The Absolute Configuration of Sulphoxides: 3-Thiacholestane Oxides and 1,8,8-Trimethyl-3-thiabicyclo[3,2,1]octane Oxides

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THE configurations of dialkyl sulphoxides have been determined by two independent methods. Johnson and McCants[1] have determined the configurations (*cis* or *trans*) of 4-*p*-chlorophenylthian oxides by dipole moment measurements. They have interrelated other 4-substituted thian oxides by comparative studies of oxidation and by equilibration. Mislow and his co-workers[2] have assigned the *S*-configuration to (+)-butyl methyl sulphoxide from its method of preparation *via* a Grignard reaction on (−)-menthyl 1-butanesulphinate of known absolute configuration and by comparison of its optical rotatory dispersion (o.r.d.) spectrum with that of more complex, naturally occurring, methyl sulphoxides of known configuration. In an attempt to correlate these methods, we have prepared cyclic sulphides from natural products of known absolute configuration, have oxidized these to sulphoxides by the methods of Johnson,[1] and have determined the o.r.d. spectra of the isomeric sulphoxides.

3-Thiacholestane (IV) was synthesized from cholest-3-en-2-one[3] (I) by a sequence of reactions involving periodate–permanganate oxidation[4] of (I) to 4-nor-2,3-secocholestane-2,3-dioic acid (II), reduction of the dimethyl ester of (II) to 4-nor-2,3-secocholestane-2,3-diol (III), conversion of (III) into its bismethanesulphonate which was treated with sodium sulphide. Oxidation of 3-thiacholestane (IV) with *m*-chloroperbenzoic acid yielded a mixture of sulphoxides which were separated by chromatography on aluminium oxide; 3-thiacholestane 3α-oxide (V), m.p. 227—229°, $\lambda_{\max}$ (Nujol) 1022, 1030, 1038 cm.$^{-1}$, n.m.r.† (C_6H_6) 28·5 (18-Me), 38 c./sec. (19-Me); 3-thiacholestane 3β-oxide (VI), m.p. 229—232°, $\lambda_{\max}$ (Nujol) 1060 cm.$^{-1}$, n.m.r. (C_6H_6) 32 (18-Me), 35·5 c./sec. (19-Me). The crude yields of (V) and (VI) were

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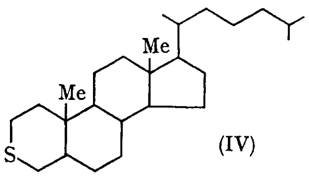
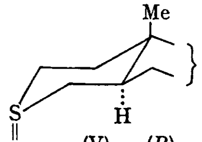
† The n.m.r. spectra were determined with a Varian Associates A-60 spectrometer and are recorded in c./sec. downfield from tetramethylsilane.

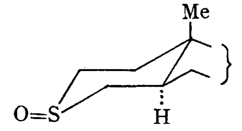
36% and 51%, respectively; the ratio of (V) : (VI) was 41 : 59.



(IV)



(V) (*R*)



(VI) (*S*)

Configurations were assigned to the sulphoxides (V) and (VI) on the following evidence: (1) Oxidation of (IV) with nitrogen tetroxide[1] produced 60 ± 2% (V) and 40 ± 2% (VI).[‡] Equilibration of either the axial oxide, (V), or the equatorial oxide, (VI), with nitrogen tetroxide also produced a mixture of oxides of this same composition, the quantity of axial oxide predominating. (2) Oxidation of (IV) with *m*-chloroperbenzoic acid[1] produced 42 ± 3% (V) and 58 ± 3% (VI), the quantity of equatorial oxide predominating. (3) The axial sulphoxide (V) was eluted first on column chromatography.[1] (4) The S=O group of the equatorial sulphoxide (VI) absorbed at higher frequency (1060 cm.$^{-1}$) in the infrared than that of the axial sulphoxide (V) (1022, 1030, 1038 cm.$^{-1}$).[5] The o.r.d. spectra of the isomeric sulphoxides, (V) and (VI), are given in Figure 1.

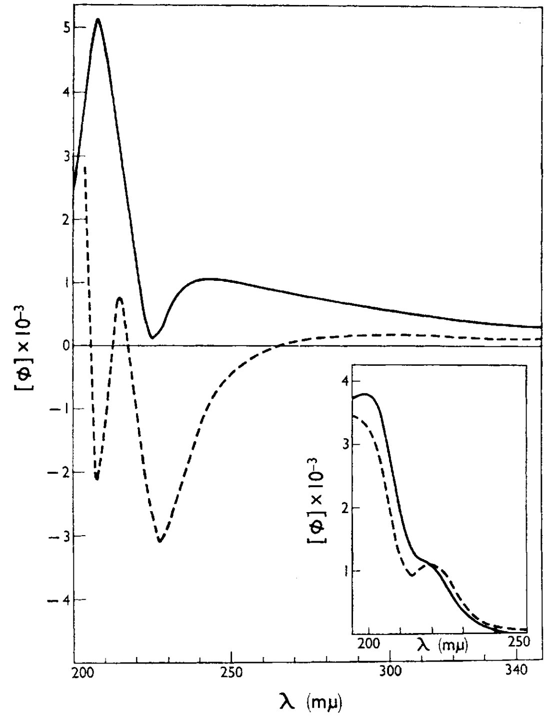


FIGURE 1. *Optical rotatory dispersion curves and ultraviolet spectra of* 3-*thiacholestane* 3α-*oxide* (V) (——) *and* 3-*thiacholestane* 3β-*oxide* (VI) (- - -). *All spectra were determined in acetonitrile solution.*

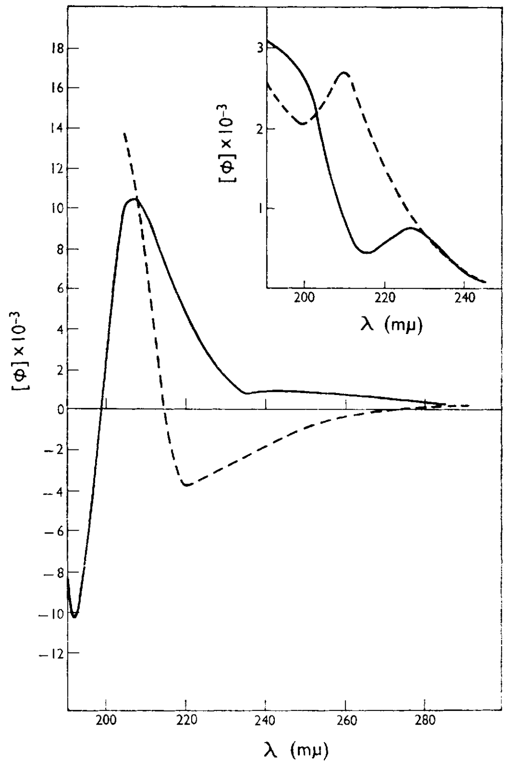


FIGURE 2. *Optical rotatory dispersion curves and ultraviolet spectra of* exo-1,8,8-*trimethyl*-3-*thiabicyclo*[3,2,1]-*octane oxide* (VII) (——) *and* endo-1,8,8-*trimethyl*-3-*thiabicyclo*[3,2,1]*octane oxide* (VIII) (- - -). *All spectra were determined in acetonitrile solution.*

Similar studies (see Figure 2) were made on the *exo*- and *endo*-1,8,8-trimethyl-3-thiabicyclo[3,2,1]-octane oxides (VII and VIII, respectively) synthesized from (+)-camphor. Configurations were

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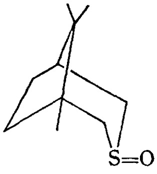
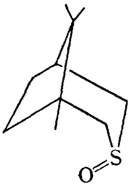
[‡] The composition of the mixtures of sulphoxides was determined from the intensity of the absorption bands of the 18- and 19-methyl groups in the n.m.r. spectra of the mixtures in benzene and from optical rotatory dispersion spectra of the mixtures.

assigned to (VII) and (VIII) from the methods of synthesis[1] [*m*-chloroperbenzoic acid → 95 ± 2% (VII), 5 ± 2% (VIII); t-butyl hypochlorite → 4 ± 2% (VII), 96 ± 2% (VIII)], from the order of elution on chromatography,[1] and from their n.m.r. spectra[6] [complex multiplet for C-5, 6, 7 H's centred at 107 c./sec. (VII); centred at 122 c./sec. (VIII)].



(VII) (*R*)



(VIII) (*S*)

The o.r.d. spectra of the sulphoxides (V), (VI), and (VII) show Cotton effects corresponding to the two electronic transitions at *ca.* 200 mμ and 220 mμ. Consequently, both the transitions are optically active. The ultraviolet spectrum of (VIII) is abnormal; however, it does correlate with the o.r.d. spectrum. The steric interactions between the S=O and the C-6 and C-7 methylene groups probably distort the molecule. The signs of the Cotton effects in the o.r.d. curves of (V), (VI), (VII), and (VIII) clearly separate the sulphoxides having the *R*-configuration from those having the *S*-configuration. Sulphoxides with a positive Cotton effect associated with the shorter wavelength transition have been assigned the *R*-configuration. However, Mislow *et al.*,[2] have shown that *S*-butyl methyl sulphoxide has a positive Cotton effect associated with this transition. The o.r.d. curves (V) and (VI), and (VII) and (VIII) are not enantiomeric. Differences (other than that of sign) between the o.r.d. spectra for the *R* and *S* epimers reflect the differences in the relative spatial positions of the hydrocarbon residues surrounding the symmetric sulphoxide chromophores. The difference between our conclusions and those of Mislow *et al.*,[2] must also result from similar differences. A related, pronounced effect of conformation on the o.r.d. spectra of sulphoxides has recently been postulated by Folli, Montanari, and Torre.[7]

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