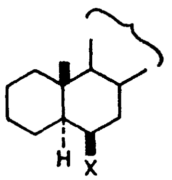
Chiroptical Properties of Steroidal βγ-Unsaturated Sulphoxides

By D. Neville Jones,* E. E. Helmy, and R. J. K. Taylor
(*The Chemistry Department, The University, Sheffield* S3 7HF)
and A. C. F. Edmonds
(*Department of Pure and Applied Science, Doncaster College of Technology, Doncaster*)

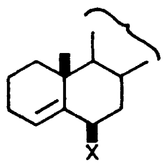
Summary The chiroptical properties of steroidal βγ-unsaturated sulphoxides are determined by the relative spatial orientation of the olefinic double bond and the lone electron pair on sulphur, and chirality at sulphur does not necessarily play a predominant role.

The chiroptical properties of alkyl allyl sulphoxides are markedly different from those of constitutionally and configurationally related dialkyl sulphoxides;[1] diastereoisomers of *S*-allyl-L-cysteine *S*-oxide and *S*-propyl-L-cysteine *S*-oxide of identical configuration at sulphur display almost enantiomeric chiroptical properties, whereas those with opposite configurations display similar o.r.d. and c.d. curves.[1b] The differences may be attributed to electronic interaction between the double bond and the sulphoxide group, the relative orientations of which could possibly influence the interaction and hence the chiroptical characteristics. We have explored this possibility with steroidal $\beta\gamma$-unsaturated sulphoxides.

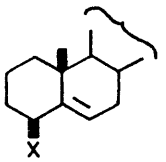
(*R*)-6β-Allylsulphinyl-5α-cholestane (I) and its (*S*)-isomer (II) displayed almost enantiomeric o.r.d. curves in ethanol (Table) in marked contrast to the behaviour of their saturated analogues (III) and (IV).[2] In view of the marked influence of the dissymmetric steroid skeleton upon the chiroptical properties of (III) and (IV),[2] the almost mirror-image relationship of the o.r.d. curves for (I) and (II) provide convincing evidence that the allylsulphinyl system predominates in determining the chiroptical properties of alkyl allyl sulphoxides. In contrast to the marked solvent dependence of the chiroptical behaviour of (+)-(*R*)-allyl methyl sulphoxide (V) and (+)-(*R*)-allyl butyl sulphoxide (VI),[1a] the o.r.d. curves for (I) and (II) in hexane were similar in shape to those in ethanol and were shifted 5—10 nm to longer wavelength. The o.r.d. curve of (II) in ethanol was similar in sign and shape to those given in water by the configurationally related (V), (VI), and the (*S*)-isomer of *S*-allyl-L-cysteine *S*-oxide,[1] suggesting as a general rule that alkyl allyl sulphoxides of stereoformula (*A*) should display o.r.d. curves in hydroxylic solvents typified by that of (II).



(I) X = (*R*) - $SO{\cdot}CH_2{\cdot}CH{:}CH_2$
(II) X = (*S*) - $SO{\cdot}CH_2{\cdot}CH{:}CH_2$
(III) X = (*R*) - $SOPr^n$
(IV) X = (*S*) - $SOPr^n$



(VII) X = (*R*) - SOMe
(VIII) X = (*S*) - SOMe



(IX) X = (*S*)-SOMe
(X) X = (*R*)-SOMe

TABLE

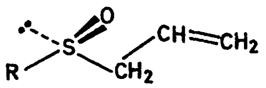
O.r.d. data for steroidal $\beta\gamma$-unsaturated sulphoxides

Dispersion characteristics[a]

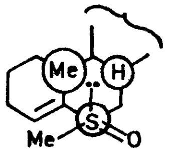
	In ethanol				In hexane			
(I)	0 (275)	6300pk (245)	0 (238)	−41000tr (218)	0 (275)	2500pk (253)	0 (247)	−19400tr (222)
(II)	0 (275)	−8300tr (243)	0 (233)	37700! (217)	−1000 (275)	−9000tr (256)	0 (246)	47300! (225)
(VII)	2800 (345)	9800pk (240)		4500tr (226)	2000 (345)	18000pk (248)	0 (238)	−48000tr (215)
(VIII)	2500 (345)	30000pk (240)	0 (232)	−30000! (225)	1030 (345)	10000pk (248)	0 (240)	−37500tr (220)
(IX)	−3000 (345)	−34000tr (237)		−17000pk (223)	−2000 (345)	−36000tr (249)	0 (236)	15000! (220)

[a] Molecular rotations at wavelengths/nm indicated in parentheses. pk = peak, tr = trough, ! = no extremum.

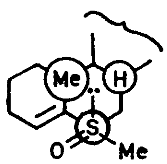
In striking contrast to the behaviour of (I) and (II), (*R*)-6β-methylsulphinylcholest-4-ene (VII) and its (*S*)-isomer (VIII) did not give antipodal o.r.d. curves in ethanol and gave similar o.r.d. curves in hexane (Table), whilst (*S*)-4β-methylsulphinylcholest-5-ene (IX) in hexane displayed an o.r.d. curve antipodal to those of (VII) and (VIII). The same relationships were observed in their c.d. behaviour, so that (VII) and (VIII) of opposite configuration at sulphur displayed similar chiroptical properties, whilst the chiroptical properties of (VIII) and (IX) which had the same configuration at sulphur were antipodal. The u.v. absorption characteristics of $\beta\gamma$-unsaturated sulphoxides have been related to spectroscopic coupling between a $\pi \rightarrow \pi^*$ transition of the double bond and a sulphoxide $n \rightarrow d$ transition,[3] and the chiroptical properties of the sulphoxides (VII), (VIII), and (IX) are rational if they are associated predominantly with the relative spatial orientation of the double bond and the lone electron pair on sulphur, because models reveal that this spatial relationship is similar in the most stable conformations (*B*) and (*C*) (projections down the S–C-6 bond) of (VII) and (VIII) respectively, whilst in the most favourable conformation (*D*) of (IX) a pseudo-enantiomeric situation pertains. In the light of this rationalisation the almost enantiomeric relationship between the o.r.d. curves of (I) and (II), and between the diastereoisomers at sulphur of *S*-allyl-L-cysteine *S*-oxide[1b] is a consequence of the conformational mobility of the allyl



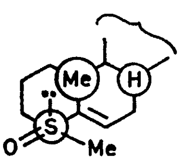
(A)



(B)



(C)



(D)

group, which allows chirality at sulphur to control the relative spatial orientation of double bond and lone electron pair on sulphur; the relative orientations within each pair of these diastereoisomeric sulphoxides are perforce antipodal.

The sulphoxides (I) and (II) were prepared from the corresponding sulphide by oxidation with peroxydodecanoic acid followed by chromatographic separation, and configurations at sulphur were established by reduction of (I) and (II) with di-imide to (III) and (IV) respectively of known absolute configuration.[2] Treatment of 5α-cholestane 5,6α-oxide with sodium methanethiolate in ethanol gave 6β-methylthiocholestan-5α-ol, which was dehydrated by thionyl chloride in pyridine to give 6β-methylthiocholest-4-ene. Oxidation of the unsaturated sulphide with peroxydodecanoic acid in light petroleum gave a mixture of (VII), m.p. 154—155°, $[\alpha]_D$ + 105° (*c* 0·4, $CHCl_3$), τ 9·07 (10-Me), 7·56 (SMe), 6·83 (6α-H), 4·29 (4-H), and (VIII), $[\alpha]_D$ + 84° (*c* 0·4, $CHCl_3$), τ 8·80 (10-Me), 7·45 (SMe), 6·85 (6α-H), 4·35 (4-H), which were separated chromatographically. Solvolysis of 6β-chlorocholest-4-ene in methanethiol gave an inseparable mixture of 6β-methylthiocholest-4-ene and 4β-methylthiocholest-5-ene which on oxidation with peroxydodecanoic acid in light petroleum gave a mixture of the sulphoxides (VII), and (VIII), together with (IX), m.p. 145°, $[\alpha]_D$ − 98° (*c* 0·6, $CHCl_3$), τ 9·06 (10-Me), 7·57 (SMe), 6·85 (4α-H), 4·33 (6-H) and (*R*)-4β-methylsulphinylcholest-5-ene (X), from which all but (X) were obtained pure by preparative t.l.c. The n.m.r. data for (VII) and (VIII) revealed the configurations at sulphur, because 10-methyl groups resonate at lower field in (*S*)-6β-alkylsulphinyl-steroids than in their (*R*)-isomers.[2] Like other allyl sulphoxides[4] the sulphoxides (VII) and (VIII) readily interconverted at 56°, so the pyrolytic method of determination of configuration at sulphur[2] was inapplicable. The close similarity of the n.m.r. spectra for (VII) and (IX) indicated that these sulphoxides were pseudoenantiomeric (*cf.* ref. 5), revealing that (IX) had the (*S*)-configuration at sulphur.

(*Received, July 26th,* 1971; *Com.* 1302.)

---

[1] (a) M. Axelrod, P. Bickart, M. L. Goldstein, M. M. Green, A. Kjaer, and K. Mislow, *Tetrahedron Letters*, 1968, **3249**; (b) P. D. Henson and K. Mislow, *Chem. Comm.*, 1969, **413**.

[2] D. N. Jones, D. Mundy, and R. D. Whitehouse, *J. Chem. Soc.* (*C*), 1969, **1668**.

[3] M. Prochazka and M. Palacek, *Coll. Czech. Chem. Comm.*, 1967, **32**, 3149.

[4] P. Bickart, F. W. Carson, J. Jacobus, E. G. Miller, and K. Mislow, *J. Amer. Chem. Soc.*, 1968, **90**, 4869; R. Tang and K. Mislow, *ibid.*, 1970, **92**, 2100; V. Rautenstrauch, *Chem. Comm.*, 1970, 526.

[5] D. N. Jones, M. J. Green, and R. D. Whitehouse, *J. Chem. Soc.* (C), 1969, 1166.