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STEREOSPECIFIC INTERACTIONS OF KETALS WITH TRIS(DIPIVALOMETHANATO)EUROPIUM (III)

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The use of shift reagents for the simplification of proton magnetic resonance spectra received tremendous attention during the last two years[1,2]. With only few exceptions[3], the published efforts describe work related to compounds having one site of association. It seemed therefore interesting to analyse the behavior of some steroidal ketals, in order to establish if such compounds show steric association preferences with $(DPM)_3Eu$.

Solutions containing 0.1 mmol of 3,3-dimethoxy-cholestane[4], 3,3-ethylenedioxy-cholestane, 3,3-ethylenedithio-cholestane and the ethylenehemithioketal of 3-cholestanone in 0.4 ml of CCl_4, were examined with a Varian Associates A-60 NMR spectrometer using simultaneously internal and external TMS as standards.

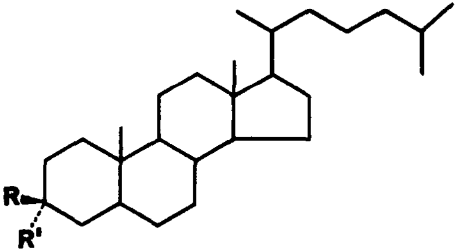
The induced chemical shifts of some of these ketals and of 3β-methoxy- and of 3α-methoxy-cholestane in the presence of increasing amounts of $(DPM)_3Eu$ are summarized in Figure 1. Figure 2 represents the PMR spectra of the adduct of 3-cholestanone with β-mercapthoethanol[5] before and after addition of the shift reagent. Table I shows the inversed slopes one gets from the quantitative studies of the compounds with the europium complex.

When both internal and external TMS are used as standards, a diamagnetically induced shift of some PMR signals, such as those of the internal TMS and of protons distant from the site of association, becomes apparent. The signals of protons which are close to the pseudocontact position are paramagnetically shifted and the sign of the values of Table I indicate the direction of the shift. Upfield shifts induced by $Eu(DPM)_3$, attributed to pseudocontact, have recently been reported[6]. We believe, however, the diamagnetic shifts to be mainly due to changes in bulk suceptibility induced by the added complex, which shifts the signals of the internal TMS upfield with equal or greater intensity than those of the protons which are located far from the site of association. Furthermore, the addition of $EuCl_3$ to a DMSO solution of a given substrate, causes non-selective upfield shifts.

On comparing the spectra which are schematically represented in Figure 1, it is possible to conclude that ketals derived from A/B trans 3-keto-steroids associate with the shift reagent only in the 3-β-position. Figure 2 also permits one to conclude that the adduct obtained by reaction of 3-cholestanone and β-mercaptho-ethanol is a mixture of equal portions of the two possible spiro derivatives, from which only the one having the oxygen atom in the pseudoequatorial position shows association with the complex, since sulfur atoms which have almost the same electronegativity than carbon atoms, do not associate.

TABLE I

Induced Chemical Shifts in ppm/mol $(DPM)_3Eu(III)$/mol steroid.



R	R'	R	R'	C_{19}	C_{18}	C_{26-27}	int. TMS
OCH_2	CH_2O	-10.7	-4.9	+0.9	+1.1	+1.2	+1.2
OCH_3	OCH_3	- 7.0	-1.9	+1.0	+1.4	+1.3	+1.4
OCH_3	H	-19.3	-19.8	-1.2	+0.7	+1.1	+1.2
H	OCH_3	- 1.9	-1.5	+0.6	+1.0	+0.9	+1.0
OH	H	-----	-19.0	-2.7	+0.6	+1.3	+1.3
H	OH	-20.0	-----	-3.1	-0.2	+0.7	+1.2
SCH_2	CH_2O	+ 0.4	+ 0.4	----	----	----	+1.0[a]
OCH_2	CH_2S	- 2.8	- 0.5	----	----	----	

[a] Determined for the equimolecular mixture of 3,3-ethylenehemithioketal isomers.

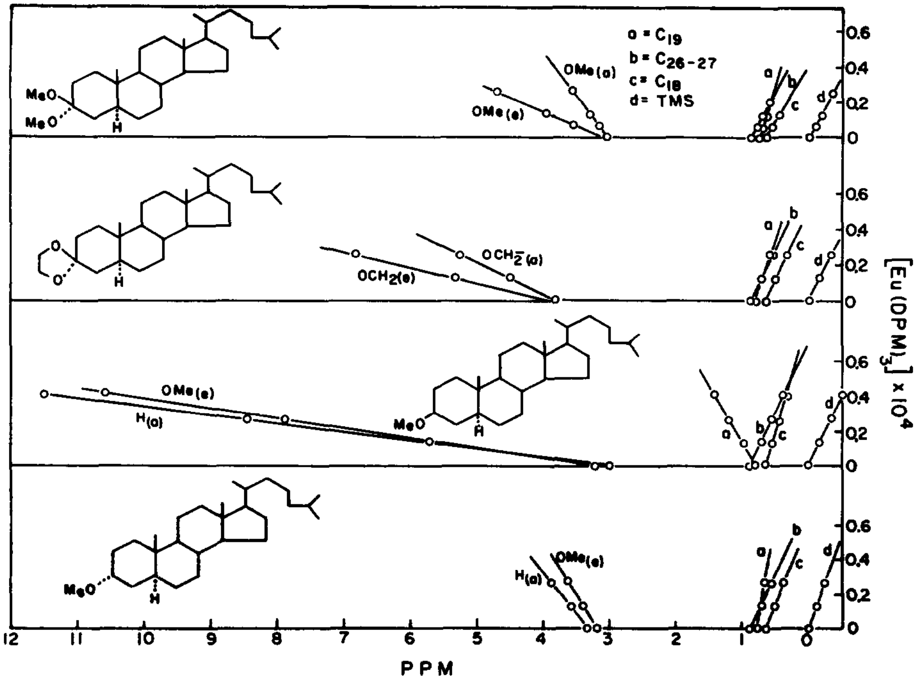


Figure 1.

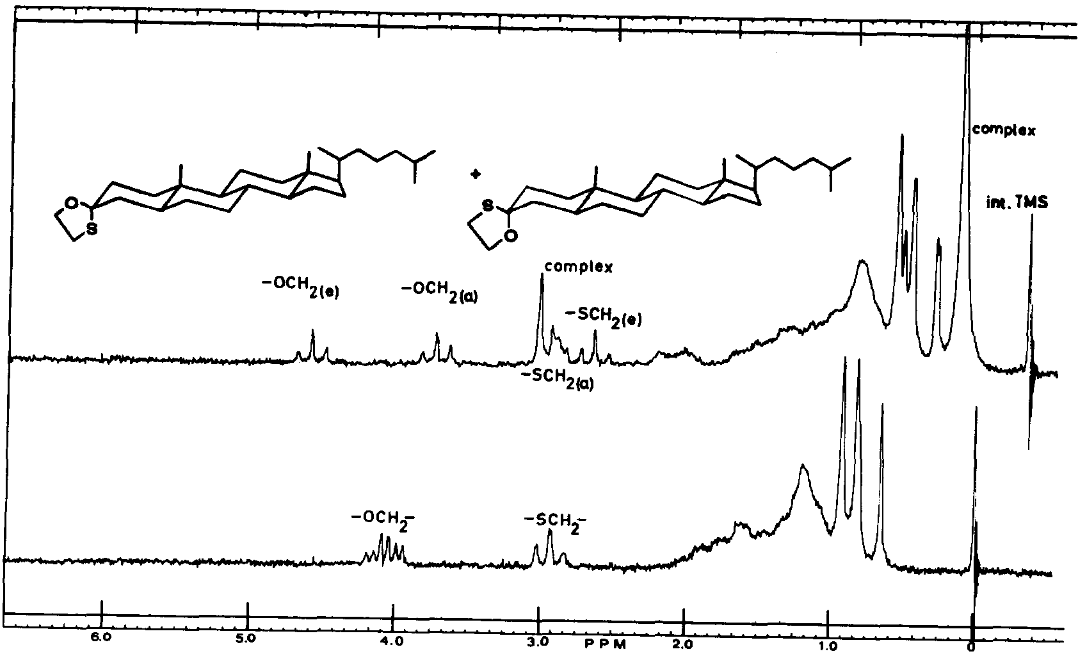


Figure 2.

The steric preference of association of $(DPM)_3Eu(III)$ with equatorial methoxyl groups appears to provide a general method for stereochemical studies. While *cis*- and *trans*-4-terbutylcyclohexanols associate with almost equal intensities[7], the mixture of the corresponding O-methyl derivatives (eq. MeO -10 and ax MeO +1.5 ppm/mole complex/mole compound) show a similar behavior as the 3-methoxy cholestanols (Table I).

Further studies are in progress and will be described elsewhere.

REFERENCES AND FOOTNOTES

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2.- J.K.M. Sanders and D.H. Williams, *J. Amer. Chem. Soc.*, **93**, 641 (1971) and references therein.

3.- D.R. Crump, J.K.M. Sanders and D.H. Williams, *Tetrahedron Letters*, 4949 (1970).

4.- The compounds used in the present work, were prepared using known procedures.

5.- This compound was considered as homogenious. See: L.F. Fieser, *J. Amer. Chem. Soc.*, **76**, 1945 (1954).

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