787. *Aspects of Stereochemistry. Part XIII.*[1] *Properties of Some Disubstituted Derivatives of 5-Hydroxy-1,3-dioxan.*

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The synthesis of a series of derivatives of 5-hydroxy-1,3-dioxan with methyl and phenyl groups *trans* to the hydroxyl group and variously in the 2-, 4-, 2,4-, and 4,6-positions is described. The pattern of intramolecular hydrogen bonding is similar for each of these compounds; the conformational implications of these results are discussed.

An analysis of the patterns of intramolecular hydrogen bonding of 1,3-*O*-benzylidene-L-erythritol and the L-threitol analogue is presented.

In the preceding paper [1] the synthesis of a series of 2-alkyl-5-hydroxy-1,3-dioxans was described for the purpose of examining the effect of bulk and orientation of the alkyl groups on the extent of intramolecular hydrogen bonding between the hydroxyl group and the oxygen atoms of the 1,3-dioxan ring. We now report on a series of disubstituted 5-hydroxy-1,3-dioxan derivatives.

The relevant compounds in the Table were obtained as follows. Reduction of 2,4-*O*-methylene-1,3,5-tri-*O*-toluene-*p*-sulphonylribitol [2] with lithium aluminium hydride in tetrahydrofuran gave 1,5-dideoxy-2,4-*O*-methyleneribitol, the toluene-*p*-sulphonate of which had a melting point (64°) identical with that reported for 1,5-dideoxy-2,4-*O*-methylene-3-*O*-toluene-*p*-sulphonylribitol obtained by reduction of 1,5-dideoxy-1,5-di-iodo-2,4-*O*-methylene-3-*O*-toluene-*p*-sulphonylribitol.[2]

Oxidation of 4,6-*O*-ethylidene-D-glucose with sodium metaperiodate and reduction of the resultant 2,4-*O*-ethylidene-D-erythrose with sodium borohydride afforded 1,3-*O*-ethylidene-L-erythritol. On conformational grounds [3] the configuration at the acetal carbon atom in 1,3-*O*-ethylidene-L-erythritol would be expected to be the same as that established [4] for 1,3-*O*-benzylidene-L-erythritol, *viz.*, with the methyl group *trans* to the 2-hydroxyl group. The close similarity of the infrared spectra in the hydroxyl stretching region for dilute solutions in carbon tetrachloride of 1,3-*O*-ethylidene- and 1,3-*O*-benzylidene-L-erythritol and of the 4-deoxy-derivatives supports this view. Further, when 1,3-*O*-ethylidene-2,4-di-*O*-toluene-*p*-sulphonyl-L-erythritol was treated with benzaldehyde at 100° in the presence of an acid catalyst, the corresponding 1,3-*O*-benzylidene derivative was obtained which was identical with the product of established total configuration [4] formed by sequential periodate oxidation, borohydride reduction, and toluene-*p*-sulphonylation of 4,6-*O*-benzylidene-D-glucose. Reduction of 1,3-*O*-ethylidene-2,4-di-*O*-methanesulphonyl-L-erythritol with lithium aluminium hydride gave 4-deoxy-1,3-*O*-ethylidene-L-erythritol which was characterised as the *p*-phenylazobenzoate.

Attempts to obtain 1,3-*O*-methylene-L-erythritol by graded acidic hydrolysis of 1,3:2,5:4,6-tri-*O*-methylene-D-mannitol to 1,3-*O*-methylene-D-mannitol followed by degradation were unsuccessful. Although 1,3:4,6-di-*O*-methylene-D-mannitol and D-mannitol were formed when the tri-*O*-methylene compound was treated with boiling 6N-hydrochloric acid for 4·5 hr., the only monomethylene compound isolated was 3,4-*O*-methylene-D-mannitol. Clearly, an acetal migration had occurred. Both 1,3- and 3,4-*O*-methylene-D-mannitol have been isolated [5] after partial methylenation of D-mannitol. Degradation of 3,4-*O*-methylene-D-mannitol by periodate oxidation and then borohydride reduction gave 2,3-*O*-methylene-D-threitol which was characterised as the di-*O*-methanesulphonate.

[1] Part XII, Baggett, Bukhari, Foster, Lehmann, and Webber, preceding paper.
[2] Hann and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 1906.
[3] Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.
[4] Foster, Haines, Homer, Lehmann, and Thomas, *J.*, 1961, 5005.
[5] Fletcher and Diehl, *J. Amer. Chem. Soc.*, 1952, **74**, 3799.

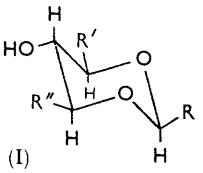
Treatment of 1,3-*O*-ethylidene-2,4-di-*O*-methanesulphonyl-L-erythritol with paraformaldehyde and an acid catalyst gave 2,4-di-*O*-methanesulphonyl-1,3-*O*-methylene-L-erythritol. An analytically pure sample of 1,3-*O*-methylene-L-erythritol could not be obtained from the methane sulphonyl derivative by hydrolysis with aqueous-methanolic potassium hydroxide, but reduction with lithium aluminium hydride gave 4-deoxy-1,3-*O*-methylene-L-erythritol which was purified by way of the *p*-phenylazobenzoate.

Infrared spectral data on 5-hydroxy-1,3-dioxan and certain derivatives.

Derivative (I)	R	R′	R″	$\nu_{max.}$ (cm.$^{-1}$) Free OH	Bonded OH	$\frac{\log_{10}(I_0/I_B)}{\log_{10}(I_0/I_F)}$ *
5-Hydroxy-1,3-dioxan †	H	H	H	3641	3596	5·70
4-Deoxy-1,3-*O*-methylene-L-erythritol	H	H	CH_3	3644	3604	0·31
trans-5-Hydroxy-2-methyl-1,3-dioxan [1]	CH_3	H	H	3633	3604	0·40
1,5-Dideoxy-2,4-*O*-methyleneribitol	H	CH_3	CH_3	3649	3602	0·28
4-Deoxy-1,3-*O*-ethylidene-L-erythritol	CH_3	H	CH_3	3643	3605	0·32
trans-5-Hydroxy-2-phenyl-1,3-dioxan ‡	Ph	H	H	3637	3604	0·32
1,3-*O*-Benzylidene-4-deoxy-L-erythritol [4]	Ph	H	CH_3	3642	3604	0·28

* The values of I_0, I_B, and I_F taken from the spectra had average magnitudes of 21, 11, and 4, respectively. † Barker, Brimacombe, Foster, Whiffen, and Zweifel, *Tetrahedron*, 1959, **7**, 10. ‡ Dobinson and Foster, *J.*, 1961, 2338.

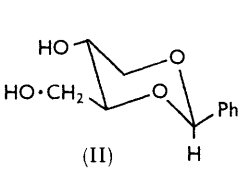
The absorptions in the hydroxyl stretching region of the infrared spectra of the alcohols in the Table were obtained on $>0{\cdot}005$M-solutions in carbon tetrachloride. Under these conditions intermolecular hydrogen bonding is negligible and the absorptions may be associated [6] with free and intramolecularly bonded hydroxyl groups. For a given alcohol the proportion of free and bonded hydroxyl groups may be assessed approximately from the relative extinction coefficients [7] or from the ratio $\log_{10}(I_0/I_B)/\log_{10}(I_0/I_F)$ where I_B and I_F refer in the usual manner to the absorptions for bonded and free hydroxyl groups. The magnitude of the ratio is proportional to the percentage of bonded hydroxyl groups; a ratio greater than unity indicates that the majority of the hydroxyl groups are bonded. From the Table it can be seen that, with the exception of 5-hydroxy-1,3-dioxan (ratio 5·70) the ratios of the other 5-hydroxy-1,3-dioxan derivatives are notably less than unity and of similar magnitude. In the preceding paper it was noted that for each member of the series of *trans*-2-alkyl-5-hydroxy-1,3-dioxans where the alkyl groups were Et, Pr^i, and Ph, the ratios were near to 0·3 and not significantly different; the ratio for the compound where the alkyl group was methyl was slightly greater. These results were taken to mean that, in these compounds, the chair forms of the 1,3-dioxan rings with axial hydroxyl groups were not significant contributors to the conformational equilibria and that intramolecular hydrogen bonding must occur in some other conformation where the bulk of the 2-substituent is not of critical importance. For reasons similar to those detailed in the preceding paper, this inference is substantiated by the results in the Table which show that a ratio near to 0·3 is also obtained when 5-hydroxy-1,3-dioxan is substituted to give a *trans*-4-methyl derivative (4-deoxy-1,3-*O*-methylene-L-erythritol), a *trans,trans*-4,6-dimethyl derivative (1,5-dideoxy-2,4-*O*-methyleneribitol), a *trans,trans*-2,4-dimethyl derivative (4-deoxy-1,3-*O*-ethylidene-L-erythritol), and a *trans,trans*-4-methyl-2-phenyl derivative (1,3-*O*-benzylidene-4-deoxy-L-erythritol). The chair conformation of the 1,3-dioxan ring with an axial hydroxyl group for each of the disubstituted derivatives would also contain two methyl groups or a methyl and a phenyl group in axial positions on the same side of the ring which is sterically a very unfavourable arrangement.[8] Since intramolecular hydrogen bonding occurs in each of the disubstituted derivatives, the chair



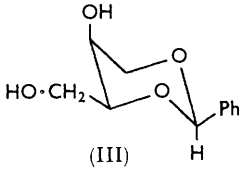
(I)

[6] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.
[7] Cole and Jefferies, *J.*, 1956, 4391.
[8] McCoubrey and Ubbelohde, *Quart. Rev.*, 1951, **5**, 364.

conformation of 5-hydroxy-1,3-dioxan with an equatorial hydroxyl group is not completely stabilised by the introduction of two equatorial groups in the 2,4- or 4,6-positions. It is unlikely that intramolecular hydrogen bonding could occur in the chair conformations of 5-hydroxy-1,3-dioxan derivatives which contain an equatorial hydroxyl group since the dihedral angle (*ca.* 180°) between the hydroxyl group and each ring-oxygen atom is larger than that (*ca.* 120°) between the hydroxyl groups in cyclopentane-*trans*-1,2-diol and intramolecular hydrogen bonding does not occur in this compound.[6] The dihedral angle between the hydroxyl group and either ring-oxygen atom in 5-hydroxy-1,3-dioxan derivatives is reduced to a minimum value of *ca.* 60° in the chair form with the hydroxyl group axial, and in other conformations such as the boat forms considered in the preceding paper. However, any deformation of the chair forms with the hydroxyl groups equatorial must be associated with an increase in non-bonded interactions the magnitude of which is difficult to assess since the ring contains two oxygen atoms and the steric requirements of their lone pairs of electrons are uncertain. Should these steric requirements be significantly less [9] than those for the hydrogen atoms in a methylene group, then the energy difference between the preferred chair conformation (equatorial hydroxyl group) and non-chair conformations will be less than that in the analogous cyclohexane derivatives and the postulation that the intramolecular hydrogen bonding observed is associated with conformations other than chair forms becomes plausible. The problem is being studied further.



(II)



(III)

It is probable that the hydroxyl group would be completely bonded to the appropriate ring-oxygen atom in those conformations of derivatives of 5-hydroxy-1,3-dioxan where the dihedral angle between these groups is near to 60°. This follows by analogy with the observation that, in *trans*-2-methoxycyclohexanol, where the minimum dihedral angle between the hydroxyl and methoxy groups is 60°, the hydroxyl group is completely bonded.[10]

Conformational instability has also been observed for 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-threitol and 2,4,5-tri-*O*-acetyl-1,3-*O*-benzylidene-L-arabitol.[4] In these compounds the 1,3-dioxan rings can exist in chair conformations with axial acetoxyl groups at position 2 and bulky equatorial groups at positions 2 and 4.

The dilute-solution spectra in the hydroxyl stretching region for 1,3-*O*-benzylidene-L-erythritol (II) (Fig. 1a) and -L-threitol [4] (III) (Fig. 1b) were more complex than those for the alcohols in the Table. An interpretation is possible by reference to the hydrogen-bonding patterns [11] for 2-methoxyethanol (3646 and 3614 cm.$^{-1}$, $\Delta\nu$ 32) and 3-methoxypropanol (3646 and 3568 cm.$^{-1}$, $\Delta\nu$ 78). The $\Delta\nu$ values, which are the arithmetical differences between the frequencies for free and bonded hydroxyl groups, reflect the size of the ring formed by intramolecular hydrogen bonding, *e.g.*, for a five-membered ring $\Delta\nu$ *ca.* 30, and for a six-membered ring *ca.* 80. The absorption at 3644 cm.$^{-1}$ for 1,3-*O*-benzylidene-L-erythritol may be assigned to free hydroxyl groups. An intramolecular hydrogen bond forming a five-membered ring may be associated with the absorption at 3614 cm.$^{-1}$ ($\Delta\nu$ 30) and probably involves the primary hydroxyl group and the neighbouring ring-oxygen atom. In view of the results discussed above, bonding of the secondary hydroxyl group to the ring-oxygen atoms may also occur in a suitable conformation but would do so only

[9] Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44.
[10] Buck, Foster, Labib, and Webber, unpublished result.
[11] Foster, Haines, and Stacey, *Tetrahedron*, 1961, **16**, 177.

to a limited extent. The absorption at 3565 cm.$^{-1}$ ($\Delta\nu$ 79) can be assigned to a hydrogen bond forming a six-membered ring and clearly involves the primary and secondary hydroxyl groups. The greater acidity of the primary hydroxyl group makes it likely that it is bonded to the oxygen atom of the secondary hydroxyl group (cf. the results of Cole and Jefferies [7]).

The spectrum for 1,3-*O*-benzylidene-L-threitol (Fig. 1b) showed four absorptions which may be assigned as follows: 3644 cm.$^{-1}$, free hydroxyl groups; 3623 cm.$^{-1}$ ($\Delta\nu$ 21), primary hydroxyl group bonded to neighbouring ring-oxygen atom; 3590 cm.$^{-1}$ ($\Delta\nu$ 54), secondary hydroxyl group bonded to ring-oxygen atoms (the $\Delta\nu$ value here is probably artificially large since it relates to the absorption for free hydroxyl groups at 3644 cm.$^{-1}$ which is most likely that for the primary hydroxyl groups); *ca.* 3545 cm.$^{-1}$ ($\Delta\nu$ 99), primary hydroxyl group bonded to the oxygen atom of the secondary hydroxyl group. The

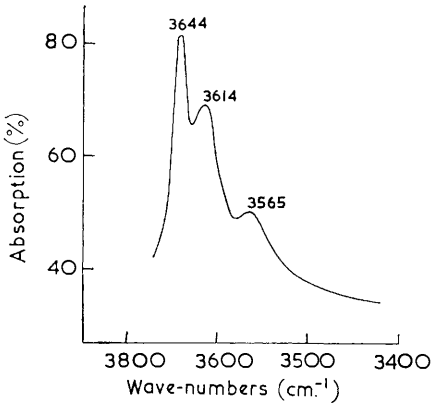


FIG. 1a.

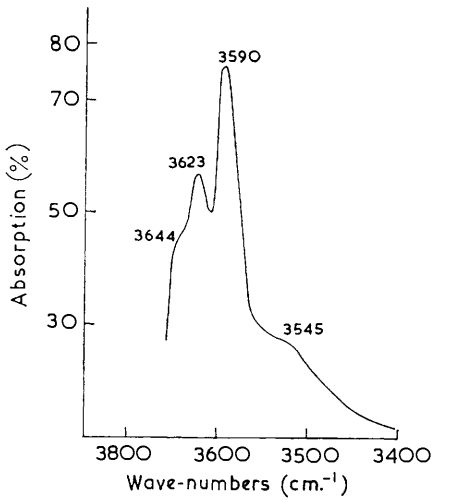


FIG. 1b.

Infrared spectra of 1,3-*O*-benzylidene-L-erythritol (*a*) and 1,3-*O*-benzylidene-L-threitol (*b*) obtained on *ca.* 0·005M-solutions in CCl_4.

large $\Delta\nu$ value associated with the last absorption may arise because the secondary hydroxyl group is bonded to the ring-oxygen atoms which would make its oxygen atom more basic and hence a better proton-acceptor and would also orient the secondary hydroxyl in a position suitable for bonding of its oxygen atom to the primary hydroxyl group.

EXPERIMENTAL

1,5-*Dideoxy*-2,4-O-*methyleneribitol*.—A solution of 2,4-*O*-methylene-1,3,5-tri-*O*-toluene-*p*-sulphonylribitol [2] (11 g., m. p. 125—126°) in tetrahydrofuran (200 ml.) was boiled under reflux with lithium aluminium hydride (8 g.) for 24 hr. The excess of reducing agent was then decomposed in the cooled solution by addition of ethyl acetate, and the alkoxides by the addition of water. The inorganic precipitate was dissolved by addition of Rochelle salt, and the solution was exhaustively extracted with ether. The dried ($MgSO_4$) extract was concentrated and the residue sublimed at 85—90°/~12 mm. Recrystallisation of the sublimate from ether–light petroleum (b. p. 60—80°) gave 1,5-*dideoxy*-2,4-O-*methyleneribitol* (1·7 g.), m. p. 94—95° (Found: C, 55·5; H, 9·2. $C_6H_{12}O_3$ requires C, 55·3; H, 9·1%). The compound volatilised on exposure to the atmosphere.

Toluene-*p*-sulphonylation in the usual way gave 1,5-dideoxy-2,4-*O*-methylene-3-*O*-toluene-*p*-sulphonylribitol, m. p. 65°. Hann and Hudson [2] record m. p. 64° for the same compound obtained by reduction of 1,5-dideoxy-1,5-di-iodo-2,4-*O*-methylene-3-*O*-toluene-*p*-sulphonylribitol.

1,3-O-*Ethylidene*-L-*erythritol*.—(*a*) A solution of 4,6-*O*-ethylidene-D-glucose [12] (20 g.; m. p. 175—177°), sodium metaperiodate (42 g.), and sodium hydrogen carbonate (16 g.) in water (500 ml.) was stored at room temperature for 2 hr. The solvent was then evaporated under diminished pressure and temperature and the residue was extracted with ethyl acetate. The syrupy 2,4-*O*-ethylidene-D-erythrose obtained on concentration of the extract was dissolved in water (100 ml.) containing concentrated aqueous ammonia (0·8 ml.) and hydrogenated at 100°/100 atm. in the presence of Raney nickel (3 g.). The cooled mixture was filtered through charcoal and evaporated and the residue sublimed at 115—120°/~12 mm. to yield 1,3-*O*-ethylidene-L-erythritol, m. p. 98—100°, $[\alpha]_D$ −52° (*c* 2·0 in H_2O), $[M]_D$ −77° (Found: C, 48·4; H, 8·2. Calc. for $C_6H_{12}O_4$ C, 48·6; H, 8·1%).

(*b*) After oxidation of 4,6-*O*-ethylidene-D-glucose (20 g.) as in (*a*) the solution was filtered and treated with saturated aqueous barium chloride till no further precipitation occurred. Insoluble material was removed and the filtrate was treated with sodium borohydride (2·5 g.) and with a further amount (0·5 g.) after 3 hr. After a further 6 hr. the pH of the solution was adjusted to 6·5—7 and the solution then basified with ammonia. The filtered solution was passed through a column (3 × 20 cm.) of Ultrasorb.[13] Elution with water removed inorganic material and subsequent elution with 50% aqueous alcohol removed the cyclic acetal. Concentration of the eluate and recrystallisation of the residue from ether–light petroleum (b. p. 40—60°) gave 1,3-*O*-ethylidene-L-erythritol (9 g.), m. p. 99·5—100°, $[\alpha]_D$ −52° (*c* 2·0 in H_2O), $[M]_D$ −77°.

When this work was complete, Barker and MacDonald [14] described 1,3-*O*-ethylidene-L-erythritol, m. p. 99·5—100·5°, $[\alpha]_D$ −54·7° in H_2O, obtained by a different procedure.

1,3-*O*-Ethylidene-L-erythritol was readily converted by conventional methods into the following derivatives: *di*-O-*acetate*, m. p. 35—36° [from light petroleum (b. p. 60—80°)], $[\alpha]_D$ −62° (*c* 1·5 in $CHCl_3$); $[M]_D$ −144° (Found: C, 51·5; H, 6·9. $C_{10}H_{16}O_6$ requires C, 51·7; H, 6·9%); *di*-O-*toluene*-p-*sulphonate*, m. p. 71—72° (from methanol), $[\alpha]_D$ −33·5° (*c* 1·0 in $CHCl_3$), $[M]_D$ −154° (Found: C, 52·5; H, 5·5. $C_{20}H_{24}O_8S_2$ requires C, 52·6; H, 5·2%); *di*-O-*methanesulphonate*, m. p. 85—86° (from methanol), $[\alpha]_D$ −44° (*c* 1·2 in $CHCl_3$), $[M]_D$ −134° (Found: C, 31·8; H, 5·3; S, 21·1. $C_8H_{16}O_8S_2$ requires C, 31·6; H, 5·3; S. 21·1%).

4-*Deoxy*-1,3-O-*ethylidene*-L-*erythritol*.—A suspension of 1,3-*O*-ethylidene-2,4-di-*O*-methanesulphonyl-L-erythritol (10 g.) in ether (70 ml.) and benzene (10 ml.) was treated dropwise with a slurry of lithium aluminium hydride (4·5 g.) in ether (50 ml.). The mixture was boiled under reflux for 12 hr. and a further amount of reductant (2 g.) added. After a further 24 hr. the excess of reductant in the cooled solution was destroyed with ethyl acetate and the alkoxides by the addition of water. The insoluble material was collected and washed with ether and the combined and dried (Na_2SO_4) filtrate and washings were concentrated. The residue was distilled at 46—49°/0·5 mm. to yield the *product* (2·3 g.) as a colourless oil which crystallised on storage, then having m. p. 24—25°, $[\alpha]_D$ −30·5° (*c* 1·0 in $CHCl_3$), $[M]_D$ −40° (Found: C, 54·8; H, 9·4. $C_6H_{12}O_3$ requires C, 54·5; H, 9·15%).

Acetal Exchange on 1,3-O-*Ethylidene*-2,4-*di*-O-*toluene*-p-*sulphonyl*-L-*erythritol*.—Hydrogen chloride was bubbled through a mixture of 1,3-*O*-ethylidene-2,4-di-*O*-toluene-*p*-sulphonyl-L-erythritol (3 g.) and freshly distilled benzaldehyde (50 ml.) which was then kept at 100—110° for 1 hr. The cooled, partially crystalline mixture was poured into methanol (400 ml.), and the product was collected and washed successively with methanol (200 ml.), water, and methanol (100 ml.). Recrystallisation of the product from benzene–chloroform gave 1,3-*O*-benzylidene-2,4-di-*O*-toluene-*p*-sulphonyl-L-erythritol (3·2 g., 92%), m. p. 185° (decomp.), $[\alpha]_D$ −49° (*c* 1·0 in $CHCl_3$), $[M]_D$ −210°. The m. p. was not depressed on admixture with the product obtained by toluene-*p*-sulphonylation of 1,3-*O*-benzylidene-L-erythritol,[4] and the infrared spectra (KCl discs) of the two di-*O*-toluene-*p*-sulphonates were indistinguishable.

Graded Acidic Hydrolysis of 1,3:2,5:4,6-*Tri*-O-*methylene*-D-*mannitol*.—A mixture of 1,3:2,5:4,6-tri-*O*-methylene-D-mannitol [15] (200 g.; m. p. 230—232°), concentrated hydrochloric acid (300 ml.), and water (300 ml.) was boiled under reflux for 4·5 hr. The solution was concentrated (to *ca.* 200 ml.) at 80° (bath)/13 mm. and unchanged starting material was removed. The filtrate was diluted with water (200 ml.) and neutralised with sodium hydrogen carbonate.

[12] Helferich and Appel, *Ber.*, 1931, **64**, 1841.
[13] Hughes and Whelan, *Chem. and Ind.*, 1958, 1228.
[14] Barker and MacDonald, *J. Amer. Chem. Soc.*, 1960, **82**, 2301.
[15] Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 138.

After storage at 0° for 3 hr. the filtered solution was concentrated to a thick syrup which was extracted with pyridine, leaving D-mannitol and inorganic material. The solvent was removed from the pyridine extract, the residue was dissolved in water (200 ml.), and the solution was continuously extracted with ether for 3 days. Concentration of the extract and recrystallisation of the residue from ethanol–ether gave 1,3:4,6-di-*O*-methylene-D-mannitol (11 g.), m. p. 207—208°, which readily gave a *di*-O-*acetate*, m. p. 163—164° (Found: C, 49·8; H, 6·15. $C_{12}H_{18}O_4$ requires C, 49·7; H, 6·25%).

The aqueous layer remaining from the ether-extraction above was concentrated to dryness. The residue was dissolved in the minimum volume of the organic phase of a butanol–ethanol–water (4 : 1 : 5) solvent system. The crude D-mannitol (*ca.* 30 g.) which crystallised on storage of the cooled solution was removed, half of the filtrate was added to a column (4·5 × 50 cm.) of powdered cellulose, and the column was eluted with the same solvent system. Fractions (50 ml.) were examined by polarimetry and paper chromatography (detection with alkaline silver nitrate [16]). 1,3:4,6-Di-*O*-methylene-D-mannitol was eluted first, followed by a monomethylene-D-mannitol contaminated with components of lower R_F value. Fractions containing the monomethylene compound were combined and concentrated, and the residue was thrice recrystallised from ethanol–water, to yield 3,4-*O*-methylene-D-mannitol [5] (7 g.), m. p. 125—126°, $[\alpha]_D$ +40·5° (*c* 1·0 in H_2O); the m. p. on admixture with 1,3-*O*-methylene-D-mannitol was depressed 15°.

Oxidation of 3,4-O-*Methylene*-D-*mannitol with Periodate.*—3,4-*O*-Methylene-D-mannitol (20 g.; contaminated with a small amount of 1,3:4,6-di-*O*-methylene-D-mannitol) was oxidised with sodium metaperiodate (45 g.), and the product was reduced with sodium borohydride (2·5 g.) by essentially the method of MacDonald *et al.*[17] After destruction of the excess of borohydride the solution was evaporated to dryness, and the residue was extracted with 1 : 1 ethyl acetate–ethanol (200 ml.). The filtered extract was concentrated and a portion (0·5 g.) of the residue (9 g.) was treated with pyridine (20 ml.) and methanesulphonyl chloride (2 ml.) at room temperature. The product was isolated in the usual manner, yielding 1,4-*di*-O-*methanesulphonyl*-3,4-O-*methylene*-D-*threitol* (0·35 g., 32%), m. p. 94—95° (from ethyl acetate), $[\alpha]_D$ +25° (*c* 0·8 in $CHCl_3$), $[M]_D$ +72° (Found: C, 29·0; H, 4·8; S, 22·4. $C_7H_{14}O_8S_2$ requires C, 29·0; H, 4·9: S, 22·1%).

2,4-*Di*-O-*methanesulphonyl*-1,3-O-*methylene*-L-*erythritol.*—(*a*) 1,3-*O*-Ethylidene-2,4-di-*O*-methanesulphonyl-L-erythritol (6 g.) and paraformaldehyde (6 g.) were shaken with benzene (50 ml.) containing concentrated sulphuric acid (3 ml.) for 4 hr. The acid was neutralised with potassium carbonate; chloroform (300 ml.) and water (300 ml.) were added and the well-shaken mixture was filtered through charcoal. The separated chloroform solution was washed thoroughly with water, dried ($CaCl_2$), and concentrated. Recrystallisation of the residue from ethyl acetate gave 2,4-*di*-O-*methanesulphonyl*-1,3-O-*methylene*-L-*erythritol* (3·5 g., 61%), m. p. 117—118°, $[\alpha]_D$ −43° (*c* 0·8 in $CHCl_3$), $[M]_D$ −125° (Found: C, 29·3; H, 4·85; S, 22·1. $C_7H_{14}O_8S_2$ requires C, 29·0; H, 4·9; S, 22·1%).

(*b*) 1,3-*O*-Ethylidene-2,4-di-*O*-methanesulphonyl-L-erythritol (5 g.) and paraformaldehyde (8 g.) were heated with concentrated hydrochloric acid (60 ml.) at 100—110° for 30 min. The solution was then stored at 0°, and the product which separated was collected, washed with water, and recrystallised from ethyl acetate to yield 2,4-di-*O*-methanesulphonyl-1,3-*O*-methylene-L-erythritol (4·2 g., 86%), m. p. 117·5—118° alone or in admixture with the product from (*a*).

4-*Deoxy*-1,3-O-*methylene*-L-*erythritol.*—A solution of 2,4-di-*O*-methanesulphonyl-1,3-*O*-methylene-L-erythritol (7 g.) in ether (50 ml.) and benzene (10 ml.) was treated with a slurry of lithium aluminium hydride (4 g.) in ether (10 ml.). The mixture was boiled under reflux for 12 hr., more reductant (1 g.) was then added, and boiling was continued for 24 hr. The product was isolated as described above for the benzylidene analogue and obtained as a colourless oil (2 g.), b. p. 62—64°/0·8 mm., which possessed a strong thiol-type odour. It was purified by conversion into the *p*-phenylazobenzoate.

A solution of the impure product (1·18 g.) in pyridine (15 ml.) was treated with *p*-phenylazobenzoyl chloride (2·67 g.), and the product isolated by the method previously described; [18] 4-*deoxy*-1,3-O-*methylene*-2-O-p-*phenylazobenzoyl*-L-*erythritol* (2·5 g., 77%), m. p. 114—115°

[16] Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444.
[17] MacDonald, Fischer, and Ballou, *J. Amer. Chem. Soc.*, 1956, **78**, 3720.
[18] Baggett, Haines, Foster, and Stacey, *J.*, 1960, 3528.

(from ethanol), was obtained (Found: C, 65·9; H, 5·45; N, 8·8. $C_{18}H_{18}N_2O_4$ requires C, 66·2; H, 5·6; N, 8·6%).

The ester (2·2 g.) was treated with a boiling solution of potassium hydroxide (2·5 g.) in ethanol (100 ml.) for 5 hr. The mixture was then stored at 0° for 2 hr., then filtered, and the filtrate concentrated. The residue was dissolved in water (50 ml.), and the solution was extracted continuously with chloroform for 12 hr. The dried ($CaSO_4$) extract was concentrated and the residue was distilled, to yield 4-*deoxy*-1,3-O-*methylene*-L-*erythritol* (0·72 g., 91%) b. p. 48—50°/0·5 mm. (Found: C, 50·8; H, 8·5. $C_5H_{10}O_3$ requires C, 50·85; H, 8·5%).

Infrared Spectra.—Details of the determination of the infrared spectra in the hydroxyl stretching region are described in the preceding paper.

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