Absolute Configuration and Optical Rotatory Dispersion of 6-Alkylsulphinyl-5α-cholestanes

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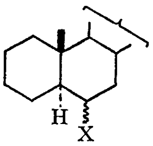
METHYL ALKYL SULPHOXIDES of (*R*)- and (*S*)-configuration at sulphur respectively exhibit negative and positive extrema near 215 nm. in their o.r.d. curves in hydrocarbon solvents.[1,2] This generalisation is useful in allocating chirality at sulphur in methylsulphinyl compounds, but similar generalisations have not been made for other dissymmetric dialkyl sulphoxides because of the paucity of available data. We have found that whereas 6-methylsulphinyl-5α-cholestanes (Ia—d; R=Me) exhibited o.r.d. behaviour in accord with the above generalisation,[3] there was no simple correlation between chirality at sulphur and o.r.d. behaviour in other 6-alkylsulphinyl-5α-cholestanes.



(Ia) X=(*R*)-6β-SOR
(Ib) X=(*S*)-6β-SOR
(Ic) X=(*R*)-6α-SOR
(Id) X=(*S*)-6α-SOR

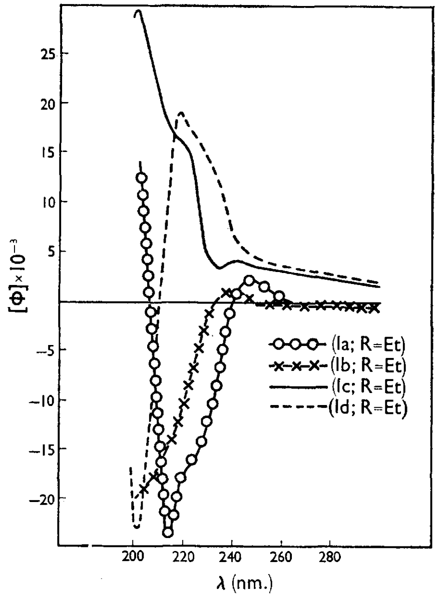


FIGURE 1. *O.r.d. curves of* 6-*ethylsulphinyl*-5α-*cholestanes in hexane.*

All the 6-alkylsulphinyl-5α-cholestanes investigated (Ia—d; R = Et, Pr^n, Pr^i, Bu^n) and (Ib and Id; R = Bu^t) displayed u.v. maxima near 210 nm. in hexane, and all except (Ic; R = Et) had shoulders near 230 nm.; both transitions were optically active (*cf.* refs. 2—4) and in ethanol both bands were displaced to shorter wavelengths, as expected for $n \rightarrow \pi^*$ transitions (*cf.* ref. 3). In sharp contrast to the behaviour of the corresponding methylsulphinyl compounds,[3] the o.r.d. curves of (*R*)- and (*S*)-6β-ethylsulphinyl-5α-cholestanes (Ia and Ib; R = Et) in hexane did not exhibit an antipodal relationship at low wavelengths (Figure 1), both being strongly negative below 210 nm. with only the (*R*)-diastereoisomer showing an extremum at 215 nm. Furthermore, both (*R*)- and (*S*)-6α-ethylsulphinyl-5α-cholestanes (Ic and Id; R = Et) in hexane displayed positive low wavelength extrema, the former at 202 nm. and the latter at 219 nm. Linear extension of the alkyl chain in the alkylsulphinyl group produced no further significant change in the o.r.d. behaviour, the curves of the 6-propylsulphinyl- and 6-butylsulphinyl-5α-cholestanes (Ia—d; R = Pr^n and Bu^n) being very similar to those of their ethyl analogues. Branching in the α-position of the alkyl group further changed the shapes of the curves, which for the four 6-isopropylsulphinyl-5α-cholestanes (Ia—d; R = Pr^i) (Figure 2) showed the same relationship between the sign of the extrema near 217 nm. and chirality at sulphur as that in the 6-methylsulphinyl-5α-cholestanes (Ia—d; R = Me),[3] but the Cotton effects in the (*S*)-6β- and (*R*)-6α-isopropylsulphoxides (Ib and Ic; R = Pr$^{\mathrm{i}}$) were very weak, and the extrema were ill-defined. The o.r.d. curves of the (*S*)-6β-t-butylsulphoxide (Ib)† {$[\Phi]_{270}$ 0; $[\Phi]_{246}$ + 6800; $[\Phi]_{242}$ 0; $[\Phi]_{217}$ − 69,600; $[\Phi]_{208}$ 0°} and the (*S*)-6α-t-butylsulphoxide (Id)† {$[\Phi]_{333}$ + 1500; $[\Phi]_{250}$ + 19,500; $[\Phi]_{239}$ 0; $[\Phi]_{217}$ − 48,700; $[\Phi]_{208}$ − 19,200°} were similar in shape to those of (*R*)-6β- and (*R*)-6α-methylsulphinyl-5α-cholestanes (Ia and Ic; R = Me) respectively, but their amplitudes were much larger.

Branching at the α-position of simple dissymmetric dialkyl sulphoxides has little effect on the o.r.d. curves,[6] and, consonantly, the shapes of the curves for the (*R*)-6β-alkylsulphinyl-5α-cholestanes (Ia; R = Me, Et, Pr$^{\mathrm{i}}$) and of the (*S*)-6β-t-butylsulphoxide (Ib; R = Bu$^{\mathrm{t}}$) are similar, as are those for the (*S*)-6α-alkylsulphoxides (Id; R = Me, Et, Pr$^{\mathrm{i}}$). However, the curves for the (*S*)-6β-alkylsulphoxides (Ib; R = Me, Et, Pr$^{\mathrm{i}}$) and (*R*)-6α-alkylsulphoxides (Ic; R = Me, Et, Pr$^{\mathrm{i}}$) [the latter should also be compared with (*S*)-6α-t-butylsulphinyl-5α-cholestane (Id; R = Bu$^{\mathrm{t}}$)] vary markedly in sign and shape according to the nature of α-branching in the alkylsulphinyl groups. It is clear that the generalisation proposed earlier for methyl alkyl sulphoxides cannot be extended to other dissymmetric dialkyl sulphoxides, at least when one of the alkyl groups is chiral. When sulphur is the sole chiral centre it appears that extension of the generalisation is valid.[6]

Osmometry indicated that the sulphoxides were monomeric in hexane at the concentrations used for o.r.d. determinations, and the o.r.d. curves had the same sign in ethanol as in hexane (although there were changes in positions of extrema and in amplitudes) so variations in monomer–dimer ratios and solvational phenomena may be excluded as major factors governing their extraordinary o.r.d. behaviour. Furthermore, this behaviour cannot be rationalised in terms of changing conformational equilibria controlled in part by the steric requirements of the alkyl group (contrast ref. 7). The 19-methyl groups in the (*R*)-6β-sulphoxides (Ia; R = Me, Et, Pr$^{\mathrm{n}}$, Pr$^{\mathrm{i}}$, and Bu$^{\mathrm{n}}$) resonated at τ 8·92 ($CDCl_3$) (within 2 Hz) and the same insensitivity to the nature of the alkyl group pertained for the other three series of sulphoxides (Ib; τ 8·79) (Ic; τ 9·10) and (Id; τ 9·16) suggesting that the conformations in $CDCl_3$ of the sulphoxides within a particular series were very similar.

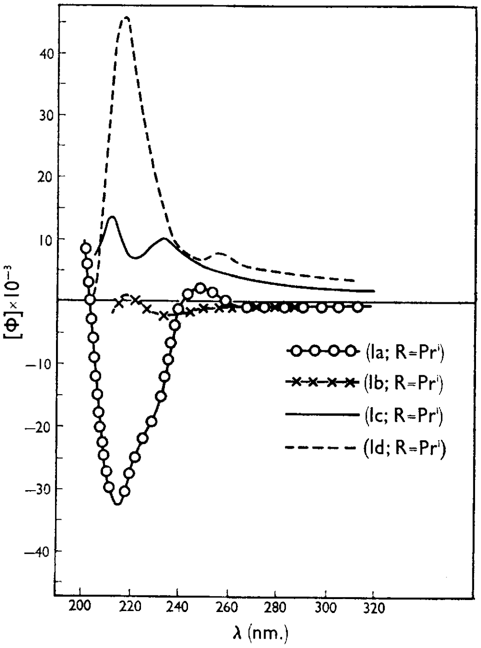


FIGURE 2. *O.r.d. curves of 6-isopropylsulphinyl-5α-cholestanes in hexane.*

The sulphoxides were prepared from 6α-methanesulphonyloxy-5α-cholestane by methods analogous to those described previously for 4-methylsulphinyl-5α-cholestanes,[2] and the configurations at sulphur were established by pyrolysis of the 6β-sulphoxides.[8]

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† These sulphoxides have analogous configurations at sulphur to those in (*R*)-6β- and (*R*)-6α-methylsulphinyl-5α-cholestanes. The reversed designation of chirality is a consequence of the Cahn–Ingold–Prelog system of nomenclature.

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