Absolute Configuration of Some Derivatives of 1,4-Oxathian *S*-Oxide

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ALTHOUGH absolute configuration has been assigned[1] to various naturally occurring asymmetric sulphoxides[2] by the *X*-ray method, no stereospecific synthesis has been reported. An approach[3] to this problem involves stereochemically defined derivatives (*e.g.* IV) of 2-hydroxy-1,4-oxathian *S*-oxide as intermediates. We now report on the first derivatives of this type.

Methyl 6-*O*-trityl-α-D-glucopyranoside with lead tetra-acetate in pyridine followed by sodium borohydride gave the syrupy diol (I) the ditosylate (m.p. 129·5—130°, $[\alpha]_D$ $-9°$)* of which, with sodium sulphide in boiling methanol, afforded (2*S*,6*R*)-2-methoxy-6-triphenylmethoxymethyl-1,4-oxathian (II, m.p. 107·5—108·5°, $[\alpha]_D$ $+$ 18°). Hydrogenolysis over palladised charcoal then yielded (2*S*,6*R*)-6-hydroxymethyl-2-methoxy-1,4-oxathian {III, b.p. 140° (bath)/0·2 mm., $[\Phi]$ $+15°$ (400), 0° (302), $-$ 2940° (243), 0° (236), $+$ 5400° (222 mμ)}. With aqueous sodium periodate[4] the sulphide (III) gave a mixture of sulphoxides (IV) ,*A* {m.p. 95—96°, $[\Phi]$ $+320°$ (400), $+835°$ (300), $+1380°$ (250), $+1880°$ (233 mμ)} and *B* {m.p. 108—108·5°, $[\Phi]$ $+385°$ (400), $+920°$ (300), $+1740°$ (250), $+2680°$ (235 mμ)} in the ratio *ca.* 10 : 1; isomer *A* was more readily eluted from

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* $[\alpha]_D$ values for $CHCl_3$, ORD curves for MeOH (*c ca.* 0·04).

[1] R. Hine and D. Rogers, *Chem. and Ind.*, 1956, 1428; K. K. Cheung, A. Kjaer, and G. A. Sim, *Chem. Comm.*, 1965, 100; *cf.* B. W. Christensen and A. Kjaer, *ibid.*, 1965, 225.

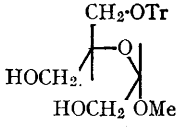
[2] A. I. Virtanen, *Angew. Chem. Internat. Edn.*, 1962, **1**, 299; A. Kjaer, *Pure Appl. Chem.*, 1963, **7**, 229.

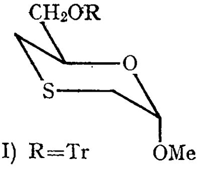
[3] K. W. Buck, F. A. Fahim, A. B. Foster, A. R. Perry, and J. M. Webber, Abs. Amer. Chem. Soc. Meeting, Atlantic City, September 1965, p. 18D.

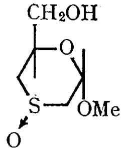
[4] N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, 1962, **27**, 282.

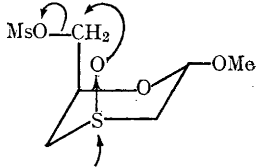
silica gel. Mixtures of similar composition were obtained when oxidation was effected with ozone or hydrogen peroxide in acetone.

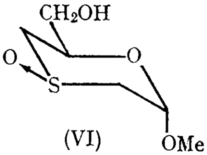
On solvolysis in water at pH 7 and 95° for 20 min. the amorphous mesylate ($[\alpha]_D$ + 64°) of sulphoxide *A* gave sulphoxide *B* in good yield whereas the mesylate (m.p. 109·5°, $[\alpha]_D$ +70°) of sulphoxide *B* reacted slowly (5% in 3 hr.) with regeneration of the parent alcohol *B* (detected chromatographically). Thus, isomer *A* may be assigned the S → O group *cis* to the hydroxymethyl group since the mesylate can then adopt a conformation (V) which will permit an intramolecular nucleophilic displacement[5] followed by attack of water on the sulphur atom of the resultant sulphoxonium salt affording the sulphoxide (*B*) with inverted configuration (*cf.* 3,6-anhydrohexopyranoside formation[6]). A similar sequence cannot occur with the mesylate of isomer *B* which has the sulphoxide and hydroxymethyl groups *trans*.


(I)


(II) R=Tr
(III) R=H


(IV)


(V)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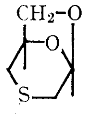
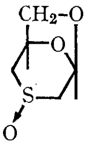
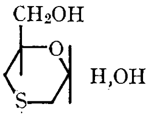

(VII)


(VIII)


(IX)

Treatment of the mesylates of sulphoxides *A* and *B* with sodium benzoate in dimethylformamide[7] followed by saponification of the resultant benzoates afforded the parent alcohols with retention of configuration.

The n.m.r. signal ($CDCl_3$, internal tetramethylsilane, Varian A60 spectrometer) for the anomeric proton of the sulphide (III) was a triplet at τ 5·16 (J 2·5 c./sec.) indicative[8] of equatorial orientation and consistent with the conformation shown (III). The sulphoxide *A* had a similar triplet at τ 4·87 (J 2·6 c./sec.) and apparently adopts conformation (VI). Thus, periodate oxidation of the sulphide (III) results in preferential equatorial oxygenation of the sulphur atom thereby contrasting with various 4-substituted thians which undergo preferential axial oxygenation.[9] Other oxidants, *e.g.* ozone, effect preferential equatorial oxygenation in each series.[10] Presumably, axial oxygenation of the sulphide (III) is hindered by the axial methoxyl group.

The S→O infrared stretching absorption for the sulphoxides (V) were as follows: *A*, 1059 (CS_2, 0·02%) and 1039 cm.$^{-1}$ (CH_2Cl_2, 0·2%); *B*, 1075

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[5] *cf.* F. Montanari, R. Danieli, H. Hogeveen, and G. Maccagnani, *Tetrahedron Letters*, 1964, 2685; D. Neville Jones and M. A. Saeed, *Proc. Chem. Soc.*, 1964, 81; J. C. Martin and J. J. Uebel, *J. Amer. Chem. Soc.*, 1964, **86**, 2936.

[6] S. Peat, *Adv. Carbohydrate Chem.*, 1946, **2**, 56.

[7] E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, 1959, **24**, 1618.

[8] N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, 1964, p. 51.

[9] C. R. Johnson, *J. Amer. Chem. Soc.*, 1963, **85**, 1020.

[10] C. R. Johnson and D. McCants, *J. Amer. Chem. Soc.*, 1965, **87**, 1109.

and 1061 cm.$^{-1}$ It is noteworthy that the absorption for the axial $S\rightarrow O$ group is at higher frequency.

By a reaction sequence similar to (I) → (IV), 1,6-anhydro-β-D-glucopyranose was converted into (1*R*,4*R*)-2,8-dioxa-6-thia-bicyclo-[3,2,1]-octane {VII, b.p. 47—49°/0·1 mm., $[\Phi]$ −210° (400), −370° (300), −2670° (239), 0° (226 mμ)} and thence to the isomeric sulphoxides (VIII), *C* {m.p. 64—66°, $[\Phi]$ −210° (400), −300° (300), 0° (259), +2860° (229), +2280° (225 mμ)} and *D* {m.p. 135°, $[\Phi]$ −460° (400), −1090° (300), −3070° (250), −5520° (233), −5790° (231), −5620° (227 mμ)} in the ratio *ca.* 9 : 1.

Little can be deduced at present from the o.r.d. curves for the sulphoxides *A*, *B*, *C*, and *D*. Equilibration of sulphoxide *C* or *D* with dioxan–water–hydrochloric acid[11] at room temperature gave a mixture with a *C* : *D* ratio of *ca.* 3 : 1. Under these conditions isomers *A* and *B* underwent equilibration at the sulphoxide group and the glycosidic centre. Treatment of an equimolar mixture of sulphoxides *A* and *B* with diborane[12] in chloroform–ether resulted in preferential reduction of isomer *B* (axial sulphoxide) to the sulphide (III). Similar treatment of sulphoxides *C* and *D* resulted in preferential reduction of isomer *D* to the sulphide (VII). Thus, isomers *C* and *D* are tentatively assigned equatorial and axial sulphoxide groups respectively.

Acidic hydrolysis of the sulphides (III) and (VII) gave the diol (IX, m.p. 92—94·5°, $[\alpha]_D$ −7° in H_2O).

Investigation of the above and related sulphoxides is continuing.

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[11] K. Mislow, T. Simmons, J. T. Melillo, and A. L. Ternay, *J. Amer. Chem. Soc.*, 1964, **86**, 1452.

[12] *cf.* D. Landini, F. Montanari, H. Hogeveen, and C. Maccagnani, *Tetrahedron Letters*, 1964, 2691.