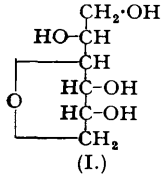
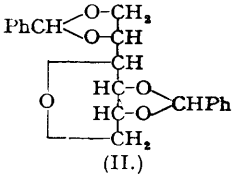
## 145. *Some Derivatives of* 3 : 6-*Anhydromannitol.*

By A. B. Foster and W. G. Overend.

Several derivatives suitable for the characterization of 3 : 6-anhydromannitol are described. The graded acid hydrolysis of 1 : 2-4 : 5-di*iso*propylidene 3 : 6-anhydromannitol yields 4 : 5-*iso*propylidene 3 : 6-anhydromannitol, the structure of which is proved. Oxidation of this by lead tetra-acetate affords derivatives of 2 : 5-anhydro-D-arabinose, the stability of which towards hydrochloric acid has been studied. The exchange reactions with iodine of ditoluene-*p*-sulphonyl and dimethanesulphonyl derivatives of 4 : 5-*iso*propylidene 3 : 6-anhydromannitol have been examined.

It is well known that the action of acids on mannitol results in the formation of a mixture of anhydromannitol derivatives. Although examined by numerous workers (Fauconnier, *Bull. Soc. chim.*, 1884, **41**, 119; *Compt. rend.*, 1885, **100**, 914; Romburgh and Burg, *Proc. Acad. Sci. Amsterdam*, 1922, **25**, 335; Wiggins, *J.*, 1945, 4; Montgomery and Wiggins, *J.*, 1948, 2204), the composition of this mixture has not been completely elucidated. However it is known that 3 : 6-anhydromannitol (mannitan) (I) is present in small but varying amounts. It was first obtained by Fauconnier (*loc. cit.*) by the action of formic or hydrochloric acid on mannitol and its structure was conclusively proved when its identity with the product obtained by reduction of 3 : 6-anhydro-D-mannose was established (Valentin, *Coll. Czech. Chem. Comm.*, 1936, **8**, 35). Treatment of 3 : 6-anhydromannitol (I) with acetic anhydride in pyridine afforded


(I.)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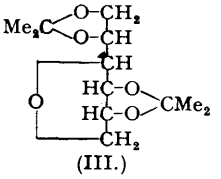
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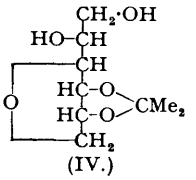
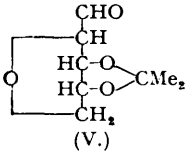

(IV.)

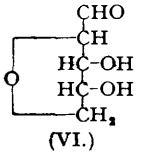
syrupy 1 : 2 : 4 : 5-tetra-acetyl 3 : 6-anhydromannitol, while a more convenient derivative for purposes of characterization was the crystalline 1 : 2 : 4 : 5-tetrabenzoate obtained by using benzoyl chloride in pyridine. (I) could readily be further characterized as its crystalline dibenzylidene derivative which was obtained by treatment with benzaldehyde either at room

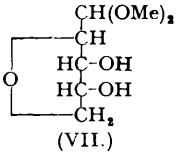
temperature in the presence of zinc chloride or preferably at elevated temperatures in an inert atmosphere (cf. Honeyman and Oldham, *J.*, 1946, 986). This derivative is probably 1 : 2-4 : 5-dibenzylidene 3 : 6-anhydromannitol (II) and its structure will be discussed in a subsequent communication.

When 3 : 6-anhydromannitol (I) was shaken with acetone containing a suitable dehydrating agent 1 : 2-4 : 5-di*iso*propylidene 3 : 6-anhydromannitol (III) was obtained in good yield. The greater lability, towards acidic reagents, of *iso*propylidene residues engaging primary and secondary hydroxyl groups [*e.g.*, (III), positions $C_{(1)}$ : $C_{(2)}$] compared with those engaging only secondary hydroxyl groups [*e.g.* (III), positions $C_{(4)}$ : $C_{(5)}$] has been noted by several workers (cf. Wiggins, *J.*, 1946, 13). When (III) was dissolved in 70% aqueous acetic acid, partial hydrolysis occurred and a crystalline mono*iso*propylidene derivative of 3 : 6-anhydromannitol was obtained. That this was 4 : 5-*iso*propylidene 3 : 6-anhydromannitol (IV) was indicated by the liberation of formaldehyde (characterized by forming a derivative with dimedone) on oxidation with periodic acid (cf. Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1476), thereby indicating the presence of the $CH_2(OH)\cdot CH(OH)\cdot$ grouping. Further hydrolysis of (IV) with mineral acid yielded 3 : 6-anhydromannitol (I). Moreover, it was shown that the rate of oxidation of (IV) by lead tetra-acetate in glacial acetic acid was closely analogous to that of an equimolecular amount of 1 : 2-*iso*propylidene D-glucofuranose. The product isolated from the lead tetra-acetate oxidation of (IV) was a liquid which readily polymerized, particularly on attempted distillation. It exhibited strong absorption in the ultra-violet region (at 2550 A.); this absorption is displaced from that normally associated with the carbonyl group (*i.e.*, 2900 A.), owing to the combined influence of the butylene oxide ring and the ketal residue. There can be little doubt that the product was 3 : 4-*iso*propylidene 2 : 5-anhydro*aldehydo*-D-arabinose (V). Treatment of (V) with N-hydrochloric acid at 100° removed the *iso*propylidene residue, yielding 2 : 5-anhydro-D-arabinose, represented in (VI) as the *aldehydo*-form. It was expected that the aldehyde group would render the adjacent anhydro-ring of (V) unstable and that on treatment with hydrochloric acid a 2-halogeno-2-deoxy-D-arabinose or 2-halogeno-2-deoxy-D-ribose would result. Either of these would form a useful precursor of 2-deoxy-D-ribose, an important sugar in biological processes (cf. Stacey *et al.*, *J.*, 1949, 1879, 2836). The ultra-violet absorption of the hydrolysis product (VI) showed a peak at 2680 A. and it may be deduced that (VI) contained a considerable proportion of the *aldehydo*-form, although it was much more weakly absorbing than (V). This was well substantiated by its treatment with methanolic hydrogen chloride, since the product isolated was not the αβ-methylglycoside which normally results from the action of this reagent on ring sugars, but the dimethyl acetal (VII). It is apparent therefore that the butylene oxide ring in 2 : 5-anhydro-D-arabinose (VI) tends to maintain the sugar in an open-chain structure, an effect similar to that encountered by Haworth, Jackson, and Smith (*J.*, 1940, 620) in the 3 : 6-anhydrohexose series.

4 : 5-*iso*Propylidene 3 : 6-anhydromannitol (IV) could also be characterized as the crystalline 1 : 2-diacetate and 1 : 2-di-*p*-nitrobenzoate. Similarly by treatment of (IV) with methane-


(V.)


(VI.)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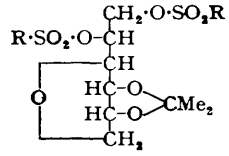
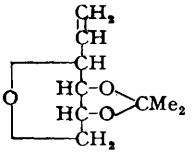
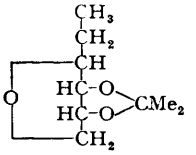

(VIII.)


(IX.)


(X.)

sulphonyl chloride or toluene-*p*-sulphonyl chloride in dry pyridine the 1 : 2-dimethanesulphonyl and 1 : 2-ditoluene-*p*-sulphonyl derivatives (VIII; R = Me and $C_6H_4Me$, respectively) were obtained. The unusual reaction of terminal vicinal ditoluene-*p*-sulphonyl derivatives of simple carbohydrates with sodium iodide in acetone under standard conditions has been noted by several workers (Hann, Ness, and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 73; Tipson and

Cretcher, *J. Org. Chem.*, 1943, **8**, 95; Karrer *et al.*, *Helv. Chim. Acta*, 1948, **31**, 784, 1611; Owen and Bladon, *J.*, 1950, 598): it involves elimination of the toluene-*p*-sulphonyl residues, liberation of iodine, and concomitant establishment of an ethylenic linkage. The 1 : 2-ditoluene-*p*-sulphonyl derivative (VIII) was heated with anhydrous acetone and sodium iodide at 125—130° for four hours, 1·84 moles of sodium toluene-*p*-sulphonate were precipitated, iodine was liberated, and the crystalline product isolated was 4 : 5-*iso*propylidene 3 : 6-anhydromannitoleen (IX). Attempts to prepare 1-iodo 4 : 5-*iso*propylidene 2-toluene-*p*-sulphonyl 3 : 6-anhydro-1-deoxymannitol by treating (VIII; R = $C_6H_4Me$) with one molecular proportion of sodium iodide in acetone under very mild conditions always resulted in precipitation of sodium toluene-*p*-sulphonate and concomitant liberation of iodine, the reactivities of the toluene-*p*-sulphonyloxy-groups being clearly similar. For comparative purposes both the 1 : 2-dimethanesulphonyl and 1 : 2-ditoluene-*p*-sulphonyl derivatives (VIII) were subjected to iodine-exchange reactions under identical, though milder, conditions than those normally employed; the latter derivative underwent 48·3% exchange and the former 43·3%; the difference in degree of exchange of methanesulphonyloxy- and toluene-*p*-sulphonyloxy-groups in standard reactions has been noted previously (Foster, Overend, Stacey, and Wiggins, *J.*, 1949, 2542) and this work is being extended.

Hydrogenation of 4 : 5-*iso*propylidene 3 : 6-anhydromannitoleen (IX) in the presence of platinum oxide readily gave 4 : 5-*iso*propylidene 3 : 6-anhydro-1 : 2-dideoxymannitol (X).

## Experimental.

*Action of Hydrochloric Acid on Mannitol.*—Mannitol (500 g.) was boiled under reflux with concentrated hydrochloric acid (2 l.) for 24 hours. After being boiled for a further 10 minutes with activated charcoal (20 g.), the solution was filtered and evaporated to a syrup at 60—70° (bath-temp.)/12—15 mm. Traces of hydrochloric acid were removed as completely as possible by repeated addition of water and re-evaporation, and the ultimate straw-coloured syrup was dissolved in ethanol (400 c.c.), and set aside at 0° for several days. The impure product which separated was collected and washed several times with ethanol. Repeated recrystallization from aqueous ethanol gave a product, m. p. 136—137°, which still contained mannitol. Distillation gave a fraction, b. p. 220—230° (bath-temp.)/0·03 mm., which crystallized on storage and after recrystallization from aqueous ethanol was obtained as large colourless plates (30 g.). It was 3 : 6-anhydromannitol (mannitan), m. p. 146—147°, $[\alpha]_D^{20}$ −26·2° in water. (Wiggins, *loc. cit.*, gives m. p. 145—147° and Valentin, *loc. cit.*, records m. p. 146—147° for the product obtained by the reduction of 3 : 6-anhydro-D-mannose.)

1 : 2 : 4 : 5-*Tetra-acetyl* 3 : 6-*Anhydromannitol.*—A solution of mannitan (1·0 g.) in dry pyridine (5 c.c.) was treated with freshly distilled acetic anhydride (2 c.c.) at room temperature for 20 hours. The reaction mixture was diluted with water (50 c.c.) and extracted with chloroform (5 × 30 c.c.), and the extract washed with water and dried ($MgSO_4$). Evaporation of the solvent gave a straw-coloured syrup from which 1 : 2 : 4 : 5-*tetra-acetyl* 3 : 6-*anhydromannitol* (0·7 g.) was obtained, b. p. 170—175° (bath-temp.)/0·05 mm., $n^{20}$ 1·4545, $[\alpha]_D^{20}$ +19·5° (*c*, 1·4 in chloroform) (Found: C, 50·8; H, 6·2. $C_{14}H_{20}O_9$ requires C, 50·6; H, 6·0%).

1 : 2 : 4 : 5-*Tetrabenzoyl* 3 : 6-*Anhydromannitol.*—Benzoyl chloride (0·82 c.c.) was cautiously added to a solution of mannitan (0·25 g.) in dry pyridine (2 c.c.), and the mixture set aside at room temperature for 5 hours. On dilution with water a syrupy product separated which did not solidify on trituration. However, when it was kept for a long time in acetone–water–ethanol colourless prisms of 1 : 2 : 4 : 5-*tetrabenzoyl* 3 : 6-*anhydromannitol* separated. After recrystallization this had m. p. 88—89° and $[\alpha]_D$ −157° (*c*, 1·5 in chloroform) (Found: C, 70·2; H, 4·9. $C_{34}H_{28}O_9$ requires C, 70·3; H, 4·8%).

*Reaction of* 3 : 6-*Anhydromannitol with Benzaldehyde.*—(a) *In the presence of anhydrous zinc chloride.* Mannitan (1·0 g.) was shaken with freshly distilled benzaldehyde (5 c.c.) and finely powdered, anhydrous zinc chloride (1·5 g.) at room temperature for 20 hours. The mixture was then treated with water and light petroleum (b. p. 60—80°), and the crystals which gradually separated were collected after 2 hours, washed alternately with the same solvents, and recrystallized from aqueous ethanol. 1 : 2-4 : 5(?)-*Dibenzylidene* 3 : 6-*anhydromannitol* (0·2 g., 9·65%) was obtained as colourless needles, m. p. 109—110°, $[\alpha]_D^{20}$ −86·4° (*c*, 0·5 in benzene) (Found: C, 69·7; H, 5·7. $C_{20}H_{20}O_5$ requires C, 70·6; H, 5·9%).

(b) *At elevated temperatures* (cf. Oldham and Honeyman, *loc. cit.*). A stream of carbon dioxide was passed through a mixture of benzaldehyde (5 c.c.) and mannitan (1·0 g.), heated at 140—145°, for 4 hours. Removal of the benzaldehyde by evaporation under diminished pressure gave a crystalline residue which was dissolved in benzene and freed from traces of benzoic acid by washing with dilute aqueous sodium hydroxide and then with water. The solution was dried ($MgSO_4$) and evaporated to dryness, yielding a residue (1·5 g., 72·4%) which after recrystallization from aqueous ethanol had m. p. 109—110° alone or on admixture with the product from (*a*) and $[\alpha]_D^{20}$ −88·1° (*c*, 1·5 in benzene). Valentin (*loc. cit.*) reports a benzylidene derivative of 3 : 6-anhydromannitol having m. p. 125—126° and $[\alpha]_D$ −48·8° in chloroform.

1 : 2-4 : 5-*Diisopropylidene* 3 : 6-*Anhydromannitol.*—3 : 6-Anhydromannitol (5 g.) was shaken mechanically for 48 hours with dry acetone (100 c.c.) containing anhydrous zinc chloride (6 g.) and a homogeneous mixture of syrupy phosphoric acid (3 c.c.) and phosphoric oxide (1·5 g.). The solution was poured into water containing an excess of sodium carbonate and the precipitated zinc carbonate

collected and washed with acetone. The combined filtrate and washings were evaporated under diminished pressure until the acetone had been completely removed, and the remaining aqueous solution was extracted with ether (5 × 100 c.c.). Evaporation of the extract after drying ($MgSO_4$) gave a syrupy residue, from which the *di*iso*propylidene* derivative (5·18 g.) was obtained as a colourless mobile liquid, b. p. 95—100° (bath-temp.)/0·01 mm., $n^{18}$ 1·4555, $[\alpha]_D^{20}$ −53·4° (*c*, 2·1 in chloroform) (Found : C, 58·8; H, 8·2. $C_{12}H_{20}O_5$ requires C, 59·0; H, 8·2%).

4 : 5-iso*Propylidene* 3 : 6-*Anhydromannitol*—1 : 2-4 : 5-Di*iso*propylidene 3 : 6-anhydromannitol (2·1 g.) was dissolved in a solvent (40 c.c.) prepared by adding water (30 c.c.) to glacial acetic acid (70 c.c.), and the hydrolysis followed polarimetrically {$[\alpha]_D^{20}$ −41·9° ⟶ −47·6° (constant) in 80 minutes} (cf. 3 : 6-anhydromannitol, $[\alpha]_D^{20}$ −29°). The solution was evaporated to dryness at 30—35° (bath-temp.)/10—12 mm., and the remaining traces of acetic acid were removed by storage *in vacuo* over phosphoric oxide and potassium hydroxide for 2 days. The syrupy residue was fractionated by extraction with water (30 c.c.), and the aqueous solution extracted with chloroform (30 c.c.). The residue remaining after the aqueous extraction was added to the chloroform solution. Evaporation of the dried ($MgSO_4$) chloroform solution gave a mobile straw-coloured syrup (0·175 g.), $[\alpha]_D^{20}$ −40·0° in ethanol : it was unchanged starting material. The aqueous solution was evaporated to dryness and the syrupy residue (1·61 g.) extracted with acetone; the undissolved material was negligible (*ca.* 5—10 mg.). The syrupy residue obtained on evaporation of the acetone solution had $[\alpha]_D^{20}$ −50·9° in ethanol and on distillation gave 4 : 5-iso*propylidene* 3 : 6-*anhydromannitol*, b. p. 125—130° (bath-temp.)/0·04 mm., $n^{20}$ 1·4785, $[\alpha]_D^{20}$ −59·1° (*c*, 0·4 in water). On storage this substance crystallized and after recrystallization from ethyl acetate–light petroleum (b. p. 60—80°) gave the product in large colourless square plates, m. p. 83—84° (Found : C, 52·5; H, 7·7. $C_9H_{16}O_5$ requires C, 52·9; H, 7·8%).

*Oxidation of* 4 : 5-iso*Propylidene* 3 : 6-*Anhydromannitol.*—(a) *With periodic acid.* The procedure followed was that of Reeves (*loc. cit.*). 4 : 5-*iso*Propylidene 3 : 6-anhydromannitol (25·3 mg.) gave the formaldehyde–dimedone derivative (39·5 mg.), m. p. 185—190°, corresponding to 140% of that expected. In a series of oxidations of this *iso*propylidene derivative the dimedone derivative isolated corresponded to 115—140% of the theoretical and had an indistinct m. p. Reeves (*loc. cit.*) records anomalous results, similar to the above, encountered in periodic acid oxidations of *iso*propylidene derivatives. Presumably hydrolysis of the *iso*propylidene residue occurs under the conditions of the experiment and interferes with the estimation.

(b) *With lead tetra-acetate.* By the method described by Hockett and McClenahan (*J. Amer. Chem. Soc.*, 1939, **61**, 1667) 4 : 5-*iso*propylidene 3 : 6-anhydromannitol (103 mg.) reduced a standard solution of lead tetra-acetate in glacial acetic acid (0·0655N.) as shown :

| Time (mins.) ..... | 15 | 35 | 55 | 90 | 115 | 215 | 425 | 900 |
|---|---|---|---|---|---|---|---|---|
| Uptake of $Pb(OAc)_4$ (moles)... | 0·208 | 0·416 | 0·566 | 0·717 | 0·792 | 0·924 | 0·943 | 0·962 |

For comparative purposes 1 : 2-*iso*propylidene D-glucofuranose (110 mg.) was oxidised under identical conditions :

| Time (mins.) ..... | 18 | 31 | 65 | 115 | 155 | 275 | 415 |
|---|---|---|---|---|---|---|---|
| Uptake of $Pb(OAc)_4$ (moles)... | 0·249 | 0·364 | 0·632 | 0·785 | 0·834 | 0·958 | 0·97 |

*Hydrolysis of* 4 : 5-iso*Propylidene* 3 : 6-*Anhydromannitol.*—A solution of the *iso*propylidene derivative (0·2 g.) in N-sulphuric acid (10 c.c.) was boiled under reflux for 5 hours. Neutralization of the acid with barium carbonate and evaporation of the solution gave a crystalline product, m. p. 146—147° alone or on admixture with 3 : 6-anhydromannitol.

3 : 4-iso*Propylidene* 2 : 5-*Anhydro*aldehydo-D-*arabinose.*—Lead tetra-acetate (10·7 g.) was added to a solution of 4 : 5-*iso*propylidene 3 : 6-anhydromannitol (5 g.) in dry benzene (80 c.c.), and the mixture agitated mechanically for 24 hours. Addition of ether (80 c.c.) precipitated inorganic material which was filtered off. The remaining solution was freed from acid by shaking it with the minimum volume of aqueous sodium hydrogen carbonate and then filtering. The aqueous solution was extracted with benzene (3 × 100 c.c.), and the combined extracts were dried ($MgSO_4$) and evaporated to dryness, yielding a straw-coloured syrup (1·35 g., 29·4%) which strongly reduced Fehling's solution. Continuous extraction of the aqueous solution with ether for 3 days gave a further yield of product (2·85 g., 67·6%). Distillation of this product resulted in extensive polymerization of the flask residues, but 3 : 4-iso*propylidene* 2 : 5-*anhydro*aldehydo-D-*arabinose* (0·2 g.) was obtained as a thick yellow liquid, strongly reducing towards Fehling's solution, b. p. 118—124° (bath-temp.)/0·03 mm., $n^{21}$ 1·4660, $[\alpha]_D^{20}$ −131·5° (*c*, 1·4 in benzene). Because of the tendency to polymerize (and hence to overheat during distillation, affording a discoloured product) it was not possible to obtain good analytical figures (Found : C, 54·0; H, 7·4. $C_8H_{12}O_4$ requires C, 55·8; H, 7·0%). It was sparingly soluble in water and moderately soluble in ether and benzene. In chloroform solution 3 : 4-*iso*propylidene 2 : 5-anhydro*aldehydo*-D-arabinose showed absorption at 2550 A. ($\varepsilon$ = 170 approx.; *c*, 78·8 mg.-%).

*Hydrolysis of the Foregoing Derivative.*—3 : 4-*iso*Propylidene 2 : 5-anhydro-*aldehydo*-D-arabinose (3·5 g.) was heated with hydrochloric acid (60 c.c.; N.) on a boiling water-bath for 3 hours. The syrupy starting material rapidly dissolved and considerable coloration of the reaction mixture occurred. The acid was neutralized with silver carbonate and the solution evaporated to dryness after removal of the silver residues. Storage of the residue over phosphoric oxide *in vacuo* afforded a colourless hygroscopic glass (1·7 g.), $[\alpha]_D^{20}$ −22° (*c*, 0·6 in water), showing an absorption band at 2680 A. ($\varepsilon$ = 20 approx.; *c*, 227·6 mg.-%). A similar product was isolated when sulphuric acid was used to effect hydrolysis. This product (1·6 g.) was boiled under reflux with 1·4% methanolic hydrogen chloride (25 c.c.) for 2 hours. The acid was neutralized with silver carbonate and the solution freed from silver residues by filtration through charcoal. Evaporation gave a syrupy residue, non-reducing towards Fehling's

solution, from which 2 : 5-*anhydro*-D-*arabinose dimethyl acetal* (1·27 g.) was obtained as a colourless viscous liquid, b. p. 115—120° (bath-temp.)/0·01 mm., $n^{18}$ 1·4700, $[\alpha]_D^{20}$ −44·4° (*c*, 0·8 in methanol) (Found : MeO, 34·0. $C_7H_{14}O_5$ requires MeO, 34·8%).

1 : 2-*Diacetyl* 4 : 5-iso*Propylidene* 3 : 6-*Anhydromannitol*.—A solution of 4 : 5-*iso*propylidene 3 : 6-anhydromannitol (0·2 g.) in dry pyridine (1 c.c.) was treated with acetic anhydride (1 c.c.) at room temperature for 48 hours. The mixture was diluted with water (40 c.c.) and extracted with chloroform (5 × 25 c.c.), and the combined extracts were washed with water, dilute sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation afforded a syrupy residue from which the *diacetate* (0·19 g.) was obtained as a colourless viscous liquid, b. p. 115—120° (bath-temp.)/0·02 mm., $n^{20}$ 1·4535. On storage the distillate crystallized and after recrystallization from aqueous ethanol had m. p. 42—44° and $[\alpha]_D^{20}$ −46·2° (*c*, 0·6 in chloroform) (Found : C, 54·5; H, 7·0. $C_{13}H_{20}O_7$ requires C, 54·2; H, 6·9%).

1 : 2-*Di*-p-*nitrobenzoyl* 4 : 5-iso*Propylidene* 3 : 6-*Anhydromannitol*.—*p*-Nitrobenzoyl chloride (2·2 mols., 0·4 g.) was added to a solution of 4 : 5-*iso*propylidene 3 : 6-anhydromannitol (0·2 g.) in dry pyridine (2 c.c.), and the mixture set aside at room temperature for 10 hours. On addition of water a syrupy product separated which crystallized on trituration. Recrystallization from acetone–water–methanol gave the *di*-p-*nitrobenzoate* as elongated prisms, m. p. 169—170°, $[\alpha]_D^{20}$ −29·6° (*c*, 0·4 in chloroform) (Found : C, 54·7; H, 4·2. $C_{23}H_{22}O_{11}N_2$ requires C, 55·0; H, 4·4%).

1 : 2-*Dimethanesulphonyl* 4 : 5-iso*Propylidene* 3 : 6-*Anhydromannitol*.—4 : 5-*iso*Propylidene 3 : 6-anhydromannitol (0·55 g.), in dry pyridine (3 c.c.), was treated with methanesulphonyl chloride (2·5 mols., 0·75 g.) at room temperature for 2·5 hours. The mixture was diluted with water (150 c.c.) and extracted with chloroform (2 × 100 c.c.), and the combined extracts were washed successively with water (twice), 0·5N-hydrochloric acid (thrice; total vol., 250 c.c.), and dilute sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation yielded a syrupy residue which crystallized on trituration with ethanol. Recrystallization from aqueous ethanol afforded the *dimethanesulphonyl* derivative (0·46 g.) as colourless needles, m. p. 85—88°, $[\alpha]_D^{20}$ −46·7° [*c*, 0·4 in chloroform–carbon tetrachloride (5 : 1)] (Found : C, 36·8; H, 5·7. $C_{11}H_{20}O_9S_2$ requires C, 36·7; H, 5·6%).

1 : 2-*Ditoluene*-p-*sulphonyl* 4 : 5-iso*Propylidene* 3 : 6-*Anhydromannitol*.—A solution of 4 : 5-*iso*propylidene 3 : 6-anhydromannitol (0·1 g.) in dry pyridine (0·5 c.c.) was treated with toluene-*p*-sulphonyl chloride (2·4 mols., 0·26 g.) at room temperature for 48 hours. Dilution with water caused separation of the *ditoluene*-p-*sulphonate* which after recrystallisation from ethanol was obtained as colourless needles, m. p. 125—126°, $[\alpha]_D^{20}$ −31·7° (*c*, 0·9 in chloroform) (Found : C, 53·7; H, 6·0. $C_{23}H_{28}O_9S_2,C_2H_5{\cdot}OH$ requires C, 53·8; H, 6·1%).

*Iodine-exchange Experiments*.—The iodine-exchange experiments were carried out under strictly comparable conditions. Solutions containing equimolecular proportions of the above methanesulphonyl or toluene-*p*-sulphonyl derivatives and sodium iodide in equal volumes of acetone were heated in sealed tubes at identical temperatures. When 1 : 2-dimethanesulphonyl 4 : 5-*iso*propylidene 3 : 6-anhydromannitol (250 mg.) was heated in acetone (10 c.c.) with sodium iodide (2·2 mols., 250 mg.), sodium methanesulphonate (70 mg.) was precipitated, corresponding to 0·866 mole of methanesulphonyloxy-group. 4 : 5-*iso*Propylidene 1 : 2-ditoluene-*p*-sulphonyl 3 : 6-anhydromannitol (355 mg.), treated as above, gave sodium toluene-*p*-sulphonate (130 mg.) corresponding to 0·966 mole of toluene-*p*-sulphonyloxy-residue. Both tubes were heated at 100—105° for 1·5 hours and in each case there was extensive liberation of iodine (cf. Foster, Overend, Stacey, and Wiggins, *loc. cit.*). The salts were collected in a sintered-glass funnel, washed well with dry acetone, and dried at 130° for 20 minutes before being weighed.

4 : 5-iso*Propylidene* 3 : 6-*Anhydromannitoleen*.—A solution of the ditoluene-*p*-sulphonyl derivative (3·0 g.) in dry acetone (25 c.c.) containing sodium iodide (3·0 g.) was heated in a sealed tube at 125—130° for 4 hours. Sodium toluene-*p*-sulphonate (2·13 g., 1·836 moles) was precipitated, and iodine liberated. After removal of the precipitated salt, the filtrate was diluted with chloroform (75 c.c.) and washed with aqueous sodium thiosulphate solution. The chloroform solution was dried ($MgSO_4$) and evaporated, and the syrupy residue distilled. 4 : 5-iso*Propylidene* 3 : 6-*anhydromannitoleen* (0·7 g.) was obtained as a colourless mobile liquid, b. p. 65—75° (bath-temp.)/0·05 mm., which rapidly crystallised on cooling and then had m. p. 23—24°, $[\alpha]_D^{17}$ +87·5° (*c*, 0·9 in methanol) (Found : C, 61·9; H, 8·5. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%).

4 : 5-iso*Propylidene* 3 : 6-*Anhydro*-1 : 2-*dideoxymannitol*.—4 : 5-*iso*Propylidene 3 : 6-anhydromannitoleen (0·65 g.), in methanol (40 c.c.), was shaken vigorously at room temperature in an atmosphere of hydrogen at a slight over-pressure in the presence of platinum oxide (50 mg.). Hydrogen (95 c.c.) was rapidly absorbed, and after removal of the catalyst and evaporation of the solvent a straw-coloured syrup was isolated from which 4 : 5-iso*propylidene* 3 : 6-*anhydro*-1 : 2-*dideoxymannitol* (0·45 g.) was obtained as a colourless mobile liquid, b. p. 50—55° (bath-temp.)/0·2 mm., $n^{17}$ 1·4330, $[\alpha]_D^{20}$ −49·1 (*c*, 0·6 in methanol) (Found : C, 61·5; H, 9·3. $C_9H_{16}O_3$ requires C, 62·8; H, 9·2%). Both this compound and its precursor were extremely hygroscopic and it was not possible to obtain good analytical data for them.

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