Tetrahedron Letters No. 38, pp.3525 - 3528, 1971. Pergamon Press. Printed in Great Britain.

APPLICATION OF PARAMAGNETIC SHIFT INDUCED BY TRIS(DIPIVALOMETHANATO)-EUROPIUM(III) TO CONFIGURATIONAL ASSIGNMENT OF SULFINYL OXYGEN IN 5α-CHOLESTAN-2α,5-EPISULFOXIDES

EXAMPLES OF UPFIELD SHIFTS DUE TO EU(DPM)$_3$

Morio Kishi, Kazuo Tori and Taichiro Komeno

Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka, Japan

and

Tetsuro Shingu

Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, Japan

(Received in Japan 28 July 1971; received in UK for publication 17 August 1971)

Although both distance and angle dependencies of paramagnetic shifts induced by tris(dipivalomethanato)complexes of the lanthanides, L(DPM)$_3$, (1,2) are apparent from the McConnell and Robertson equation for the pseudo-contact shift (3), the latter factor has so far been neglected in studies, except in those by a British group (2), owing probably to the lack of encounter with actual examples of up- or downfield shifts due to Eu(DPM)$_3$ or Pr(DPM)$_3$, respectively. Since a few examples of these shifts were reported quite recently (4), it seems worthwhile to present here some additional examples of upfield shifts due to Eu(DPM)$_3$, which have been experienced in the course of a study of steroidal episulfoxides.

In a previous paper (5), the isomeric bridge-top sulfoxides of a 7-thiabicyclo[2.2.1]heptane system, 5α-cholestane-2α,5-syn- and -anti-episulfoxides, were reported to require unusually drastic conditions for the exchange reaction of their sulfinyl oxygen. Of the two sulfoxides, the isomer thermodynamically more stable and less mobile on chromatography was assigned the anti-structure (II), and the less stable and more mobile one the syn-structure (III). These structures are consistent with the anisotropic shielding effects of their S→O bonds (6) obtained from their PMR spectra (5).

In order to obtain confirmatory evidence for the stereochemistry of the sulfinyl groups, we have used the paramagnetic shifts induced by Eu(DPM)$_3$ (7) in their 100-MHz PMR spectra in CDCl$_3$. The spectra of

5α-cholestane-2α,5-episulfide (I) and its sulfone (IV) were also examined. The results obtained are shown in the TABLE. The $H_{1\alpha}$- and $H_{1\beta}$-signals in the spectra of the compounds examined with various concentrations of $Eu(DPM)_3$ were assigned by double resonance experiments where the $H_{2\beta}$ signals were spin-decoupled, and in some cases by triple resonance techniques including spin-tickling. Plotting the chemical shifts of assignable protons against the molar ratios of $Eu(DPM)_3$/substrate gave the S-values, defined as the difference in chemical shift between the proton resonance without $Eu(DPM)_3$ and with an equimolar ratio of $Eu(DPM)_3$/substrate (8).

The S-value for $H_{1\alpha}$ is much larger in III than in II; those for $H_{1\beta}$, H_{18}, and H_{19} are larger in III than in II. From these results, the configurations of sulfinyl oxygens in II and III were confirmed unambiguously. No shifts were observed for I, as expected (9). The S-values for sulfone protons were found to be smaller than those for the corresponding sulfoxides protons, suggesting that the ability of sulfonyl oxygens to complex with $Eu(DPM)_3$ is less than that of the sulfinyl oxygen; this relationship is similar to that between an amine oxide and a nitro group.

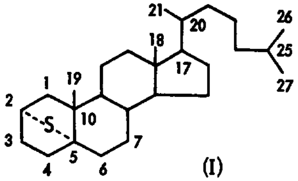
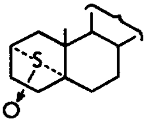
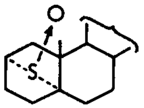
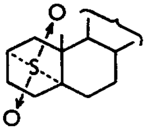
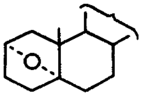
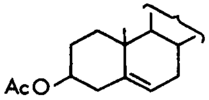
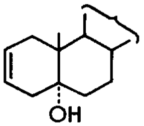
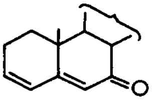
The most interesting finding concerns the behavior of the C_{20} and C_{25} methyl signals of the *syn*-sulfoxide (III). These methyl signals were shifted to higher fields on each addition of $Eu(DPM)_3$. This demonstrates that the angular dependency of lanthanide-induced shifts should not be neglected, and, further, provides confirmatory evidence for the structure of III, and accordingly, for that of II. The hydrocarbon side-chain must be extended towards the back-side direction of sulfinyl oxygen in III, $3\cos^2\theta_i$ being smaller than 1 in the McConnell and Robertson equation (3), where θ_i is the angle between the crystal field axis of the complex and the radius vector from the metal to the proton i.

Similar phenomena were also found in the paramagnetic shifts of both C_{20} and C_{25} methyl or the C_{25} methyl signals in the 100-MHz spectra of 5α-cholestan-2α,5-epoxide (V) (10), 3β-acetoxycholest-5-ene (VI), 5-hydroxy-5α-cholest-2-ene (VII) (10), and cholesta-3,5-dien-7-one (VIII), as listed in the TABLE. It is of considerable interest that the hydrocarbon side-chain signals are shifted upfield in VI, whereas those for the corresponding alcohol are moved to downfield.

The 100-MHz PMR, PMDR, and PMTR spectra were recorded on a Varian HA-100 spectrometer operating in the frequency-swept and TMS-locked mode.

TABLE

Chemical Shifts (δ, ppm Downfield from Internal TMS) and S-Values by $Eu(DPM)_3$ (Plus Sign Denotes a Downfield Shift) in $CDCl_3$

Compounds		Proton signals							
		$H_{1\alpha}$	$H_{1\beta}$	$H_{2\beta}$	H_3	C_{10}-Me	C_{13}-Me	C_{20}-Me	C_{25}-Me
 (I)	δ	1.85	1.31	3.61		0.92	0.64	0.89	0.85
	S	~0	~0	0.02		~0	~0	~0	~0
 (II)	δ	1.78	1.29	3.42		1.01	0.66	0.89	0.85
		(-0.07)	(-0.02)	(-0.19)		(+0.09)	(+0.02)	(0.00)	(0.00)
	S	3.3	3.0	5.0		2.3	1.0	0.16	~0
 (III)	δ	2.84	1.79	3.28		1.10	0.67	0.89	0.85
		(+0.99)	(+0.48)	(-0.33)		(+0.18)	(+0.03)	(0.00)	(0.00)
	S	13.0	5.0	5.0		4.0	1.2	-0.45	-0.50
 (IV)	δ	2.13	1.44	2.92		1.00	0.67	0.89	0.85
		(+0.28)	(+0.13)	(-0.69)		(+0.08)	(+0.03)	(0.00)	(0.00)
	S	2.0	1.3	2.5		1.2	1.0	0.06	~0
 (V)	δ	1.21	1.29	4.37		0.94	0.64	0.89	0.84
	S	6.2	6.0	11.0		4.4	0.60	-0.13	-0.21
 (VI)	δ				4.58	1.01	0.67	0.91	0.86
	S				12.0	1.2	0.08	-0.12	-0.07
 (VII)	δ					0.88	0.67	0.89	0.85
	S					5.5	1.5	0.23	-0.18
			H_4	H_6					
 (VIII)	δ		6.08	5.58	6.15	1.10	0.70	0.92	0.86
	S		0.40	11.2	0.40	4.2	4.4	1.5	-0.18

Values in parentheses are shift values due to S-oxidation.

REFERENCES

1. J. K. M. Sanders and D. H. Williams, J. Amer. Chem. Soc. 93, 641 (1971); C. C. Hinckley, M. R. Klotz and F. Patil, J. Amer. Chem. Soc. 93, 2417 (1971); D. R. Crump, J. K. M. Sanders and D. H. Williams, Tetrahedron Letters 4419 (1970); C. Beauté, Z. W. Wolkowski and N. Thoai, Tetrahedron Letters 817 (1971); Z. W. Wolkowski, Tetrahedron Letters 821 (1971).
2. J. Briggs, G. H. Frost, F. A. Hart, G. P. Moss and M. L. Staniforth, Chem. Commun. 749 (1970); J. Briggs, F. A. Hart and G. P. Moss, Chem. Commun. 1506 (1970); J. Briggs, F. A. Hart, G. P. Moss and E. W. Randall, Chem. Commun. 364 (1971).
3. H. M. McConnell and R. E. Robertson, J. Chem. Phys. 29, 1361 (1958).
4. T. H. Siddall, III, Chem. Commun. 452 (1971); M. R. Willcott, J. F. M. Oth, J. Thio, G. Plinke and G. Schröder, Tetrahedron Letters 1579 (1971); P. H. Mazzochi, H. J. Tamburin and G. R. Miller, Tetrahedron Letters 1819 (1971).
5. M. Kishi and T. Komeno, Tetrahedron Letters 2641 (1971).
6. W. O. Siegl and C. R. Johnson, Tetrahedron 27, 341 (1971), and references therein.
7. R. R. Fraser and Y. Y. Wigfield, Chem. Commun. 1471 (1970).
8. A. F. Cockerill and D. M. Rackham, Tetrahedron Letters 5149 (1970).
9. D. R. Crump, J. K. M. Sanders and D. H. Williams, Tetrahedron Letters 4949 (1970).
10. T. Komeno, H. Itani, H. Iwakura and K. Nabeyama, Chem. Pharm. Bull. (Tokyo) 18, 1145 (1970).