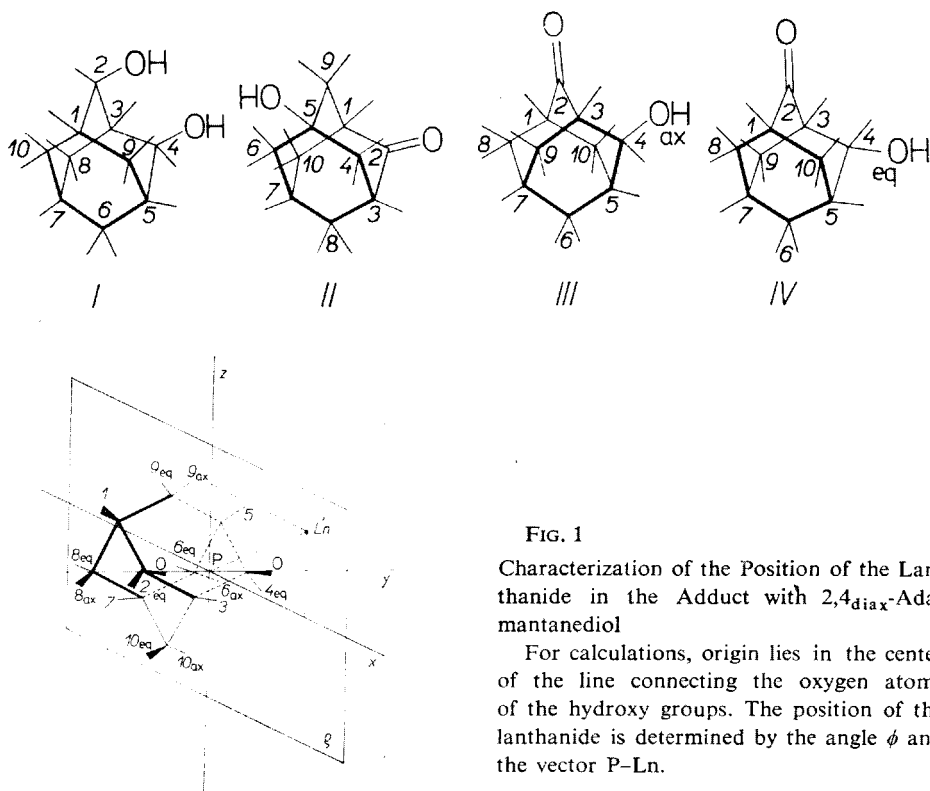


FIG. 1

Characterization of the Position of the Lanthanide in the Adduct with 2,4_{diax}-Adamantane-1,3-diol

For calculations, origin lies in the center of the line connecting the oxygen atoms of the hydroxy groups. The position of the lanthanide is determined by the angle ϕ and the vector P–Ln.

The derivative *I* is a symmetrically substituted diol, with the combination of the parameters *a*) and *c*). Its experimental spectrum displays a regular location of the resonance signals of the protons, corresponding to the symmetrical structure of the complex adduct. Fig. 1 shows the mean most probable position of the lanthanide with respect to the two functional groups. Based on the agreement of the sets of experimental and calculated bound chemical shifts (Table J), coordination of one molecule of the shift reagent to one molecule of the substrate with equal probability to the two functional groups is assumed. The position of Eu corresponds to the average position between the oxygen atoms of the two functional groups determined by the distances Eu–O 3.7 Å and angles $\psi = 0.0^\circ$, $\phi = 112.7^\circ$ with the magnitude of the optimization criterion $P = 1.43$ (Fig. 1).

In the case of the compound *II*, the spectrum with the shift reagent resembles closely that of 1-adamantanol (Fig. 2). One molecule of the reagent is probably coordinated to the hydroxy group of the substrate. The keto group does not probably affect the coordination of the shift reagent; its effect appears only at R_p values as high as ~ 1 (Fig. 3, splitting of the resonance signal of the proton).

Comparison of the sets of the experimental and calculated data indicates the position of Eu in the complex adduct in the distance of 2.1 Å from the oxygen atom of the hydroxy group (Fig. 4, Table I). This distance of Eu in the derivative *II* differs only slightly from that in 1-adamantanol¹².

The derivatives *III* and *IV* represent disubstituted derivatives differing only in the position of the hydroxy group. In these cases, the solving of the coordination of the shift reagent was the most complicated. The position of Eu in the complex adduct

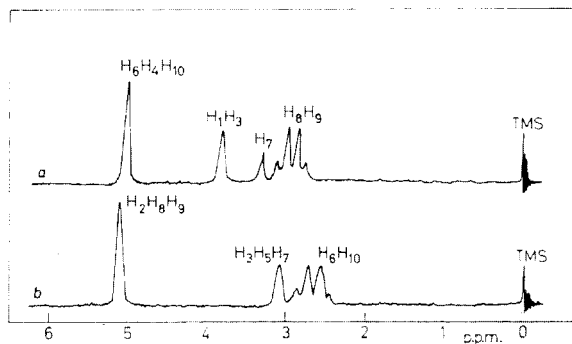


FIG. 2

Comparison of Spectra of *a* 1-Adamantanol and *b* 5-Hydroxy-2-adamantanone in the Presence of the Shift Reagent

R_p 0.2, concentration of the substrate 0.32M.

molecule can be determined by using spatial representation (Fig. 5). The comparison of the sets of measured and calculated bound shifts showed the distance $\text{Eu}-\text{O}$ 2.5 \AA and the angles $\psi = 17^\circ$, $\phi = 46^\circ$ for *III* and $\text{Eu}-\text{O}$ distance 2.4 \AA , $\psi = 350^\circ$, $\phi = 70^\circ$ for *IV*.

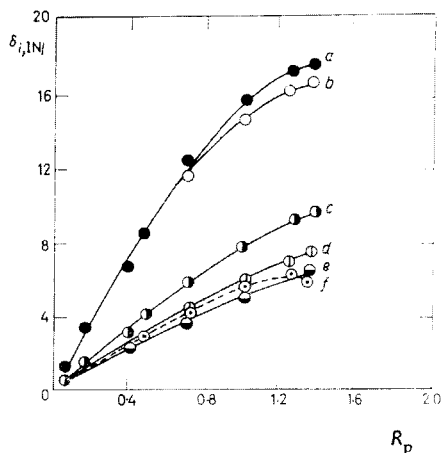


FIG. 3

Dependence of $\delta_{i,IN} = \delta_{i,obs} - \delta_i$ on R_p for the Compound *II*

Concentration of *II* $0.32M$; protons: *a* 4_{ax} ; 10_{ax} ; *b* 4_{eq} , $6_{ax,eq}$; *c* $1,3$; *d* 8_{ax} , 9_{ax} ; *e* 8_{eq} , 9_{eq} ; *f* 7 .

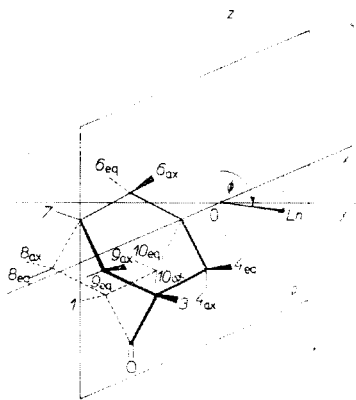


FIG. 4

Characterization of the Position of the Lanthanide in the Adduct with 5-Hydroxy-2-adamantanone

For calculations, origin lies in the heteroatom of the hydroxy group. The position of the lanthanide is determined by the angle ϕ and the vector $\text{Eu}-\text{O}$.

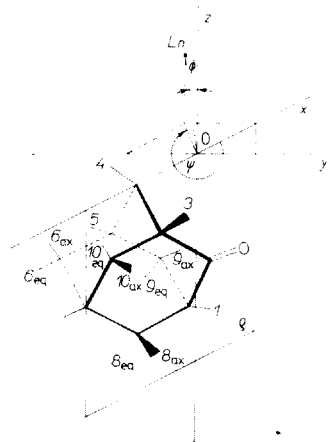


FIG. 5

Characterization of the Position of the Lanthanide in the Adduct with 4-Hydroxy-2-adamantanone

For calculations, origin lies in the heteroatom of the functional group. The position of the lanthanide is determined by the angles ψ and ϕ and the vector $\text{Eu}-\text{O}$.

From the results it was, however, apparent that the experimental bound chemical shift for the proton in the position 1 in the derivative *III* was extremely high in comparison with the calculated value. When this proton was not considered, another possibility of coordination of the shift reagent was obtained, determined by a more convenient optimization criterion for the angles $\psi = 37^\circ$, $\phi = 54^\circ$ and the Eu-O distance of 2.2 Å (Table II.).

The application of the computational method based on the assumption of the mean position of the Eu atom of the shift reagent between the two functional groups proved to be possible. A more unambiguous determination of the coordination of the shift reagent to disubstituted substrates will be possible only after having procured a higher number of data on further disubstituted derivatives of adamantane.

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