APPLICATION OF SHIFT REAGENTS IN NMR ANALYSIS OF 1-ADAMANTANOL

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The effect of some experimental factors on the values of induced shifts was studied on systems of 1-adamantanol with a series of shift reagents. Among the paramagnetic ions, Eu, Pr, Yb, and Nd are the most suitable for routine work. Solutions of the complex adducts are time-stable, the dependence of the induced shifts on the ratios of the concentration of the shift reagent to that of the substrate (R_p) is linear up to R_p 0·7. The spatial arrangement of the adducts with the reagents $Ln(DPM)_3$ (DPM 2,2,6,6-tetramethyl-3,5-heptanedione) is the same in all instances. The distance oxygen-lanthanide lies in the range of 2·0—2·1 Å. This value, however, represents only the projection of the real distance in the connecting line carbon–oxygen. The highest shifts were found for solutions in CCl_4 and CS_2. The values of the induced shifts decrease with increasing temperature.

In the recent years, several papers were published on the application of the shift reagents in NMR spectroscopy[1,2], particularly for the study of structural problems. The formation of the adduct between the substance analyzed (substrate) and the shift reagent brings about resolution of the complex NMR spectrum of the substance itself, which facilitates the elucidation of the structure. In this work we are concerned with some general problems of the application of the shift reagents $Ln(DPM)_3$ and $Ln(FOD)_3$ (Ln lanthanide, DPM 2,2,6,6-tetramethyl-3,5-heptanedione, FOD 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione) in order to specify the physical nature of the interaction between the substrate and the shift reagent.

For the study of the effect of experimental factors (concentration ratio of the substrate to the shift reagent, type of the lanthanide atom and the shift reagent ligand, solvent, temperature, and time), 1-adamantanol was chosen as the substrate, a compound possessing a high symmetry of the core skeleton, which can be easily prepared and purified. It is one of the fundamental derivatives of adamantane, serving as the starting compound for our NMR study[3] of the structure of bitopic and polytopic oxygen-containing adamantane derivatives.

EXPERIMENTAL

Preparation of the reagents. 2,2,6,6-Tetramethyl-3,5-heptanedione (DPM) was prepared by Claisen condensation[4], its purity was checked by gas chromatography. The individual shift reagents were prepared according to[5], their purity was checked by melting point measurements and elemental analysis. In the case of the reagents Eu(FOD)$_3$, Yb(FOD)$_3$ and Pr(FOD)$_3$, commercially available chemicals of Willow Brooks Labs., Inc., New Jersey, U.S.A. were used. All the reagents were kept in a vacuum dessicator over P$_2$O$_5$.

1-*Adamantanol* was prepared by hydrolysis of 1-bromoadamantane[6] and purified by sublimation and recrystallization. Its purity was cofirmed by IR, NMR, and mass spectroscopy.

Preparation of samples. The substrate and the reagent were weighed directly in the cell. The solvent (0·5 ml) was supplied with a syringe and the amount added was weighed. Samples containing the shift reagent of the type Ln(DPM)$_3$ had to be heated for dissolving. The following solvents were used: CDCl$_3$ 99% deuterium; CCl$_4$ reagent grade; C$_6$D$_6$ 98·1% deuterium; CD$_3$COCD$_3$ Merck, Darmstadt; CS$_2$ pure, Laborchemie, Apolda. NMR spectra were measured on NMR spectrometers Tesla BS 477 (60 MHz) and Varian XL-100-15 (100 MHz) at the temperatures 27° and 37°C, respectively. Tetramethylsilane was used as internal standard. The positive sign was ascribed to chemical shifts occurring in the direction of descending intensity of magnetic
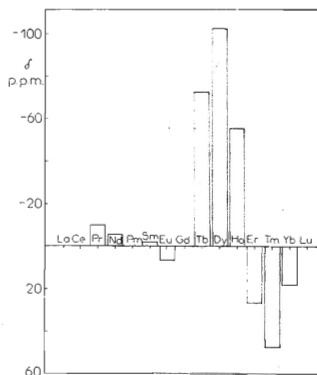

Fig. 1

Dependence of the Induced Shift of β-Protons of 1-Adamantanol on the Atomic Number of the Central Ion of the Ln(DPM)$_3$ Type Shift Reagent
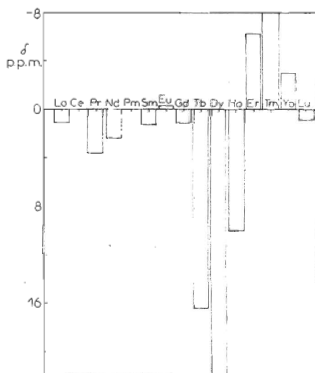
Concentration of 1-adamantanol 25 mg//0·5 ml CDCl$_3$; R_p 0·5.

Fig. 2

Dependence of the Chemical Shift of Protons of the Tert-butyl Group of the Reagent Ln(DPM)$_3$ on the Atomic Number of the Central Ion

Conditions as for Fig. 1.

field. The induced shifts were calculated according to the relation

$$\Delta\delta^i = \delta^i_{OBS} - \delta^i, \qquad (1)$$

where δ^i_{OBS} is the chemical shift measured after the addition of the shift reagent and δ^i the chemical shift in the free substrate; the superscript pertains the i-th proton of the substrate.

The dependence of the induced shift $\Delta\delta^i$ on the ratio of the shift reagent to the substrate R_p was evaluated by using the least squares method. The calculations were performed on a digital computer Tesla 200. The values of the angles and distances obtained from Dreiding Stereomodels (Büchi Laboratoriums-Technik AG) were used for the calculations.

RESULTS AND DISCUSSION

Effect of the Central Ion

In order to determine the effect of the central ion, we investigated mixtures of 1-adamantol with a series of reagents Ln(DPM)$_3$ $(c_S = 25.0$ mg in 0.5 ml CDCl$_3$, ratio of the analytical concentrations of the reagent and the substrate R_p 0.500). The measured induced shifts of the protons of 1-adamantanol are given in Fig. 1, the chemical shifts of the tert-butyl group of the shift reagent are shown in Fig. 2. The halfwidths of the signals of the protons of 1-adamantanol are summarized in Table I.

For the selection of the most suitable central ion two criteria must be taken into consideration: the reagent must cause sufficiently high induced shifts, and at the same time the broadening of the signals themselves must be as low as possible. These two

TABLE I

Halfwidths (Hz) of Signals of Protons of 1-Adamantol for Reagents of the Type Ln(DPM)$_3$ (Ln lanthanide); R_p 0.5.

Ln	H$_\beta$	H$_\gamma$	H$_{\delta a}$	H$_{\delta b}$
La	5	16	6	6
Pr	6	5	24	24
Nd	7	6	16	11
Sm	10	6	—	—
Eu	6	25	25	16
Tb	—	17	34	20
Dy	150	22	24	28
Ho	—	12	23	20
Er	68	16	16	19
Tm	70	11	22	20
Yb	32	10	10	12
Lu	5	12	8	8

requirements are in a sense mutually excluding. The results of the analysis of the spectra indicate that the most common use of Eu(DPM)$_3$ and Pr(DPM)$_3$ as shift reagents is justified. The halfwidths of the signals of the β protons (Table I) suggest Yb(DPM)$_3$ and Nd(DPM)$_3$ as additional suitable shift reagents. For the γ and δ_a protons the halfwidths of the signals are similar, only with Eu(DPM)$_3$ the two resonance lines coincide at the given ratio R_p 0·5. For the measurements of more complex spectra, reagents leading to higher shifts can be also recommended; it must be, however, taken into account that along with the increasing induced shifts their uncertainty increases, too, due to the broadening of the signals. The same effect can be achieved also by increasing the ratio R_p. Reagents with La, Sm, Gd, or Lu as the central ions cannot be used at all. For La, Lu, and Sm the induced shifts are too low to allow any practical application. Gd yields a single, highly broadened signal, so that the induced shifts cannot be measured[7] (they were therefore formally put equal to zero in the plots). The order of the magnitudes of the shifts for the system treated is analogous to those reported by Nasser Ahmad[8] and Horrocks[9] for other substrates.

In addition to the reagents with proton ligand of the type DPM, reagents with the fluorine-containing diketone FOD were measured as well. No significant differences appeared on the comparison of the values of the induced shifts. The position of the signals of the tert-butyl group, however, is shifted to lower values with respect to tetramethylsilane, if FOD is used, which could interfere in some instances (superposition of resonance signals). The relatively highest shift was observed for Yb(FOD)$_3$. The difference lies, however, in the higher solubility of the shift reagents containing FOD and in their higher stability towards some functional groups (*e.g.*, the group —COOH (ref.[10])).

In order to test the effect of the solvent on the magnitude of the induced shifts, measurements with the reagents Yb(DPM)$_3$, Pr(DPM)$_3$, Eu(DPM)$_3$, Yb(FOD)$_3$, Pr(FOD)$_3$, and Eu(FOD)$_3$ were carried out in various solvents, *viz.* CDCl$_3$, CCl$_4$, C$_6$D$_6$, CS$_2$, and CD$_3$COCD$_3$, under constant conditions (c_S = 12·5 mg in 0·5 ml, R_p 0·2). The induced shifts in the individual solvents were then expressed as relative values with respect to those in CCl$_4$ (100%).The shifts of the β protons of the substrate expressed in this way are summarized in Table II. The data are in general in a good agreement with those published recently[11−14]. The induced shifts occurring in CCl$_4$, CDCl$_3$, C$_6$D$_6$, and CS$_2$ lie very close to each other. In the case of acetone, (CD$_3$)$_2$CO, the values of the induced shifts are very low, which is in accordance with the assumption that acetone behaves as a substrate.

The induced shifts obtained with the reagents Ln(FOD)$_3$ are slightly lower than those observed when the reagents Ln(DPM)$_3$ are used. A similar trend was found by Shapiro and coworkers[15], who explain it in terms of the different ratios of the reagent to the substrate in the complex adducts; this could be confirmed only if the nature of coordination of the reagent and the substrate were known.

TABLE II

Relative Induced Shifts of β Protons of 1-Adamantanol in Systems with the Reagents Ln(DPM)$_3$ and Ln(FOD)$_3$ in Various Solvents

R_p 0·2; induced shifts in CCl$_4$ represent 100%.

Reagent	C$_6$D$_6$	CDCl$_3$	CS$_2$	(CD$_3$)$_2$CO
Eu(DPM)$_3$	82·6	83·5	103·0	5·0
Yb(DPM)$_3$	72·6	87·0	107·0	2·7
Pr(DPM)$_3$	81·0	87·5	93·3	5·9
Eu(FOD)$_3$	78·6	96·5	97·7	1·0
Yb(FOD)$_3$	94·6	99·1	106·1	2·1
Pr(FOD)$_3$	96·5	92·8	98·6	5·8

TABLE III

Measured[a] and Calculated[b] Values Δ^i_{OBS}, Δ^i_C for the Systems 1-Adamantanol–Ln(DPM)$_3$

c Distance oxygen–lanthanide (Å), P agreement factor, K constant.

Ln	c	K	P	H$_\delta$b	H$_\gamma$	H$_\delta$a	H$_\beta$
Pr	2·05	−1248·6	0·083	−[a]5·09 −[b]5·68	−6·45 −8·04	−7·10 −7·07	−20·2 −19·36
Nd	2·08	−772·3	0·092	−[a]2·99 −[b]3·47	−3·87 −4·92	−4·39 −4·33	−12·42 −11·85
Sm	1·85	−118·0	0·16	−[a]0·43 −[b]0·58	−0·76 −0·83	−0·43 −0·72	−2·162 −1·98
Tb	2·01	−9946·8	0·070	−[a]43·43 −[b]45·86	−53·61 −64·97	−56·03 −56·99	−162·2 −156·37
Ho	2·06	−7782·1	0·071	−[a]33·73 −[b]35·29	−41·01 −49·98	−43·47 −43·94	−124·71 −120·317
Er	2·11	3415·5	0·074	[a]14·28 [b]15·19	17·51 21·51	18·76 18·96	53·77 51·77
Tm	2·04	6511·1	0·075	[a]27·58 [b]29·75	34·40 42·14	36·46 37·01	105·51 101·45
Yb	2·02	2652·3	0·078	[a]11·78 [b]12·19	13·87 17·27	14·76 15·15	43·24 41·56
Dy	2·05	−15285·0	0·071	−[a]66·33 −[b]69·55	−81·01 −98·50	−85·26 −86·56	−246·2 −237·2
Eu	2·03	1076·0	0·097	[a]4·39 [b]4·92	5·34 6·97	6·07 6·126	17·66 16·79

The effect of concentration of the shift reagent was investigated in mixtures of the substrate with the various shift reagents in $CDCl_3$. The reagent was added gradually to the sample. The values of the induced shifts increased linearly in the interval of values $R_p \sim 0.1$ to 0.7. The correlation coefficients of the dependences $\Delta\delta^i$ vs R_p in that interval were higher than 0.99. Extrapolation of these dependences to $R_p \to 0$ gave values of the shifts very close to those of pure 1-adamantanol in $CDCl_3$. The slopes of the dependences for the protons in the molecule of 1-adamantanol are given in Table III.

Errors due to the evaporation of the solvent can occur at the common way of sample handling. We followed the changes of the induced shift in dependence on the volume of the added solvent in the concentration range of $0.1-0.5M$ (Fig. 3). The analysis of this dependence suggests that the influence of the evaporation can be neglected if the samples are prepared carefully.

We examined also the time stability of the solutions of the complex adducts in the above solvents. We found the equilibrium of the reaction between the substrate and the shift reagent to be established immediately after the dissolution; the values of the induced shifts do not change with time up to ten days (cells sealed with paraffin).

The temperature dependence of the induced shifts in the system $Eu(DPM)_3$–1-adamantanol was measured in solutions in $CDCl_3$, CCl_4, and C_6D_6. The slopes of the plots log $\Delta\delta^i$ vs log T for the β-protons are -2.91, -2.42, and -2.58, resp.
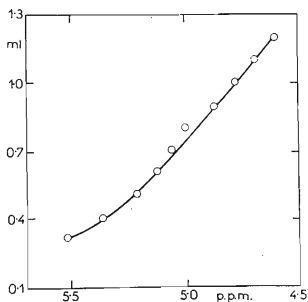

Fig. 3

Dependence of the Induced Shift of β-Protons 1-Adamantanol on the Volume of $CDCl_3$

Concentration of 1-adamantanol 0.1 to 0.5M; R_p 0.2.
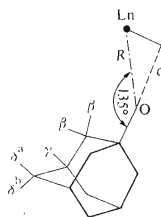
Fig. 4

Position of the Lanthanide in the Complex Adduct of $Ln(DPM)_3$ with 1-Adamantanol

c Distance oxygen—lanthanide, R assumed distance oxygen—lanthanide.

According to Bleaney[16] the induced shifts are linearly dependent on T^{-2}. In our temperature interval (26 to 60°C) the magnitude of the exponent is lower. These deviations can be attributed to the change of the equilibrium constant with temperature.

Geometry of the Complex Adduct

The slopes of the plots $\Delta\delta^i$ vs R_p were used for the elucidation of the structure of the complex adducts. We solved the equation $\Delta^i_{OBS} = K(3\cos\theta - 1)/r^3_i$, where Δ^i_{OBS} is the slope of the plot $\Delta\delta^i$ vs R_p for a constant concentration of the substrate[17], θ is the angle between the vector joining the lanthanide atom with the i-th proton and the principal magnetic axis, r_i is the magnitude of the above vector, and K is a constant. We used the method of simulation of spectra combined with the nonlinear regression method[18,19] for solving the equation. As the evaluation parameter we applied the agreement factor introduced by Willcott[20] for the solution of such systems, viz. $P = (\sum(\Delta^i_{OBS} - \Delta^i_C)^2/\sum(\Delta^i_{OBS})^2)^{1/2}$, where Δ^i_C are the calculated values of the shifts. The values Δ^i_C for all the reagents $Ln(DPM)_3$ are given in Table III. The position of the lanthanide ion was found on the prolonged joining line carbon–oxygen (Fig. 4). The distance from the oxygen atom, c, lies in the range of $2.0-2.1$ Å (Table III) except for the complex with Sm. This distance is almost the same in all cases; this is in accordance with the magnitude of the ionic or covalent radii[21,22], which are for the lanthanide group almost the same, too (~ 1.6 Å). The absolute value of the distance c is, however, lower than the sum of the covalent radii of oxygen $(0.73$ Å$)$ and the lanthanide in question. The comparison of this value with other measured distances, e.g. in systems of $Eu(DPM)_3$ with alcohols, also shows that the distance c is by $0.5-1$ Å lower [23]. This can be explained assuming that in the molecule of the complex adduct the reagent rotates around the joining line carbon–oxygen. In such case the distance c represents the projection of the actual distance R in the axis carbon–oxygen. (Fig. 4)[23].

The distance oxygen–lanthanide is often assumed[20] to be approximately 3 Å. For this distance we have calculated the position of the lanthanide to be tilted by about 135° with respect to the axis carbon–oxygen. A similar result was obtained by Demarco[24] in the system $Eu(FOD)_3$–1-adamantanol.

A simplified model calculation has been also suggested[25–28] for 1-adamantanol. In such case the heteroatom of the functional group is considered as the centre of paramagnetism in the molecule of the complex adduct and the distance oxygen-i-th proton is taken into calculations[26]. The linear equation of the form $\log \Delta^i_{OBS} = \log k - n \log r'_i$ is then solved; here k is a constant, r'_i the distance of the i-th proton from the oxygen atom, and n the slope. We carried out these calculations as well and found the mean value of the slope $n = 1.98$ (correlation coefficients were 0.98). The applicability of the relation for structure analysis was often discussed; we think that it can be used in some cases to express the structure approximately.

The relation seems to yield the best approximation for the rotation[29] of the lanthanide complex around the joining line carbon-oxygen, such as in the case of 1-adamantanol.

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