113. *Dithiols. Part VII. 5 : 6-Sorbitoleen and 1 : 2-Mannitoleen as Intermediates for the Preparation of Dithiols.**

By PETER BLADON and L. N. OWEN.

By the action of sodium iodide, in acetone solution, on 5 : 6-ditosyl or 5 : 6-*dimethanesulphonyl* 1 : 3-2 : 4-*diethylidene sorbitol,* 1 : 3-2 : 4-*diethylidene* 5 : 6-*sorbitoleen* is obtained (cf. Hann, Ness, and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 73); similarly 5 : 6-*dimethanesulphonyl* 1 : 2-3 : 4-*di*iso*propylidene mannitol* gives 1 : 2-3 : 4-*di*iso*propylidene* 5 : 6-*mannitoleen.* Removal of the protecting groups by acid hydrolysis then yields 5 : 6-*sorbitoleen* and 1 : 2-mannitoleen. Acetylation, followed by addition of bromine and reaction of the *dibromides* with potassium thiolacetate, gives the hexa-acetyl 5 : 6-dithiohexitols as mixtures of stereoisomers.

Addition of hypobromous acid to the tetra-acetates of 5 : 6-sorbitoleen and 1 : 2-mannitoleen, followed by reaction with sodium acetate, gives hexa-acetyl L-iditol and hexa-acetyl D-sorbitol respectively, and thus provides a new method for the interconversion of hexitols.

EXPERIMENTS directed towards the synthesis of hydroxy-dithiols of the general formula $HO{\cdot}CH_2{\cdot}[CH(OH)]_n{\cdot}CH(SH){\cdot}CH_2{\cdot}SH$ have been described where $n = 0$ (Stocken, *J.*, 1947, 592), and where $n = 1$ and 2 (Evans, Fraser, and Owen, *J.*, 1949, 248). For the synthesis of the corresponding compound where $n = 3$, an unsaturated alcohol $HO{\cdot}CH_2{\cdot}[CH(OH)]_3{\cdot}CH{:}CH_2$ was required, and our attention was therefore directed towards the preparation of the hexitol derivatives, 1 : 2-mannitoleen and 5 : 6-sorbitoleen.

It has been known for some time that there are exceptions to Oldham and Rutherford's rule (*J. Amer. Chem. Soc.*, 1932, **54**, 366) in that secondary toluene-*p*-sulphonyl derivatives in the carbohydrate field will, in certain cases, react with sodium iodide in acetone solution. For example, both the tosyloxy-groups in 2 : 5-ditosyl 1 : 4-3 : 6-dianhydromannitol (Hockett, Fletcher, Goepp, and Sheffield, *ibid.*, 1946, **68**, 930), and one in 2 : 5-ditosyl 1 : 4-3 : 6-dianhydrosorbitol (*idem, ibid.*, p. 927) react with the reagent at 120° (see also Folkers *et al.*, *ibid.*, 1948, **70**, 2325; Tipson, Clapp, and Cretcher, *J. Org. Chem.*, 1947, **12**, 133). Of particular interest is the behaviour of vicinal tosyloxy-groups; Levene and Mehltretter (*Enzymologia*, 1937, **4**, ii, 232) found that when tritosyl glycerol was heated with sodium iodide in acetone all the groups were displaced, with the formation of an unsaturated compound, free iodine, and sodium toluene-*p*-sulphonate. Similar results were obtained by using tetratosyl erythritol (Tipson and Cretcher, *J. Org. Chem.*, 1943, **8**, 95), and in this case the unsaturated product was butadiene. More recently, Karrer, Schick, and Schwyzer (*Helv. Chim. Acta*, 1948, **31**, 784) have shown that the ditosyl derivatives of glyceraldehyde and of its acetal give acraldehyde.

In the hexitol series, a similar reaction was first observed by Hann, Ness, and Hudson (*loc. cit.*), who briefly reported that heating of 5 : 6-ditosyl 1 : 2-3 : 4-dibenzylidene sorbitol with sodium iodide in acetone at 100° resulted in precipitation of sodium toluene-*p*-sulphonate, liberation of iodine, and formation of 1 : 2-3 : 4-dibenzylidene 5 : 6-sorbitoleen. At the time of this publication, the exact nature of the linking of the benzylidene residues in the parent compound was uncertain, but in view of later work (Angyal and Lawler, *J. Amer. Chem. Soc.*, 1944, **66**, 837) the unsaturated compound must be formulated as 1 : 3-2 : 4-dibenzylidene 5 : 6-sorbitoleen (I).

The first stage in the reaction is undoubtedly the replacement of the primary tosyloxy-group by iodine. It is possible that the resulting intermediate product, containing a secondary tosyloxy-group and an iodine atom on adjacent carbon atoms, is unstable and breaks down directly to the unsaturated compound; more probably, however, the secondary tosyloxy-group in this intermediate undergoes replacement to form the vicinal di-iodide, a type of compound which is known to be unstable, and which then loses iodine in the usual way:

$$R{\cdot}CH(OTs){\cdot}CH_2{\cdot}OTs \longrightarrow R{\cdot}CH(OTs){\cdot}CH_2I \longrightarrow R{\cdot}CHI{\cdot}CH_2I \longrightarrow R{\cdot}CH{:}CH_2$$

In utilising this reaction for the preparation of 5 : 6-sorbitoleen, 1 : 3-2 : 4-diethylidene sorbitol was converted into 5 : 6-ditosyl 1 : 3-2 : 4-diethylidene sorbitol (II) (Wiggins, *J.*, 1946, 388; Sullivan, *J. Amer. Chem. Soc.*, 1945, **67**, 837), which reacted readily with sodium iodide in acetone at 100° and gave 1 : 3-2 : 4-*diethylidene* 5 : 6-*sorbitoleen* (III); the same product was also obtained from 5 : 6-*dimethanesulphonyl* 1 : 3-2 : 4-*diethylidene sorbitol* under the same conditions. Removal of the ethylidene residues from (III) by acid hydrolysis gave 5 : 6-*sorbitoleen* (IV) as a viscous liquid which could be distilled in high vacuum without decomposition; the overall yield from ditosyl diethylidene sorbitol was 70—80%. On

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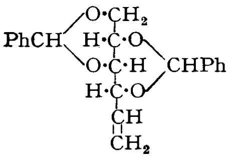
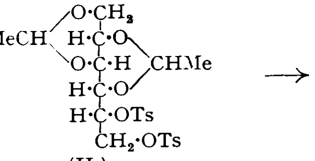
* A preliminary note on part of this work appeared in *Nature*, 1949, **163**, 140.

acetylation, with acetic anhydride and sodium acetate, it gave crystalline *tetra-acetyl* 5 : 6-*sorbitoleen* (V), which took up bromine in carbon tetrachloride solution and gave a *dibromide*, which partly crystallised.

The addition of bromine to (V) can theoretically give two products, (VI) and (VII), and the solid isomer must correspond to one of these formulæ, the other being present in the liquid portion. There is, however, no means of deciding which formula should be allocated to a particular isomer. The liquid and the crystalline substance were separately treated with potassium thiolacetate in boiling ethanol; both yielded syrups, but that derived from the crystalline dibromide slowly deposited a solid *hexa-acetyl* 5 : 6-*dithiohexitol*, (VIII) or (IX). In the reaction of the dibromides with potassium thiolacetate, partial epimerisation occurs on $C_{(5)}$; the solid product, therefore, does not necessarily possess the same (unknown) configuration as the crystalline dibromide. Deacetylation of the combined thiolacetate syrups with methanolic barium methoxide gave a crude barium salt of the 5 : 6-dithiohexitol (X).


(I.)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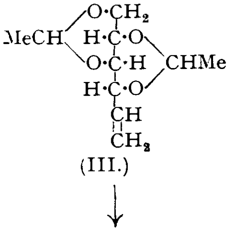
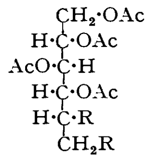

(III.)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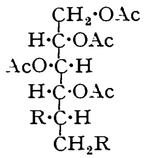
(VI; R = Br.)
(VIII; R = SAc)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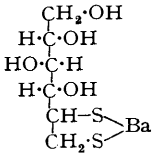
(VII; R = Br.)
(IX; R = SAc.)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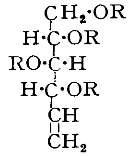
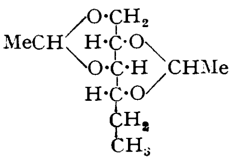
(X.)


$$\begin{array}{c} \mathrm{CH_2\cdot OR} \\ \mathrm{H\cdot C\cdot OR} \\ \mathrm{RO\cdot C\cdot H} \\ \mathrm{H\cdot C\cdot OR} \\ \mathrm{CH} \\ \| \\ \mathrm{CH_2} \end{array}$$
(IV; R = H.)
(V; R = Ac.)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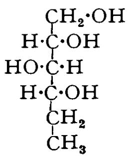
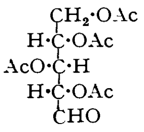
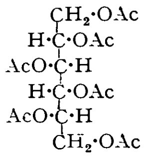
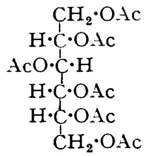

$$\begin{array}{c} \mathrm{CH_2\cdot OH} \\ \mathrm{H\cdot C\cdot OH} \\ \mathrm{HO\cdot C\cdot H} \\ \mathrm{H\cdot C\cdot OH} \\ \mathrm{CH_2} \\ \mathrm{CH_3} \end{array}$$
(XII.)


$$\begin{array}{c} \mathrm{CH_2\cdot OAc} \\ \mathrm{H\cdot C\cdot OAc} \\ \mathrm{AcO\cdot C\cdot H} \\ \mathrm{H\cdot C\cdot OAc} \\ \mathrm{CHO} \end{array}$$
(XIII.)


$$\begin{array}{c} \mathrm{CH_2\cdot OAc} \\ \mathrm{H\cdot C\cdot OAc} \\ \mathrm{AcO\cdot C\cdot H} \\ \mathrm{H\cdot C\cdot OAc} \\ \mathrm{AcO\cdot C\cdot H} \\ \mathrm{CH_2\cdot OAc} \end{array}$$
(XIV.)


$$\begin{array}{c} \mathrm{CH_2\cdot OAc} \\ \mathrm{H\cdot C\cdot OAc} \\ \mathrm{AcO\cdot C\cdot H} \\ \mathrm{H\cdot C\cdot OAc} \\ \mathrm{H\cdot C\cdot OAc} \\ \mathrm{CH_2\cdot OAc} \end{array}$$
(XV.)

Several other reactions were carried out on derivatives of 5 : 6-sorbitoleen. Hydrogenation of 1 : 3-2 : 4-diethylidene 5 : 6-sorbitoleen (III) over Raney nickel gave 1 : 3-2 : 4-*diethylidene* 5 : 6-*dideoxysorbitol* (XI), from which 5 : 6-*dideoxysorbitol* (XII) (*tetra-acetate*) was obtained by acid hydrolysis. Ozonolysis of tetra-acetyl 5 : 6-sorbitoleen (V) afforded a small yield of tetra-acetyl *aldehydo*-L-xylose (XIII) (cf. Major and Cook, *J. Amer. Chem. Soc.*, 1936, **58**, 2474; Wolfrom *et al.*, *ibid.*, 1931, **53**, 4379; 1944, **66**, 204). It was also possible to convert (V) into hexa-acetyl L-iditol; reaction of the unsaturated compound with *N*-bromosuccinimide in water and ether (a convenient source of hypobromous acid; see Raphael, *J.*, 1949, S 44) gave a non-crystalline bromohydrin of uncertain structure, and probably consisting of a mixture of isomers. This, on being heated with sodium acetate in acetic anhydride and acetic acid, gave a syrup from which hexa-acetyl L-iditol (XIV) was obtained in crystalline form; the yield was low, but no evidence was found of the presence of hexa-acetyl sorbitol (XV), the other possible product. Hexa-acetyl L-iditol was also obtained by treatment of the crystalline tetra-acetyl sorbitoleen dibromide, (VI) or (VII), with potassium acetate; this, however, does not prove the configuration of the original dibromide.

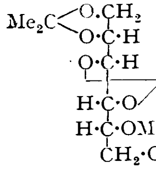
For the preparation of 1 : 2-mannitoleen and its derivatives the starting material was 1 : 2-3 : 4-di*iso*propylidene mannitol (Wiggins, *J.*, 1946, 13). Treatment with methanesulphonyl chloride in pyridine gave crystalline 5 : 6-*dimethanesulphonyl* 1 : 2-3 : 4-*di*iso-*propylidene mannitol* (XVI); the corresponding 5 : 6-*ditosyl* compound was a liquid. When (XVI) was heated in acetone solution with sodium iodide, it gave 1 : 2-3 : 4-*di*iso*propylidene* 5 : 6-*mannitoleen* (XVII) as a mobile liquid. In the distillation of the crude reaction product, free iodine was liberated, indicating the presence of an iodine-containing compound, comparatively stable at moderate temperatures, but broken down when more strongly heated. Furthermore, from the non-volatile residue a small quantity of a water-soluble solid was obtained, which was identified as 1 : 2(or 5 : 6)-mannitoleen (XVIII). The mechanism of the formation of this compound, which involves the loss of the *iso*propylidene residues, is obscure; it appears that it must be produced during the distillation, since it is practically insoluble in chloroform and would not have been extracted from aqueous solution by this solvent during the working-up process. It was obtained in good yield from the di*iso*propylidene compound by acid hydrolysis, the overall yield from the dimethanesulphonyl derivative being 45%.

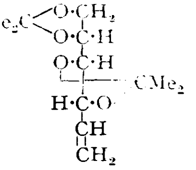
Acetylation of 1 : 2-mannitoleen gave the crystalline tetra-acetate, which reacted with bromine in carbon tetrachloride to give a solid dibromide, which was separated by fractional crystallisation into two *isomers*, m. p.s 111—112° and 76°. The optical rotations of these were almost identical, which suggested that they were polymorphic forms of the same substance, but a mixture of them melted over the range between their individual m. p.s and it was not possible to convert one form into the other. They must therefore be the structural isomers (XIX) and (XX), although there is no means of deciding the individual allocation of formulæ.

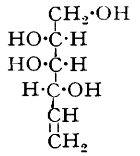
Treatment of both dibromides with potassium thiolacetate in boiling ethanol gave the hexa-acetyl 5 : 6-dithiohexitols, presumably mixtures of (XXI) and (XXII).

Tetra-acetyl 1 : 2-mannitoleen reacted with hypobromous acid to give a liquid bromohydrin, which on treatment with sodium acetate gave hexa-acetyl D-sorbitol (XV); none of the other possible product (hexa-acetyl D-mannitol) was encountered.

Unsuccessful attempts were made to prepare an unsaturated compound from 3 : 4-ditosyl 1 : 2-5 : 6-di*iso*propylidene mannitol and from 3 : 4-*dimethanesulphonyl* 1 : 2-5 : 6-*di*iso*propylidene mannitol* (XXIII). When these compounds were heated with sodium iodide in acetone at 110°, the sodium sulphonate was obtained in theoretical yield, and iodine was liberated, but none of the expected material could be isolated. Possibly the *iso*propylidene residues were eliminated during the reaction.

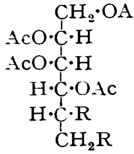

(XVI.) (Ms = Me·SO$_2$.)


(XVII.)



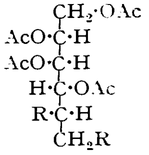
$$\begin{array}{c}\mathrm{CH_2{\cdot}OH}\\ \mathrm{HO{\cdot}C{\cdot}H}\\ \mathrm{HO{\cdot}C{\cdot}H}\\ \mathrm{H{\cdot}C{\cdot}OH}\\ \mathrm{CH}\\ \| \\ \mathrm{CH_2}\end{array}$$

(XVIII.)



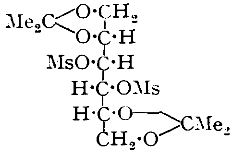
$$\begin{array}{c}\mathrm{CH_2{\cdot}OAc}\\ \mathrm{AcO{\cdot}C{\cdot}H}\\ \mathrm{AcO{\cdot}C{\cdot}H}\\ \mathrm{H{\cdot}C{\cdot}OAc}\\ \mathrm{H{\cdot}C{\cdot}R}\\ \mathrm{CH_2R}\end{array}$$

(XIX; R = Br.)
(XXI; R = SAc.)



$$\begin{array}{c}\mathrm{CH_2{\cdot}OAc}\\ \mathrm{AcO{\cdot}C{\cdot}H}\\ \mathrm{AcO{\cdot}C{\cdot}H}\\ \mathrm{H{\cdot}C{\cdot}OAc}\\ \mathrm{R{\cdot}C{\cdot}H}\\ \mathrm{CH_2R}\end{array}$$

(XX; R = H.)
(XXII; R = SAc.)


(XXIII.)

Since the completion of this work, Karrer and Davis (*Helv. Chim. Acta*, 1948, **31**, 1611) have reported experiments on the preparation of 1 : 2-mannitoleen from 1 : 2-3 : 4-di*iso*-propylidene mannitol by a method similar to that described above. Their results (with the ditosyl compound), however, differ in some respects from those obtained by us with the dimethanesulphonyl derivative. They found that treatment with sodium iodide in acetone gave 1 : 2-mannitoleen directly, and they failed to isolate the di*iso*propylidene compound, which was the main product in our experiments. Furthermore, the direct yield from the ditosyl di*iso*propylidene mannitol is only half of the overall yield obtained from the dimethane-sulphonate.

EXPERIMENTAL.

5 : 6-*Ditosyl* 1 : 3-2 : 4-*Diethylidene Sorbitol*.—1 : 3-2 : 4-Diethylidene sorbitol (Bladon and Owen, preceding paper) (47 g.) in dry pyridine (250 c.c.) was treated with a solution of toluene-*p*-sulphonyl chloride (80 g., 2·1 mols.) in pyridine (160 c.c.) with cooling, and then set aside at room temperature for 21 hours. Addition of water (1500 c.c.) precipitated a solid, which was washed with water and with ethanol. This ditosyl derivative (45 g.), m. p. 169—170°, was sufficiently pure for most purposes;

further recrystallisation from acetone–ethanol raised the m. p. to 170—172°, $[\alpha]_D^{21}$ $-12{\cdot}0°$ (*c*, 1·7 in chloroform). Wiggins (*loc. cit.*) gives m. p. 173°, $[\alpha]_D$ $-12{\cdot}6°$; Sullivan (*loc. cit.*) gives m. p. 172°, $[\alpha]_D^{23}$ $-12{\cdot}8°$. It was obtained only as a by-product by these workers.

5 : 6-*Dimethanesulphonyl* 1 : 3-2 : 4-*Diethylidene Sorbitol*.—1 : 3-2 : 4-Diethylidene sorbitol (4·7 g.) was added slowly to a cooled solution of methanesulphonyl chloride (5·8 g.) in dry pyridine (12 c.c.). The mixture was set aside at 0° overnight and then diluted with water, which precipitated a viscid oil; a portion crystallised on trituration with methanol, and the main bulk was then seeded. The solid was well washed with water and recrystallised from methanol to give irregular prisms of the *dimethanesulphonate* (5·4 g.), m. p. 152—153°, $[\alpha]_D^{21}$ $-5{\cdot}2°$ (*c*, 1·0 in chloroform) (Found : C, 37·0; H, 6·3; S, 16·3. $C_{12}H_{22}O_{10}S_2$ requires C, 36·9; H, 5·7; S, 16·4%).

1 : 3-2 : 4-*Diethylidene* 5 : 6-*Sorbitoleen*.—(i) The ditosyl compound (41 g.), anhydrous sodium iodide (90 g.), and pure acetone (600 c.c.) were heated in a pressure bottle at 100° for 6 hours. The precipitated sodium toluene-*p*-sulphonate (29·5 g., 100%) was filtered off from the cooled reaction product, and well washed with cold acetone. The dark brown filtrate was evaporated to small bulk, and the residue was shaken with a solution of sodium thiosulphate (37·5 g.) in water (250 c.c.) to remove free iodine. The solution was then extracted with chloroform (4 × 50 c.c.); evaporation of the dried (Na_2SO_4) extracts gave a solid residue (15·4 g.), which on recrystallisation from ethyl acetate gave needles (10·9 g., 73%) of 1 : 3-2 : 4-*diethylidene* 5 : 6-*sorbitoleen*, m. p. 120—122°, raised on further recrystallisation to 122—123°, $[\alpha]_D^{21}$ $-23{\cdot}8°$ (*c*, 1·1 in chloroform) (Found : C, 60·4; H, 7·9. $C_{10}H_{16}O_4$ requires C, 60·05; H, 8·1%).

(ii) Similar treatment of 5 : 6-dimethanesulphonyl 1 : 3-2 : 4-diethylidene sorbitol (1·95 g.) with sodium iodide (6·0 g.) in acetone (40 c.c.) for 6 hours at 100° gave sodium methanesulphonate (1·6 g., 100%), and, from the chloroform extracts, 1 : 3-2 : 4-diethylidene 5 : 6-sorbitoleen (1·0 g.), which on recrystallisation from ethyl acetate formed needles (0·6 g.), m. p. 122—124°.

5 : 6-*Sorbitoleen*.—1 : 3-2 : 4-Diethylidene 5 : 6-sorbitoleen (15 g.) was heated with N-sulphuric acid (10 c.c.) and water (20 c.c.) at 100° for 11 hours under nitrogen. The cooled solution was then extracted once with ether to remove a small amount of oily impurity, and neutralised by the addition of a slight excess of barium hydroxide solution, followed by treatment with carbon dioxide. After being heated, to assist coagulation of the barium sulphate, it was filtered, the solid being well washed with hot water. Evaporation of the filtrate under reduced pressure gave a syrup, which was taken up in hot ethanol (50 c.c.), treated with charcoal, filtered, and evaporated to yield 5 : 6-*sorbitoleen* (10·8 g.), a small portion of which was distilled at 100—130° (air-bath)/0·0001 mm.; n_D^{19} 1·5068, $[\alpha]_D^{19}$ $+19{\cdot}8°$ (*c*, 3·8 in water) (Found : C, 48·5; H, 8·3. $C_6H_{12}O_4$ requires C, 48·6; H, 8·2%).

Tetra-acetyl 5 : 6-*Sorbitoleen*.—5 : 6-Sorbitoleen (7·4 g.) was heated with acetic anhydride (40 c.c.) and fused sodium acetate (5 g.) for 9 hours on the steam-bath. The solution was then poured into cold water (400 c.c.) and well stirred to decompose the excess of acetic anhydride. The *tetra-acetate* separated as a white solid (12·5 g., 80%), which was collected and recrystallised from aqueous methanol; it formed small prisms, m. p. 57—58·5°, $[\alpha]_D^{21}$ $-13{\cdot}6°$ (*c*, 1·2 in chloroform) (Found : C, 52·8; H, 6·2. $C_{14}H_{20}O_8$ requires C, 53·15; H, 6·4%). Extraction of the aqueous solution with chloroform gave a further quantity (2·6 g.) of the same material.

Reaction of Tetra-acetyl 5 : 6-*Sorbitoleen with Bromine*.—A solution of bromine (8·8 g.) in carbon tetrachloride (40 c.c.) was added to a well-stirred and cooled solution of the tetra-acetate (15·8 g.) in the same solvent (150 c.c.), the temperature being kept at *ca.* 15° during the addition (2 hours) and for a further hour. A small quantity of solid which had separated was taken into solution by addition of a little chloroform, and the solution was washed with sodium hydrogen carbonate containing some sodium thiosulphate, and then with water, dried (Na_2SO_4), and evaporated to a syrup (25·7 g.). This was dissolved in warm ethanol (50 c.c.) and cooled to 0°, whereupon a solid crystallised. After being kept at 0° for 12 hours, it was collected and washed with ethanol (yield, 12·1 g.; m. p. 135—145°); recrystallisation from acetone gave small prisms of the *dibromide*, m. p. 152—154°, $[\alpha]_D^{18}$ $-21{\cdot}4°$ (*c*, 1·3 in chloroform) (Found : C, 35·5; H, 4·4; Br, 33·3. $C_{14}H_{20}O_8Br_2$ requires C, 35·3; H, 4·2; Br, 33·6%).

Evaporation of the ethanolic filtrate gave a syrup (10·4 g.), $[\alpha]_D^{21}$ $+7{\cdot}6°$ (*c*, 12 in chloroform), which contained the stereoisomeric dibromide (Found : Br, 32·0%).

Hexa-acetyl 5 : 6-*Dithiohexitol*.—(*a*) The crystalline dibromide (11·9 g.) and potassium thiolacetate (6·8 g.) were heated under reflux in ethanol (125 c.c.) for 7 hours. Water (250 c.c.) was then added, and the mixture was extracted with ether. Evaporation of the dried (Na_2SO_4) extracts gave a red syrup, which partly crystallised when kept for a week. The solid (3·5 g.; m. p. 86—87°) was freed from oil by trituration with cold methanol; recrystallisation from methanol then gave flat needles of the *hexa-acetyl* 5 : 6-*dithiohexitol*, m. p. 87—89°, $[\alpha]_D^{21}$ $+49{\cdot}4°$ (*c*, 2·8 in chloroform) (Found : C, 46·5; H, 5·9; S, 13·5. $C_{18}H_{26}O_{10}S_2$ requires C, 46·3; H, 5·6; S, 13·7%). Light absorption : max. 2300 A., $\varepsilon = 7900$.

(*b*) The liquid dibromide (9·8 g.), potassium thiolacetate (5·7 g.), thiolacetic acid (0·3 c.c.), and ethanol (40 c.c.) were heated under reflux for 6 hours. The product, isolated as described above, failed to crystallise, and was distilled, to yield the hexa-acetyl dithiohexitol (7·8 g.), b. p. 140—160°/0·001 mm., n_D^{20} 1·4895, $[\alpha]_D^{21}$ $-17{\cdot}8°$ (*c*, 1·5 in chloroform) (Found : C, 47·4; H, 5·8; S, 13·65%). Light absorption : max. 2290 A., $\varepsilon = 5000$.

Deacetylation. The syrupy hexa-acetate (21·3 g.) was dissolved in methanol (250 c.c.) and treated at −20° with 1·07N-methanolic barium methoxide (103 c.c.), air being excluded. The temperature was then allowed to rise to 0°, and stirring continued for a further 45 minutes. The precipitated barium salt was collected, washed with methanol and with ether, and dried under reduced pressure over calcium chloride and finally over phosphoric oxide; yield, 9·3 g. (Found : C, 28·6; H, 5·4; S, 17·6; thiol S, 10·8; Ba, 26·4. $C_6H_{12}O_4S_2Ba$ requires C, 20·6; H, 3·5; S, 18·4; Ba, 39·3%). The analysis, as usual with these compounds, indicated considerable contamination with other products; earlier work has shown that the deacetylation of acetylated polyhydroxy-dithiols does not proceed smoothly (cf. Part III, *J.*, 1949, 248; Part VI, preceding paper).

1 : 3-2 : 4-*Diethylidene* 5 : 6-*Dideoxysorbitol*.—1 : 3-2 : 4-Diethylidene 5 : 6-sorbitoleen (3 g.) in ethyl acetate (35 c.c.) was hydrogenated at ordinary temperature and pressure over Raney nickel catalyst; the filtered solution was then evaporated to a solid residue (3 g.), m. p. 84—86°. Recrystallisation from

light petroleum (b. p. 60—80°) gave 1 : 3-2 : 4-*diethylidene* 5 : 6-*dideoxysorbitol*, m. p. 85—86°, $[\alpha]_D^{2}$ +7·8° (*c*, 1·7 in chloroform) (Found : C, 59·55; H, 8·6. $C_{10}H_{18}O_4$ requires C, 59·4; H, 9·0%).

5 : 6-*Dideoxysorbitol*.—The diethylidene compound (3 g.) was heated on the steam-bath for 7 hours under reflux with methanol (5 c.c.) and 0·45N-sulphuric acid (10 c.c.). The cooled solution was extracted once with ether to remove a trace of oil, and was heated and treated with a slight excess of barium hydroxide solution, the excess then being removed with carbon dioxide. The barium salts were removed by filtration, and well washed with hot water; evaporation of the filtrate under reduced pressure gave a syrup, which was dissolved in warm methanol, filtered, and again evaporated to give 5 : 6-*dideoxysorbitol* (2·2 g.). A small portion, distilled at 150—160°(bath)/0·0001 mm., had n_D^{24} 1·4825, $[\alpha]_D^{21}$ +5·7° (*c*, 2·0 in water) (Found : C, 47·5; H, 9·5. $C_6H_{14}O_4$ requires C, 48·0; H, 9·4%).

Acetylation of 5 : 6-dideoxysorbitol (1·7 g.) with acetic anhydride (15 c.c.) and sodium acetate (1 g.) at 100° for 12 hours, gave *tetra-acetyl* 5 : 6-*dideoxysorbitol* (3·7 g.), b. p. 100—120°/0·0001 mm., n_D^{21} 1·4415, $[\alpha]_D^{21}$ +6·3° (*c*, 2·6 in chloroform) (Found : C, 53·0; H, 7·3. $C_{14}H_{22}O_8$ requires C, 52·8; H, 7·2%).

Tetra-acetyl aldehydo-L-*Xylose*.—Tetra-acetyl 5 : 6-sorbitoleen (0·5 g.) in ethyl acetate (10 c.c.) was treated with a stream of ozonised oxygen at −30° until no more ozone was absorbed. The solution was then shaken with hydrogen, in the presence of Raney nickel (1·5 g.), until no more was absorbed and evaporated under reduced pressure to an oil, which crystallised on the addition of light petroleum (b. p. 40—60°). Recrystallisation from dry ether gave tetra-acetyl *aldehydo*-L-xylose, m. p. 85—87°, $[\alpha]_D^{21}$ +17·6° (*c*, 1·0 in chloroform), which restored the colour to Schiff's reagent. Major and Cook (*loc. cit.*) give m. p. 90—91°, $[\alpha]_D^{20}$ +22·5° (*c*, 2 in absolute chloroform) (cf. also Wolfrom *et al.*, *loc. cit.*).

Hexa-acetyl L-*Iditol*.—(*a*) A solution of tetra-acetyl sorbitoleen (0·53 g.) in ether (5 c.c.) was shaken with *N*-bromosuccinimide (0·35 g.) and water (15 c.c.) overnight. The ethereal layer was separated, the aqueous portion was extracted twice with ether, and the combined extracts were dried (Na_2SO_4) and evaporated. The residue was heated on the steam-bath with acetic anhydride (1·5 c.c.), acetic acid (1·5 c.c.), and sodium acetate (0·5 g.) for 26 hours (a crystalline precipitate of sodium bromide began to appear after 6 hours) and then stirred with water. The solution was extracted thrice with chloroform, and the extracts were washed with aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated to a syrup (0·65 g.), which was dissolved in dry ether containing a little methanol and treated with light petroleum (b. p. 40—60°). Hexa-acetyl L-iditol (0·2 g.) was obtained, m. p. 118—120°, $[\alpha]_D^{22}$ −26·8° (*c*, 1·0 in chloroform). Hann and Hudson (*J. Amer. Chem. Soc.*, 1942, **64**, 925) give m. p. 121—122° (corr.), $[\alpha]_D^{20}$ −25·5° (chloroform); Meyer and Reichstein (*Helv. Chim. Acta*, 1946, **29**, 161) give m. p. 119·5—120·5°, $[\alpha]_D^{19}$ −26·1° ± 2° (*c*, 0·9 in chloroform). Evaporation of the mother-liquors gave a syrup, from which no more solid material could be obtained.

(*b*) The crystalline dibromide of tetra-acetyl 5 : 6-sorbitoleen (0·7 g.; m. p. 152—153°), fused potassium acetate (1·25 g.), acetic acid (7·5 c.c.), and acetic anhydride (2·5 c.c.) were heated on a sand-bath under reflux for 60 hours. The mixture gradually darkened, and a precipitate of potassium bromide slowly appeared. The cooled mixture was then poured into water (40 c.c.) and extracted with chloroform. The extracts were washed with sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated to a syrup. This was dissolved in a little methanol and treated with ether and light petroleum (b. p. 40—60°), whereupon crystals (0·2 g.) gradually separated. Recrystallisation from methanol–ether gave hexa-acetyl L-iditol, m. p. (and mixed m. p. with that obtained by the first method) 118—120°, $[\alpha]_D^{17}$ −26·6° (*c*, 1·2 in chloroform).

5 : 6-*Dimethanesulphonyl* 1 : 2-3 : 4-*Di*iso*propylidene Mannitol*.—To a solution of 1 : 2-3 : 4-di*iso*propylidene mannitol (Wiggins, *J.*, 1946, 13) (7·6 g.) in dry pyridine (18 c.c.) was added a solution of methanesulphonyl chloride (8·6 g.) in pyridine (18 c.c.), the temperature being kept below 20°. The mixture was set aside at 0° for 12 hours and then poured into water (250 c.c.). The precipitated oil crystallised on nucleation with a sample which had been caused to solidify by trituration with methanol. The solid was collected and well washed with water. One recrystallisation from methanol gave 10·65 g., m. p. 117—118°. Further recrystallisation from the same solvent gave pure 5 : 6-*dimethanesulphonyl* 1 : 2-3 : 4-*di*iso*propylidene mannitol*, m. p. 118—120°, $[\alpha]_D^{20}$ +25·1° (*c*, 2·0 in chloroform) (Found : C, 39·95; H, 6·3; S, 15·3. $C_{14}H_{26}O_{10}S_2$ requires C, 40·2; H, 6·3; S, 15·3%).

5 : 6-*Ditosyl* 1 : 2-3 : 4-*Di*iso*propylidene Mannitol*.—Similar treatment of 1 : 2-3 : 4-di*iso*propylidene mannitol (1·3 g.) in pyridine (6 c.c.) with toluene-*p*-sulphonyl chloride (2·1 g.) gave an oil on addition of water to the reaction mixture. It was isolated by chloroform extraction; the extracts were washed with hydrochloric acid, sodium hydrogen carbonate solution, and with water, dried (Na_2SO_4), and evaporated to a viscous oil (2·2 g.). This crude *ditosyl* derivative had $[\alpha]_D^{21}$ +12·1° (*c*, 4 in chloroform) (Found : S, 10·6. $C_{26}H_{34}O_{10}S_2$ requires S, 11·2%).

1 : 2-3 : 4-*Di*iso*propylidene* 5 : 6-*Mannitoleen*.—5 : 6-Dimethanesulphonyl 1 : 2-3 : 4-di*iso*propylidene mannitol (14·4 g.), sodium iodide (42 g.), and acetone (280 c.c.) were heated in a pressure bottle at 100° for 6½ hours. The precipitated sodium methanesulphonate (11·1 g.) was filtered off and washed with acetone. The filtrate and washings were evaporated to small bulk, and the residue was stirred with a solution of sodium thiosulphate (20 g.) in water (200 c.c.) and extracted 5 times with chloroform (50-c.c. portions). The dried (Na_2SO_4) extracts were evaporated to an oil (7·6 g.) which was distilled, b. p. 40°/0·1 mm.; the distillate contained free iodine, and it was therefore dissolved in chloroform and washed with sodium thiosulphate solution. The recovered oil on distillation gave colourless 1 : 2-3 : 4-*di*iso*propylidene* 5 : 6-*mannitoleen* (5·2 g.), b. p. 41°/0·1 mm., n_D^{23} 1·4401, $[\alpha]_D^{21}$ −5·5° (*c*, 2·4 in chloroform) (Found : C, 63·4; H, 8·6. $C_{12}H_{20}O_4$ requires C, 63·1; H, 8·8%).

A higher-boiling fraction and the still residue from the first distillation were combined, and oily material and iodine were removed by extraction with chloroform. The crystalline residue, on recrystallisation from methanol saturated with light petroleum (b. p. 40—60°) gave 1 : 2-mannitoleen as short needles, m. p. 147—149°, $[\alpha]_D^{20}$ +30·9° (*c*, 1·0 in water) (Found : C, 48·6; H, 7·9. Calc. for $C_6H_{12}O_4$: C, 48·6; H, 8·2%).

Hydrolysis of 1 : 2-3 : 4-*Di*iso*propylidene* 5 : 6-*Mannitoleen*.—A solution of the di*iso*propylidene compound (5·0 g.) in 0·3N-sulphuric acid (15 c.c.) was heated on the steam-bath for 7 hours in a slow stream of nitrogen. The solution was then cooled and extracted once with ether to remove oily impurities. The acid was neutralised by addition, to the hot solution, of barium hydroxide solution in slight excess, followed by carbon dioxide. The barium salts were filtered off and washed with water, and the filtrate and washings were evaporated under reduced pressure. The solid residue was dissolved in warm methanol (100 c.c.) and the solution was filtered and evaporated, the residue being dried by evaporation with benzene and ethanol. Recrystallisation from ethanol–ethyl acetate gave 1 : 2-mannitoleen (2·25 g.), m. p. 144—148°, raised on further recrystallisation to m. p. 147—148°, $[\alpha]_D^{20}$ +30·0° (*c*, 1·0 in water). Karrer and Davis (*loc. cit.*) give m. p. 148·5—149°, $[\alpha]_D^{18}$ +33·4° (in water).

Tetra-acetyl 1 : 2-*Mannitoleen.*—1 : 2-Mannitoleen (2·0 g.), acetic anhydride (10 c.c.), and fused sodium acetate (1·0 g.) were heated on the steam-bath for 12 hours. The reaction mixture was then poured into water and stirred to decompose excess of anhydride. The mixture was cooled to 0°, and the solid was collected (yield, 4·3 g.; m. p. 79—82°). Recrystallisation from methanol gave plates of the tetra-acetyl derivative, m. p. 80—81°, $[\alpha]_D^{22}$ +49·4° (*c*, 1·0 in chloroform) (Found: C, 53·1; H, 6·0. Calc. for $C_{14}H_{20}O_8$: C, 53·15; H, 6·4%). Karrer and Davis (*loc. cit.*) give m. p. 81·5°.

Reaction of Tetra-acetyl 1 : 2-*Mannitoleen with Bromine.*—A solution of bromine (1·8 g.) in carbon tetrachloride (30 c.c.) was added slowly to a solution of the tetra-acetate (3·15 g.) in carbon tetrachloride (50 c.c.), the temperature being kept below 20°. Stirring was then continued for two hours, and the solution was washed with sodium hydrogen carbonate solution, containing a little sodium thiosulphate. A small quantity of oil, not soluble in the carbon tetrachloride, was brought into solution by addition of some chloroform, and the solution was dried (Na_2SO_4) and evaporated to an oil (4·7 g.). This was dissolved in methanol (12 c.c.), and the solution was cooled to 0°, and kept thereat overnight. The solid (2·1 g.; m. p. 85—100°) was collected and recrystallised from methanol to give the first *dibromide* as hexagonal plates, m. p. 111—112°, $[\alpha]_D^{21}$ +43·8° (*c*, 1·1 in chloroform) (Found: C, 35·5; H, 4·3; Br, 33·1. $C_{14}H_{20}O_8Br_2$ requires C, 35·3; H, 4·2; Br, 33·6%).

The main methanolic filtrate was evaporated to a solid residue, which on recrystallisation twice from light petroleum (b. p. 60—80°) and four times from ethyl acetate–light petroleum (b. p. 60—80°) gave cubes of the isomeric *dibromide*, m. p. 76°, $[\alpha]_D^{21}$ +45·5° (*c*, 1·1 in chloroform) (Found: C, 35·3; H, 4·3; Br, 33·6%).

The first dibromide (1·3 g.; crude) was heated under reflux with a solution of potassium thiolacetate (0·9 g.) in ethanol (15 c.c.) for 8 hours. The bisthiolacetate was isolated in the usual way and formed a syrup (1·1 g.), $[\alpha]_D^{21}$ +25·4° (*c*, 2·6 in chloroform), which failed to crystallise. Light absorption: max. 2290 A., $\varepsilon = 6500$. The second dibromide (1·9 g.), similarly treated, also gave a syrup (1·6 g.), $[\alpha[_D^{23}$ +21·8° (*c*, 3·0 in chloroform); light absorption: max. 2290 A., $\varepsilon = 7000$.

Reaction of Tetra-acetyl 1 : 2-*Mannitoleen with Hypobromous Acid.*—The tetra-acetate (0·27 g.), *N*-bromosuccinimide (0·19 g.), water (7 c.c.), and ether (3 c.c.) were shaken together for 17 hours. The ethereal layer was removed, and the aqueous portion was extracted twice with ether. The combined extracts were dried (Na_2SO_4) and evaporated. The crude bromohydrin (0·35 g.) was heated with acetic acid (1 c.c.), acetic anhydride (1 c.c.), and fused sodium acetate (0·25 g.) for 24 hours on the steam-bath. The reaction mixture was cooled, shaken with water for some time, and extracted with chloroform. The extracts were washed ($NaHCO_3$ solution), dried (Na_2SO_4), and evaporated to a syrup, which partly crystallised. The solid was removed and washed with ethanol–light petroleum (b. p. 40—60°), to give hexa-acetyl sorbitol, (0·08 g.), m. p. and mixed m. p. 96—98°, $[\alpha]_D^{20}$ +9·0° (*c*, 1·0 in chloroform).

3 : 4-*Dimethanesulphonyl* 1 : 2-5 : 6-*Diisopropylidene Mannitol.*—To a solution of methansulphonyl chloride (7·15 g.) in dry pyridine (15 c.c.), cooled in ice, was added powdered 1 : 2-5 : 6-di*iso*propylidene mannitol (Baer, *J. Amer. Chem. Soc.*, 1945, **67**, 338) (6·6 g.), during *ca.* 5 minutes. After being kept at 0° overnight, the mixture was diluted with water (200 c.c.). The precipitated solid was collected, washed with water, and recrystallised from methanol to give the *dimethanesulphonate* (9·0 g.), m. p. 143—144°, $[\alpha]_D^{24}$ −5·2 (*c*, 2·4 in chloroform) (Found: C, 39·7; H, 6·3. $C_{14}H_{26}O_{10}S_2$ requires C, 40·2; H, 6·3%).

Reactions of the 3 : 4-*Disulphonates with Sodium Iodide.*—(*a*) 3 : 4-Ditosyl 1 : 2-5 : 6-di*iso*propylidene mannitol (Brigl and Grüner, *Ber.*, 1934, **67**, 1969) (2·9 g.), sodium iodide (6·0 g.), and acetone (40 c.c.) were heated in a sealed tube for 2 hours at 80°; no reaction occurred. Heating was continued for 12 hours at 110°; iodine was then liberated, and from the cooled reaction product the theoretical amount of sodium toluene-*p*-sulphonate (1·9 g.) was removed by filtration. The filtrate was worked up as previously described, but gave only a trace of dark oil from the chloroform extracts.

(*b*) The corresponding 3 : 4-dimethanesulphonate (12·5 g.), sodium iodide (36 g.), and acetone (250 c.c.) were heated in a pressure bottle at 100° for 55 hours. The precipitated sodium methanesulphonate amounted to only 2·2 g. (23%); the dark filtrate, containing free iodine, was returned to the bottle and heated for 15 hours at 125—135°. The reaction had now gone to completion (total yield of sodium methanesulphonate, 9·5 g.), and the mixture was worked up as before. The only identifiable product from the chloroform extractions was mesityl oxide.

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IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
S. KENSINGTON, LONDON, S.W.7.

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