Absolute Configuration and Optical Rotary Power of Methylsulphinyl Steroids

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IT has been suggested that alkyl methyl sulphoxides of the (*R*)-configuration at sulphur exhibit a negative Cotton effect near 200 mμ[1] (*cf.* ref. 2). This relationship has been verified for the sulphinylamino-acids,[3] type $MeSO{\cdot}[CH_2]_n{\cdot}CH(NH_2){\cdot}CO_2H$, where $n = 1$ and 2. Substantiation of the relationship is important in view of the potential utility of the o.r.d. method for determining the absolute configuration of sulphoxides.[4] We have, therefore, determined the o.r.d. spectra of some methylsulphinyl steroids, the absolute configurations of which were defined by pyrolysis.[5] We found no simple relationship between the o.r.d. curves and chirality at sulphur; the expected Cotton effect near 200 mμ was usually accompanied by another Cotton effect of opposite sign near 230 mμ, which in some cases was the dominant feature of the o.r.d. spectrum.

3β-Acetoxy-(*R*)-5α-methylsulphinylcholestane[6] (Ia) (λ_{max} 217 mμ) displayed a positive, and the diastereomeric (*S*)-sulphoxide (Ib) (λ_{max} 215 mμ, shoulder at *ca.* 230 mμ) a negative Cotton effect centred at 232 mμ (Figure 1). The 230 mμ transition is optically active,† whilst the shorter-wavelength band is not manifestly so. Conversely, in (*S*)-methylsulphinylbutane (λ_{max} 206 mμ, shoulder at 215 mμ) only the 206 mμ band appears to be optically active,[1] and in cyclic sulphoxides both transitions show optical activity.[7] The 3β-acetoxy-group does not materially influence the o.r.d. spectra, since (*R*)- and (*S*)-5α-methylsulphinylcholestanes [(Ic) and (Id)] gave curves similar to those of (Ia) and (Ib) respectively.‡

(*R*)-4β- and (*R*)-4α-Methylsulphinyl-5α-cholestanes, (IIa) and (IIc), gave a first extremum at *ca.* 216 mμ of a negative Cotton effect, whilst (*S*)-4β- and (*S*)-4α-methylsulphinyl-5α-cholestanes (IIb) and (IId), showed a first extremum at *ca.* 216 mμ of a positive Cotton effect (Figure 2). Both (*S*)-sulphoxides, (IIb) and (IId), also displayed a negative Cotton effect at 230—240 mμ, whilst the (*R*)-4β-sulphoxide (IIa) had an extremum at 240 mμ, consistent with that of a positive Cotton effect with a hidden second extremum. The (*R*)-4α-sulphoxide (IIc) showed no Cotton effect at 230—240 mμ. All the sulphoxides had u.v. maxima near 211 mμ, and all except the (*R*)-4α-sulphoxide (IIc) displayed a shoulder at *ca.* 230 mμ; both transitions are optically active. Above 300 mμ the (*R*)- and (*S*)-4β-sulphoxides (IIa) and (IIb) showed positive, and the (*R*)- and (*S*)-4α-sulphoxides (IIc) and (IId) negative plain curves, so these are not indicative of sulphoxide chirality (*cf.* ref. 4). Osmometry indicated that the sulphoxides were monomeric in hexane at the concentrations used for o.r.d. measurements.

(*R*)- and (*S*)-4β-Methylsulphinyl-5α-cholestanes (IIa) and (IIb) were prepared by oxidation of 4β-methylthio-5α-cholestane with peroxylauric acid. After chromatographic (thin-layer) separation, the (*R*)-sulphoxide (IIa) was characterised[5] by decomposition in boiling benzene to 5α-cholest-3-ene, the diastereomeric sulphoxide being inert. The (*R*)- and (*S*)-4β-sulphoxides (IIa) and (IIb) with potassium t-butoxide in dimethyl sulphoxide gave the (*R*)-4α- and (*S*)-4α-sulphoxides (IIc) and (IId), inversion at carbon not being accompanied by inversion at sulphur.[5,8] Oxidation of the (*R*)-4β-

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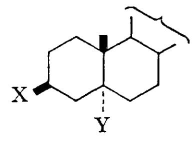
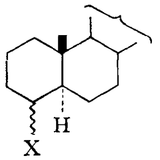
† The 230 mμ band is masked in the 3β-acetoxy-(*R*)-5α-sulphoxide (Ia), but a shoulder at *ca.* 230 mμ appeared in the u.v. spectrum of the corresponding 3β-hydroxy-(*R*)-5α-sulphoxide.

‡ (*R*)-5α-Methylsulphinylcholestane (Ic) decomposed before accurate o.r.d. investigation, but its o.r.d. spectrum was qualitatively similar to that of (Ia).



(I)



(II)

	X	Y		X
a	OAc	(*R*)-SOMe	a	(*R*)-4β-SOMe
b	OAc	(*S*)-SOMe	b	(*S*)-4β-SOMe
c	H	(*R*)-SOMe	c	(*R*)-4α-SOMe
d	H	(*S*)-SOMe	d	(*S*)-4α-SOMe

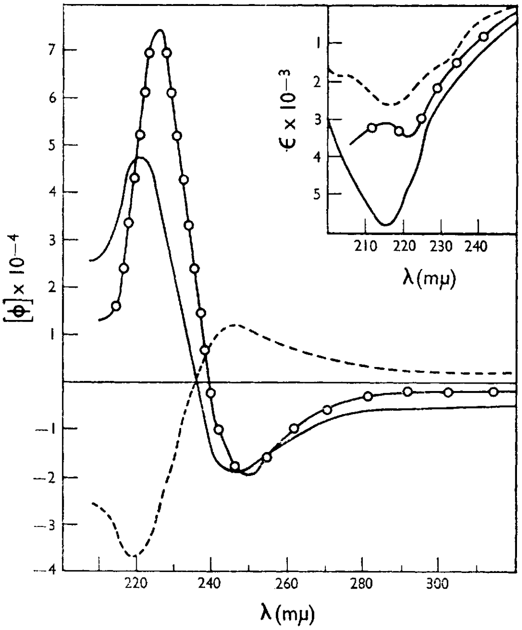


FIGURE 1. *Optical rotatory dispersion curves and ultraviolet spectra of* 3β-*acetoxy*-(*R*)-5α-*methylsulphinylcholestane* (Ia) (- - - - - -), 3β-*acetoxy*-(S)-5α-*methylsulphinylcholestane* (Ib) (————), *and* (S)-5α-*methylsulphinylcholestane* (Id) (—o—o—). *All spectra were determined in hexane solution.*

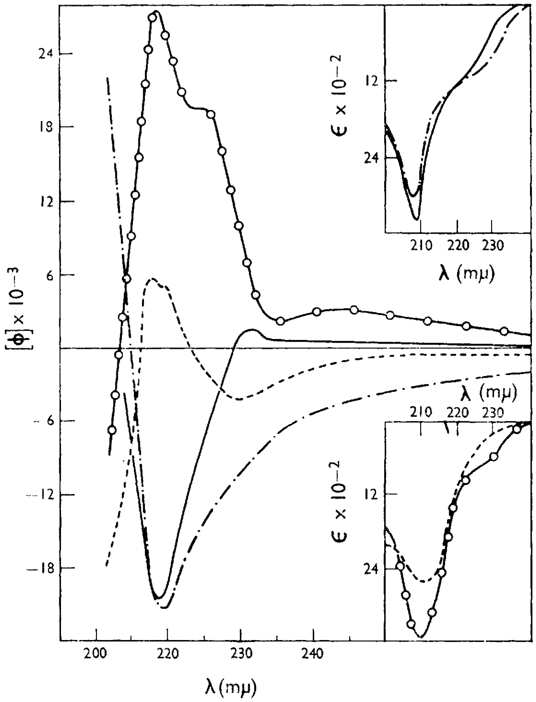


FIGURE 2. *Optical rotatory dispersion curves and ultraviolet spectra of* (R)-4β-*methylsulphinyl*-5α-*cholestane* (IIa) (————), (S)-4β-*methylsulphinyl*-5α-*cholestane* (IIb) (—o—o—), (R)-4α-*methylsulphinyl*-5α-*cholestane* (IIc) (—·—·—), *and* (S)-4α-*methylsulphinyl*-5α-*cholestane* (IId) (- - - - -). *All spectra were determined in hexane solution.*

and (*S*)-4β-sulphoxides (IIa) and (IIb) gave the same 4β-sulphone, and the (*R*)-4α- and (*S*)-4α-sulphoxides (IIc) and (IId) gave the same 4α-sulphone, confirming the stereochemical relationships about sulphur. (*R*)- and (*S*)-5α-Methylsulphinylcholestanes (Ic) and (Id) were prepared by oxidation of 5α-methylthiocholestane. After chromatographic separation, one sulphoxide in boiling benzene gave cholest-4-ene (83%) and cholest-5-ene (17%), indicating that it had the (*R*)-configuration at sulphur,[5] whilst the other sulphoxide gave cholest-4-ene (56%) and cholest-5-ene (44%). Both sulphoxides gave the same sulphone on oxidation.

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