Tetrahedron Letters No.59, pp. 5153-5158, 1970. Pergamon Press. Printed in Great Britain.

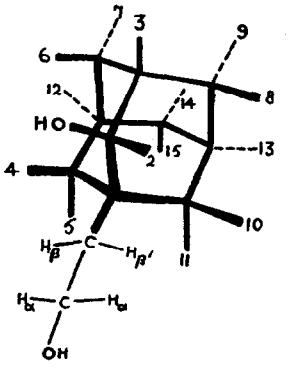
ELUCIDATION OF THE PMR SPECTRUM OF 2-HYDROXY-1-(2-HYDROXYETHYL)ADAMANTANE IN PRESENCE OF TRIS(DIPIVALOMETHANATO)EUROPIUM III

By Anthony F. Cockerill and David M. Rackham

(Lilly Research Centre, Erl Wood Manor, Windlesham, Surrey, England)
(Received in UK 2 November 1970; accepted for publication 18 November 1970)

In the preceding publication,[1] we discussed the influence of the NMR shift reagent tris(dipivalomethanato)europium III [$Eu(dpm)_3$] on the spectra of a number of monohydroxyadamantanes and cyclopentanol. We found that the magnitude of the induced change in the chemical shift of hydrogens was linearly related to the molar ratio of the shift reagent to the substrate (Equation 1). The size of the shift parameter S was in turn a linear function of r^{-2}, where r is the separation between the hydrogen nucleus and the average position of the periphery of the lone pairs of the oxygen atom (taken as a measure of the mean position of the europium atom).[2] In this publication, we illustrate the use of the r–S relationship to elucidate the spectrum of 2-hydroxy-1-(2-hydroxyethyl)adamantane (Figure 1) in the presence of $Eu(dpm)_3$. The spectra of this substrate and its complex are shown in Figures 2 and 3. To simplify the discussion, the proton numbers in the substrate are listed in Figure 1 and the signal positions and their relative magnitudes are described by letters and numbers, respectively in Figure 3.

Figure 1



(1) $\delta_\varepsilon = \delta + \underline{S}\,[\mathrm{Eu(dpm)_3/substrate}]$

(δ_ε and δ are in ppm. relative to TMS)

.The hydroxyl protons, appearing initially at 3.7δ , move rapidly on addition of small concentrations of $Eu(dpm)_3$ to a field too low to be measured on the normal PMR sweep widths. Continual interpretation of the spectrum, in the presence of increasing amounts of $Eu(dpm)_3$, enables clear assignment of signals a and 2b to $H_{(2)}$ and $2H_{(\alpha)}$, respectively. Double resonance studies demonstrate coupling between signals c and d, both e and f to 3g and h to 3k.

(2) $\delta_\varepsilon = \delta + 25.0\,[\{Eu(dpm)_3\}_{\underline{s}}/\mathrm{substrate}] + 5.80\,[\{Eu(dpm)_3\}_{\underline{p}}/\mathrm{substrate}]$

where $Eu(dpm)_3 = \{Eu(dpm)_3\}_{\underline{s}} + \{Eu(dpm)_3\}_{\underline{p}}$

The presence of two hydroxyl groups provides two potential complexing sites for the europium atom of the shift reagent. If interaction between these two sites does not occur, it should be possible to predict the spectrum from a knowledge of the behaviour of model compounds, 2-hydroxyadamantane and 1-(2-hydroxyethyl)adamantane, by using a modification of Equation 1 (see Equation 2). The subscripts s and p refer to complex associated with the secondary and primary hydroxyls, respectively and 25.0 and 5.80 to the appropriate S values for the $H_{(2)}$ proton, values of δ_ε and δ being those observed for the dihydroxy compound. This approach however, predicts greater complexing to the secondary hydroxyl and too many protons with δ_ε values below 6 than are actually observed under the experimental conditions which are illustrated in Figure 3. Obviously some interaction occurs between the hydroxyl groups causing the position of the europium atom bonded to them to be vastly different from that occupied in the model compounds.

Figure 2

PMR spectrum of 2-hydroxy-1-(2-hydroxyethyl)-adamantane at 100 MHz.

substrate 26.1 mg./0.5 ml. $CDCl_3$

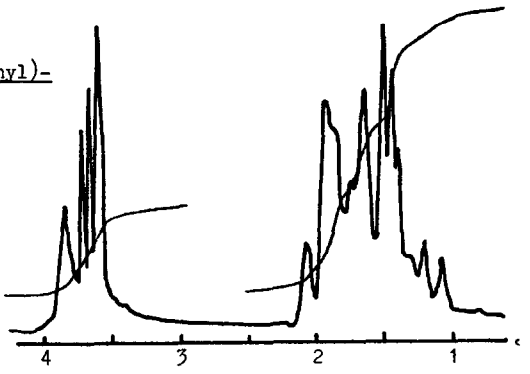
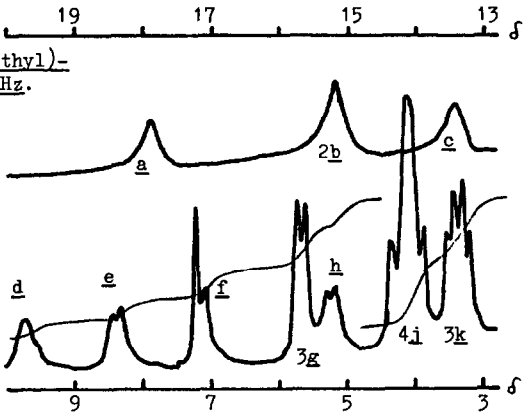


Figure 3

PMR spectrum of 2-hydroxy-1-(2-hydroxyethyl)-adamantane containing $Eu(dpm)_3$ at 100 MHz.

substrate 26.1 mg./0.5 ml. $CDCl_3$

$Eu(dpm)_3$/substrate = 0.74

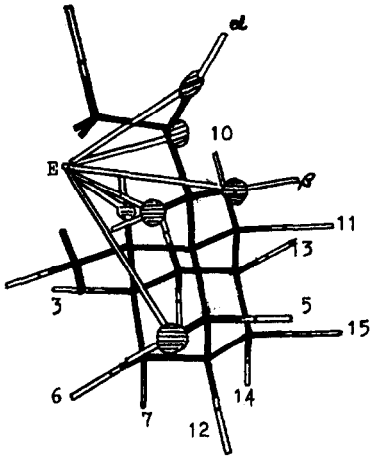


The shift reagent causes peak broadening so only geminal(11-13 Hz.) and not vicinal coupling constants (2-3 Hz.) are observed.[3] The broad nature of the signals c and d is consistent with these being due to $H_{(\alpha)}$ and $H_{(\beta)}$. From a knowledge of the behaviour of the model compounds, signal e is most probably H_4. Further assignment requires a knowledge of the average position of the europium atom. This can be achieved by using the r-S approach.

Signals a-e can be clearly interpreted for a variety of $Eu(dpm)_3$/substrate ratios, enabling calculation of the respective S values. Using the graphical relationship between r^{-2} and S, the distance of each of these six hydrogens from the average

Figure 4

Prentice-Hall framework molecular model of 2-hydroxy-1-(2-hydroxyethyl)adamantane. The bond spacers, which are fixed to the centre of the hydrogen nuclei by the shaded adhesive spheres, intersect at point E, which is taken as the average position of the Eu atom in the complex with $Eu(dpm)_3$.



position of the europium atom was calculated(Table 1).Bond spacers equivalent in length to the respective r values were then attached to the nucleus of each hydrogen atom (Prentice Hall framework molecular models) and the conformation of the molecule and the positional direction of the spacers was varied until all six spacers intersected at a point(Fig.4).This position, which was taken as the average position occupied by the europium atom, was situated on a line joining the hydroxyl functions, but much closer to the primary function. This observation mitigates against a chelation complex, in which the europium should have been spaced symmetrically between the hydroxyl groups, but accords with independent association with the two hydroxyl functions, the uncomplexed hydroxyl exerting a weak attractive force on the metal cation, thus constraining the conformation of the molecule. The separations of the remaining hydrogen nuclei from this intersection point were measured and converted into appropriate S values. The theoretically predicted δ_E values for the conditions of Fig.3 were calculated from Equation 1. Values of δ for each proton were taken as the average of the values for the corresponding protons in the model compounds.[3,4] All the relevant data are listed in Table 1.

The coupling between h and 3k requires a geminal methylene in which the difference between the r parameters for the constituent hydrogens is quite considerable. $H_{(6)}$ and $H_{(7)}$ fit this requirement most adequately. However, the predicted δ_E values are much larger than those observed. This is not surprising, for close examination of

Table 1

Calculated S and r values for 2-hydroxy-1-(2-hydroxyethyl)adamantane

$H_{(n)}$	$\delta^{2\text{-OH}}$	$\delta^{2\text{-EtOH}}$	δ	Scalc.	r(Å)	$\delta_{\varepsilon(calc)}$	$\delta_{\varepsilon(obs)}$	signal
2	3.75	-	3.62	18.3	2.69	17.9	17.9	a
α	-	3.74	3.65	16.5	2.85	15.2	15.2	2b
β	-	1.33	1.25	19.4	2.63	13.4	13.4	c
β'	-	1.33	1.33	11.5	3.41	9.7	9.7	d
4	1.80	1.55	1.67	9.5	3.73	8.4	8.4	e
5	1.68	1.55	1.61	5.7	4.75	5.8	5.7	3g
3	1.88	1.95	1.92	6.4	4.56	6.6	5.7	3g
6	1.80	1.73	1.77	6.4	4.56	6.5	5.3	h
7	1.68	1.72	1.70	3.2	6.19	4.1	3.4	3k
8	1.68	1.72	1.70	3.1	6.31	4.0	4.0	4j
9	1.82	1.67	1.75	4.6	5.37	4.8	4.4	4j
10	1.82	1.53	1.67	6.9	4.32	6.7	7.1	f
11	1.68	1.55	1.61	5.4	4.95	5.6	5.7	3g
12	1.80	1.95	1.87	3.5	6.06	4.4.	4.4	4j
13	1.80	1.95	1.87	3.1	6.31	4.2	4.2	4j
14	1.70	1.70	1.70	2.8	6.62	3.8	3.5	3k
15	1.70	1.70	1.70	2.6	7.00	3.6	3.3	3k

The signals due to the protons above the line were interpreted before application of the r-S relationship. The parentheses indicate geminal methylene pairs. $H_{(n)}$ refer to Figure 1. $\delta^{2\text{-OH}}$ refer to the chemical shifts of the corresponding hydrogen atoms relative to TMS in 2-hydroxyadamantane.[3] $\delta^{2\text{-EtOH}}$ refer to 1-(2-hydroxyethyl)adamantane.[4] δ values are the average of the $\delta^{2\text{-OH}}$ and $\delta^{2\text{-EtOH}}$ values, unless interpretable directly. $\delta_{\varepsilon(calc)} = \delta + S_{calc.} 0.74$. $\delta_{\varepsilon(calc)}$ and $\delta_{\varepsilon(obs)}$ apply to a ratio of $Eu(dpm)_3$/substrate of 0.74. Error in $S_{calc.}$ is ± 3%. Error in r is ± 0.06 Å.

the models reveals that the oxygen nucleus of the 2-hydroxy group lies directly on the lines joining the "europium centre" and the hydrogen nuclei. Some dampening of the electrical effect of the europium might be expected and comparison of theoretical and experimental S values for both protons shows that this is of the order of 30%. A slightly smaller discrepancy exists for $H_{(3)}$, assigned to 3g. Again some, but less shielding by the oxygen is apparent, this amounting to a 20% reduction.

For the remaining protons, agreement between theoretical and experimental δ_E values is excellent considering the approximations made. Signal f is clearly $H_{(10)}$ and 3g contains $H_{(5)}$ and $H_{(11)}$. Area 4j includes tertiary protons $H_{(12)}$ and $H_{(13)}$ and the methylene pair $H_{(8)}$ and $H_{(9)}$ (the small discrepancy for this proton may arise due to complete eclipsing of the "europium centre" by $H_{(2)}$. Finally area 3k is completed by $H_{(14)}$ and $H_{(15)}$, the small difference in this case being entirely analogous to the results observed with model compounds.

Although the r-S method outlined in this text is very approximate, the close agreement between experimental and predicted spectra gives support to the approach. The simplicity and rapidity of the procedure could make this a useful laboratory method. Complications may arise if heteroatom nuclei are sited between the europium and hydrogen centres.

We thank Mr. T.H.Hotten for the sample of 2-hydroxy-1-(2-hydroxyethyl)-adamantane and Mr. J.Bloxsidge of the University of Surrey for recording the 100 MHz. spectra.

References

1. A.F.Cockerill and D.M.Rackham, preceding paper.
2. As explained previously[1], we find this relationship satisfactory for interpretative purposes, although it is possibly less soundly based theoretically than the r^{-3} relationship (C.C. Hinckley, J. Amer. Chem. Soc., 1969, 91, 5160.), which arose when the distances between the europium atom and the hydrogen nuclei were estimated.
3. F.W. van Deursen and P.K. Korver, Tetrahedron Letters, 1967, 3923.
4. δ values for 1-(2-hydroxyethyl)adamantane were obtained by extrapolation of the S curves to zero concentration of $Eu(dpm)_3$.