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THE EFFECT OF $Eu(DPM)_3$ ON THE NMR SPECTRA OF BIFUNCTIONAL COMPOUNDS

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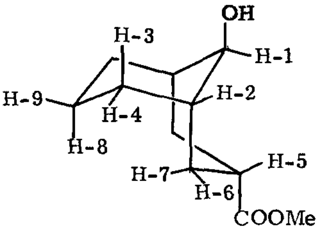
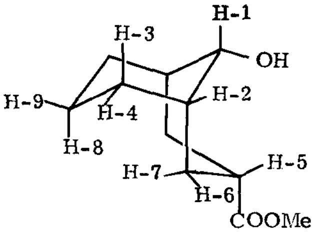
Although the n.m.r. shift reagent $Eu(DPM)_3$ has been used extensively in studying monofunctional compounds,[2] it has only been used in a limited way in studying bifunctional compounds. Gradients (called G or Δ, and given in p.p.m./mole of $Eu(DPM)_3$ per mole of substrate) have been reported[3] for bifunctional compounds at low concentrations of the shift reagent. Variations of proton shift ratios[4] as the concentration of $Eu(DPM)_3$ is changed have also been reported, both for a bifunctional compound[5] and for a mixture of two monofunctional compounds.[6] In each of the latter cases, the two functional groups were the same. Consequently the equilibrium constants for complex formation at the two sites are similar, any differences being due to steric effects alone; hence only small variations in the proton shift ratios were observed.

We report here the first clear example, illustrated by the $Eu(DPM)_3$-shifted spectra of trans- and cis-9-hydroxybicyclo[3,3,1]nonane-endo-3-carboxylates[7] (**1** and **2**), of a phenomenon which can often be observed when there is more than one kind of functional group in the molecule. The proton assignments are based on initial chemical shifts, coupling constants, and double irradiation experiments. It can be seen from the graphs, and by comparing the proton shifts and the gradients at 0.3 and 1.6 molar equivalents of $Eu(DPM)_3$, that the proton shift ratios vary greatly with the concentration of the shift reagent. Initially the $Eu(DPM)_3$ complexes almost entirely with the hydroxy group (see the gradients for the protons H-1 and H-2 at 0.3 molar equivalents of $Eu(DPM)_3$), whereas at higher concentrations, as complexing at the hydroxy group approaches saturation, the $Eu(DPM)_3$ begins to complex appreciably with the ester group (see the entries for H-6, H-7, H-8, and the OMe group, which have gradients larger at 1.6 than at 0.3 molar equivalents of $Eu(DPM)_3$). We observe a striking consequence of this effect as $Eu(DPM)_3$ is added to a solution of **1**. The signal from the methoxy group starts off as the signal at lowest field except for that from H-1. When Eu(DPM)$_3$ is added, all of the high field signals move downfield past the signal from the methoxy group; but then, as complexing at the methoxycarbonyl group becomes important, the latter signal rapidly overtakes those from H-4, H-6, and H-9, and would no doubt overtake most of the others, except that the solubility limit is reached at this point.



(**1**)

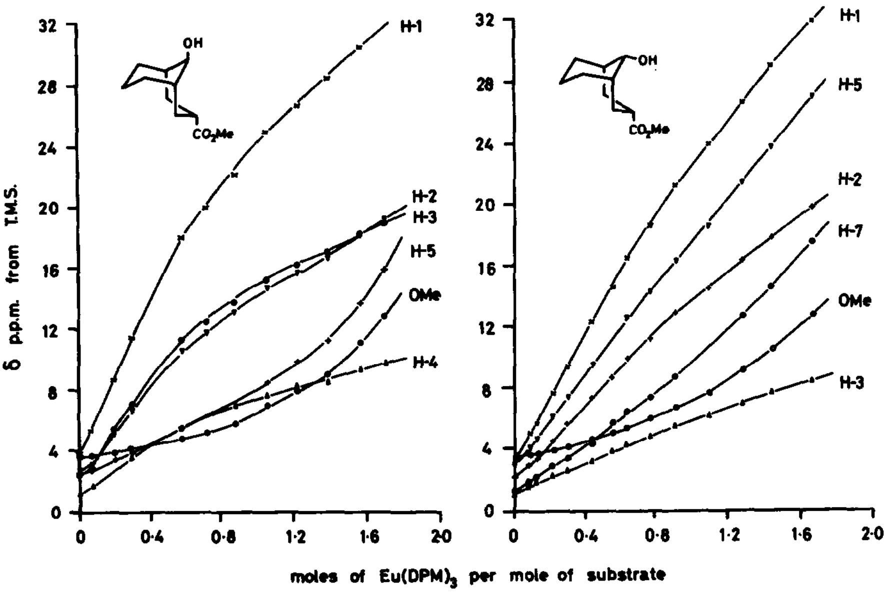


(**2**)

This behaviour is in agreement with some theoretical calculations[8] and with the observation[8] that complex formation has 1:1 stoichiometry at each site, and has equilibrium constants for a hydroxy group and an ester group in the ratio of about 10 to 1. The variation in the proton shift ratios is less marked for **2**, because the hydroxy group in this case is more hindered than it is in **1** and will have a smaller equilibrium constant, and also because the two functional groups, being closer together, cause the same signals to shift. In general, the change in proton shift ratios will be greater the larger the ratio of the equilibrium constants. In the limit, the proton shifts will curve off to a maximum equal to the total shift produced by complete complexation at both sites, but lack of solubility of Eu(DPM)$_3$ prevents this limit being reached. It is only in the event of the two equilibrium constants being accidentally the same that there will be no change in proton shift ratios as Eu(DPM)$_3$ is added to the solution.

The data in the table are consistent with a predominantly boat-chair conformation (although possibly flattened), as has been reported for other endo-substituted bicyclo[3, 3, 1]-nonanes.[9] We note, for **2** in particular, the very large shift of the signal from H-5 at 0.3 molar equivalents of Eu(DPM)$_3$, when the reagent is complexing mainly at the hydroxy group. The data for **1** are less illuminating, although the relatively small gradient for H-8 at 1.6 molar equivalents of Eu(DPM)$_3$ indicates a boat-chair conformation.[10]

Over the entire range of addition of Eu(DPM)$_3$, very little change occurs in coupling constants, where these can be measured, or in half-height widths, where they cannot, indicating that only slight changes can be taking place in the conformation as a result of complex formation.[11]



Shifts[a] and Gradients[b] observed on Addition of $Eu(DPM)_3$ to Solutions[c] of **1** and **2**.

	1				**2**			
	0.3 Molar Equivalents[d]		1.6 Molar Equivalents[d]		0.3 Molar Equivalents[d]		1.6 Molar Equivalents[d]	
	Shift	Gradient	Shift	Gradient	Shift	Gradient	Shift	Gradient
H-1	7.6	26	27.4	12	6	22	29.5	16.5
H-2	4.7	15.5	16.4	8.5	3.6	13	17.7	10.5
H-3	5.1	18	16.1	5.5	1.3	5	6.9	5
H-4	2.5	8.5	8.3	4	1.3	4.5	6.2	4.5
H-5	~2	~6	11.6	12.5	4.3	16	24.2	15.5
H-6			10.0	9	3.0	11	17.1	13.5
H-7			12.5	12.5	2.2	8.5	16.4	14.5
H-8			10.3	8	1.4	5.5	10.0	9
H-9			6.9	3.5	0.7	3	4.1	2.5
OMe	0.5	2.5	8.0	11	0.8	3	9.3	11

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[a] Expressed in p.p.m. downfield from the position of resonance in the absence of $Eu(DPM)_3$. [b] Expressed in p.p.m./mole of $Eu(DPM)_3$ per mole of substrate. [c] Approximately 0.1 molar in CCl_4. [d] Moles of $Eu(DPM)_3$ per mole of substrate.

FOOTNOTES AND REFERENCES

1. Address correspondence to this author; present address: Department of Chemistry, Fourah Bay College, University of Sierra Leone, Freetown, Sierra Leone.
2. J. K. M. Sanders and D. H. Williams, J. Amer. Chem. Soc., 93, 641 (1971), and references therein.
3. H. Hart and G. M. Love, Tetrahedron Letters, 625 (1971); C. C. Hinckley, M. R. Klotz, and F. Patil, J. Amer. Chem. Soc., 93, 2417 (1971).
4. The "proton shift ratio" is simply the ratio of the shifts for any specified pair of protons at a stated concentration of Eu(DPM)$_3$. For monofunctional compounds, these ratios are normally constant over the entire range of addition of Eu(DPM)$_3$, although changes in stoichiometry observed[8] with fluorinated shift reagents can cause the shift ratios to vary dramatically.
5. H. van Brederode and W. G. B. Huysmans, Tetrahedron Letters, 1695 (1971).
6. G. M. Whitesides and D. W. Lewis, J. Amer. Chem. Soc., 92, 6979 (1970).
7. I. Fleming and S. W. Hanson, to be published.
8. J. K. M. Sanders, S. W. Hanson, and D. H. Williams, submitted for publication.
9. W. N. Speckamp, J. Dijkink, A. W. J. D. Dekkers, and H. O. Huisman, Tetrahedron, 27, 3143 (1971) and references therein; M. R. Vegar and R. J. Wells, Tetrahedron Letters, 2847 (1971).
10. The coupling constants, signal shapes, and half-height widths are also consistent with boat-chair conformations for these endo-substituted bicyclo[3, 3, 1] nonanes.[7]
11. Even large Eu(DPM)$_3$-induced changes in conformation, although affecting the coupling constants, should have only very marginal effects on the proton shift ratios and on the shape of a plot of proton shift against moles of Eu(DPM)$_3$ per mole of substrate.