933. *Methyl 2,3-Anhydro-α-D-mannoside and 3,4-Anhydro-α-D-altroside and their Derivatives. Part I.*

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The interconversion of methyl 2,3-anhydro-α-D-mannoside and 3,4-anhydro-α-D-altroside has been studied, and that of their 6-*O*-triphenylmethyl ethers. A neighbouring *trans*-*O*-acetyl group has been shown to have a significant effect on the rate and direction of ring-opening of these epoxides by dilute acetic acid. Paper-chromatographic methods have been developed for the study of vicinal epoxides.

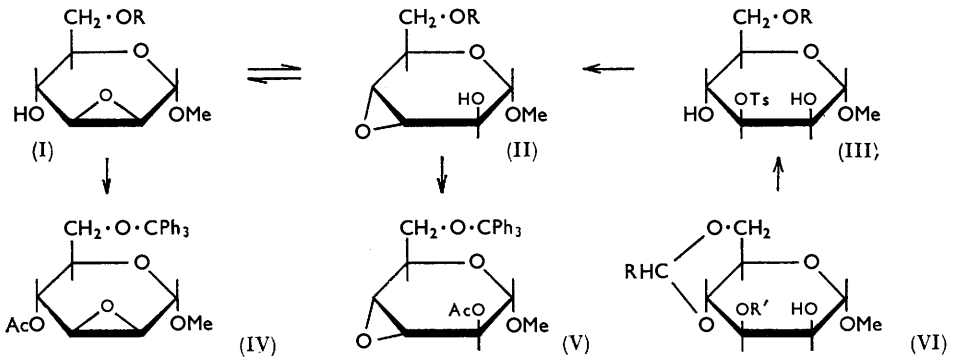
Vicinal epoxides may undergo intramolecular ring-scission under alkaline conditions with formation of a new ring system when a neighbouring hydroxyl group is suitably situated.[1,2] When the new ring is also three-membered the phenomenon has been called "epoxide migration."[3] The first example of the latter was discovered by Kohler, Richtmyer, and Hester.[4] In the carbohydrate series, Lake and Peat[5] described the case of methyl 2,3-anhydro-β-D-mannoside, which partly isomerised to the 3,4-anhydro-altroside, and later examples were discovered by Buchanan,[6] Newth,[7] and Angyal and Gilham.[3] We were interested in studying Lake and Peat's system in the α-series for two reasons: to find out which isomer predominated in the equilibrium, and to study the hydrolysis of the anhydro-compounds by acidic reagents before and after the introduction of a neighbouring *trans*-*O*-acetyl group into the molecule.

Methyl 2,3-anhydro-α-D-mannoside (I; R = H) was prepared in good yield by mild acid hydrolysis of its 4,6-*O*-benzylidene compound.[8] The physical constants agree with those given by Jeanloz and Jeanloz,[9] rather than those given by Myers and Robertson.[10] It gave, in good yield, a crystalline triphenylmethyl ether (I; R = CPh_3), whose acetate (IV) was also crystalline. Treatment of the glycoside (I; R = H) with aqueous alkali led

[1] Peat, *Adv. Carbohydrate Chem.*, 1946, **2**, 37.
[2] Newth, *Quart. Rev.*, 1959, **13**, 30.
[3] Angyal and Gilham, *J.*, 1957, 3691.
[4] Kohler, Richtmyer, and Hester, *J. Amer. Chem. Soc.*, 1931, **53**, 205.
[5] Lake and Peat, *J.*, 1939, 1069.
[6] Buchanan, *Chem. and Ind.*, 1954, 1484; *J.*, 1958, 995.
[7] Newth, *J.*, 1956, 441.
[8] Gut and Prins, *Helv. Chim. Acta*, 1947, **30**, 1223.
[9] Jeanloz and Jeanloz, *J. Amer. Chem. Soc.*, 1958, **80**, 5692.
[10] Myers and Robertson, *J. Amer. Chem. Soc.*, 1943, **65**, 8.

to the formation of a new anhydro-sugar with lower R_F values in the usual paper-chromatographic solvents, together with some methyl altroside. The new anhydro-sugar, presumably (II; R = H), was formed in small amount and it seemed impracticable to prepare it in this way. Another possible route was the more direct one, by alkali treatment of a 3-sulphonate of methyl α-D-mannoside, *e.g.*, (III; R = H).

Aspinall and Zweifel,[11] and Honeyman and Stening,[12] have shown that unimolecular



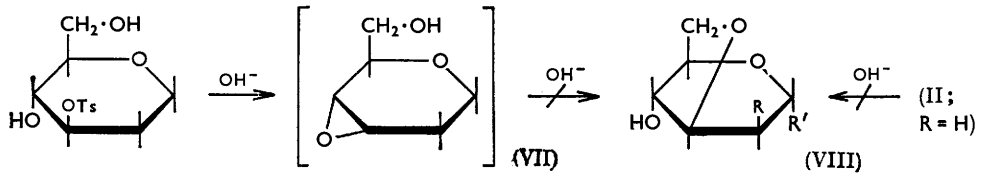
toluene-*p*-sulphonylation of methyl 4,6-*O*-ethylidene-α-D-mannoside (VI; R = Me, R′ = H) gives the equatorial 3-isomer (VI; R = Me, R′ = Ts). The acetal (VI; R = Me, R′ = H) is difficult to purify and improvements in the synthesis of the benzylidene derivative[13] (VI; R = Ph, R′ = H) were therefore explored. By use of 98% formic acid as solvent and catalyst the mono-*O*-benzylidene compound was prepared from methyl α-D-mannoside. Its structure (VI; R = Ph, R′ = H) has been proved by Honeyman and Shaw[14] who have shown that the dialdehyde produced by periodate oxidation is identical with that from methyl 4,6-*O*-benzylidene-α-D-glucoside. Reaction of the benzylidene compound with an excess of toluene-*p*-sulphonyl chloride in pyridine yielded the disulphonate; monosulphonylation gave a little disulphonate together with the monosulphonate (VI; R = Ph, R′ = Ts). Acid hydrolysis of the latter gave the crystalline glycoside (III; R = H) which was unattacked by sodium metaperiodate and is therefore the 3-toluene-*p*-sulphonate; it was also characterised as its triacetate. Great difficulty was experienced in converting the sulphonate into the anhydroaltroside (II; R = H) without formation of anhydromannoside (I; R = H). The best method was based on that of Charalambous and Percival.[15] The sulphonate was dissolved in hot water, and aqueous alkali was added dropwise until the solution was permanently alkaline; the syrupy anhydroaltroside (II; R = H) was then isolated in 79% yield after chromatography. Triphenylmethylation followed by chromatography on silica afforded crystals of the triphenylmethyl ether (II; R = CPh_3) in low yield. This ether exists in two crystalline forms, m. p. 104° and m. p. 135—136°, having different infrared spectra (KBr disc). Acetylation of the ether gave the crystalline 2-acetate (V) which was later used for nucleation purposes.

The triphenylmethyl ether (II; R = CPh_3) and its 2-acetate (V) were prepared in useful quantities by treatment of methyl 3-*O*-toluene-*p*-sulphonyl-6-*O*-triphenylmethyl-α-D-mannoside (III; R = CPh_3), as its crystalline monohydrate, with sodium methoxide. By careful choice of reaction conditions, the formation of anhydromannoside was minimised. Acetylation of the crude product gave a mixture of acetates (V) and (IV), separable by crystallisation. Catalytic deacetylation was accomplished without epoxide migration.

[11] Aspinall and Zweifel, *J.*, 1957, 2271.
[12] Honeyman and Stening, *J.*, 1957, 2278.
[13] Robertson, *J.*, 1934, 330.
[14] Honeyman and Shaw, *J.*, 1959, 2454.
[15] Charalambous and Percival, *J.*, 1954, 2443.

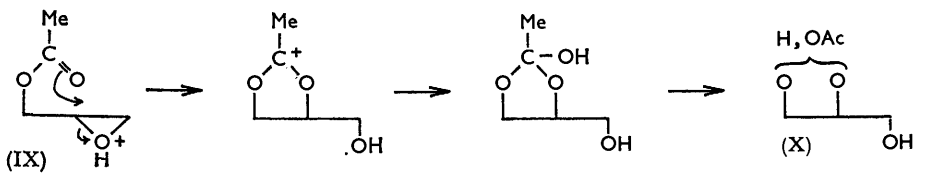
Quantitative measurements of the positions of equilibrium were not carried out. It was clear, however, that in the case of the glycosides (I and II; R = H), as well as their triphenylmethyl ethers, the equilibrium was largely in favour of the 2,3-anhydromannoside isomer. The anhydroaltroside (II; R = CPh_3) could be converted into the anhydromannoside (I; R = CPh_3) in an isolated yield of 79%; paper chromatography of the mother-liquors showed the presence of both isomers in roughly equal amounts. Similarly, isomerisation of the anhydromannoside (I; R = CPh_3) led to recovery of starting material (84%); chromatography of the remainder, followed by acetylation, yielded a small quantity of anhydroaltroside (V).

Theoretical predictions as to which should be the more stable isomer are more complicated than in the inositol series.[3] In one of the two half-chair conformations[16] of the anhydromannoside, the 1-methoxyl is the only axial group and it can be argued that this conformation would be expected to be more stable than either half-chair conformation of the anhydroaltroside. However, we prefer not to be dogmatic at this stage, since similar reasoning[7] suggests that methyl 3,4-anhydro-6-*O*-triphenylmethyl-α-D-galactoside should predominate at equilibrium over the corresponding 2,3-anhydroguloside; in practice comparable amounts of both isomers appear to be present.[6, 17]



When methyl 2,3-anhydro-α-D-mannoside was heated with N-sodium hydroxide, methyl altroside was the major product detected chromatographically, together with a trace of methyl idoside. Methyl 3,6-anhydro-α-D-mannoside (VIII; R = OH, R′ = OMe), which might have been formed by ring-opening of the 3,4-anhydroaltroside (II; R = H) by the 6-hydroxyl group, was not detected. This agrees with the finding of Foster, Stacey, and Vardheim[18] that 1,5:3,4-dianhydro-2-deoxy-D-ribohexitol (VII) suffers normal ring scission in aqueous alkali and yields no 3,6-anhydro-compound (VIII; R = R′ = H).

The directing influence of a *trans-O*-acetyl group on the acidic ring-opening of vicinal epoxides has been described.[19] The reaction, analogous to the stereospecific bromination of 3-benzamidocyclohexene by Winstein, Goodman, and Boschan,[20] involves the sequence (IX) ⟶ (X). The anhydro-sugars described above were suitable for further study of



the neighbouring group effect. The reactions are easily studied chromatographically by the methods described earlier,[19] supplemented by a spray reagent for triphenylmethyl ethers[21] and one for anhydro-sugars; the latter spray depends on the formation of alkali

[16] Ferrier and Overend, *Quart. Rev.*, 1959, **13**, 265; cf. Huber and Schier, *Helv. Chim. Acta*, 1960, **43**, 129.
[17] Oldham and Robertson, *J.*, 1935, 685; Buchanan, unpublished work.
[18] Foster, Stacey, and Vardheim, *Acta Chem. Scand.*, 1958, **12**, 1819.
[19] Buchanan, *J.*, 1958, 2511.
[20] Winstein, Goodman, and Boschan, *J. Amer. Chem. Soc.*, 1950, **72**, 2311; Goodman, Winstein, and Boschan, *ibid.*, 1958, **80**, 4312.
[21] Applegarth and Buchanan, *J.*, 1960, 4706.

when a vicinal epoxide is heated with sodium iodide.[22] In several cases the products were isolated, after acetylation.

In one series of experiments the four triphenylmethyl ethers (I; R = CPh_3), (II; R = CPh_3), (IV), and (V) were separately heated in 80% acetic acid at 100°. The results are summarised in Table 1.

TABLE 1.

Anhydro-sugar	Time of loss of CPh_3 group * (min.)	Time (hr.) of disappearance of epoxide *	Configuration of product(s)
(I; R = CPh_3)	<10	⩾4	Altroside
(IV)	<10	*ca.* 0·5	Altroside
(II; R = CPh_3)	<10	⩾4	Idoside > mannoside
(V)	<10	<1	Mannoside ⩾ idoside

* Extent of reaction greater than 95%.

In the first pair of experiments above, altroside isomers are produced in both cases and the stereospecific effect of the acetyl group is not apparent; the rate of reaction is, however, considerably faster in the case of the acetate. The production of an altrose derivative is in agreement with the work of Newth and Homer [23] who obtained methyl 3-chloro-3-deoxy-α-D-altroside in high yield by the action of hydrochloric acid on the 4,6-*O*-benzylidene derivative of the sugar (I; R = H).

In the second pair of experiments, the acetyl group not only increased the reaction rate, but also led to a high yield (82% isolated) of the mannoside isomer, the product to be expected if the acetyl group participates. The final mother-liquors showed in addition the presence of traces of an unidentified sugar and of methyl idoside. When no neighbouring acetyl group was present the idoside isomer predominated and its presence was proved by isolation.

EXPERIMENTAL

Infrared spectra were measured for potassium bromide discs. Light petroleum refers to the fraction of b. p. 40—60°. Comparison of materials with authentic substances was made, unless stated otherwise, by mixed m. p. determinations and infrared spectra.

Chromatographic Methods.—Adsorption chromatography was carried out on neutral alumina (Woelm) and silica gel (Messrs. Hopkin and Williams). For some separations involving triphenylmethyl ethers silica gel was washed with dilute ammonia and reactivated at 150° for 3 hr. before use (instructions from Messrs. Hopkin and Williams).

Paper chromatography of free sugars and glycosides not containing triphenylmethyl groups was carried out on Whatman no. 1 or no. 4 paper with the following solvent systems: (A) butan-1-ol–pyridine–water (3 : 1 : 1, v/v); (B) butan-2-one saturated with water, the chromatogram being pre-equilibrated for a few hours before running; (C) butan-1-ol–water (86 : 14, v/v). Triphenylmethyl ethers were chromatographed in (D), dimethyl sulphoxide–di-isopropyl ether.[24]

Reducing sugars were detected by using aniline phthalate,[25] α-glycols with periodate and Schiff's reagent,[26] and triphenylmethyl ethers with perchloric acid.[21] Vicinal epoxides were detected by spraying with a solution of sodium iodide (5 g.) and Methyl Red (0·01 g.) in butan-1-ol (100 c.c.) and heating the paper at 140° for a few minutes: yellow spots appeared on a red background. Some R_F values are in Table 2.

Methyl 2,3,4,6-*Tetra*-O-*acetyl*-α-D-*idoside*.—Methyl 4,6-*O*-benzylidene-α-D-idoside (0·65 g.) was suspended in 0·005N-sulphuric acid (20 c.c.) and kept at 60° for 1 hr. The cooled solution was extracted with chloroform (3 times), and the aqueous layer neutralised with barium carbonate. The filtrate, after removal of solids, was evaporated to dryness and treated overnight at room temperature with acetic anhydride (5 c.c.) in pyridine (10 c.c.). The *ac etate* was

[22] Ross, *J.*, 1950, 2257.
[23] Newth and Homer, *J.*, 1953, 989.
[24] Wickberg, *Acta Chem. Scand.*, 1958, **12**, 615.
[25] Partridge, *Nature*, 1949, **164**, 443.
[26] Baddiley, Buchanan, Handschumacher, and Prescott, *J.*, 1956, 2818.

TABLE 2.

R_F values.

Anhydro-sugar	Solvent A	B *	C	D *
Me 2,3-anhydro-α-D-alloside			0·42	
Me 3,4-anhydro-α-D-altroside	0·64	0·45	0·51	
Me 3,4-anhydro-α-D-galactoside			0·47	
Me 2,3-anhydro-α-D-guloside			0·44	
Me 2,3-anhydro-α-D-mannoside	0·69	0·61	0·57	
Me 2,3-anhydro-α-D-taloside			0·42	
5,6-Anhydro-1,2-*O*-isopropylidene-α-D-glucose †			0·77	
Me 3,4-anhydro-6-*O*-trityl-α-D-altroside				0·57
Me 2,3-anhydro-6-*O*-trityl-α-D-mannoside				0·75

* Absolute R_F values not reproducible. † Appeared as soon as the sprayed paper was dry.

isolated in chloroform. It crystallised from light petroleum as needles (0·34 g., 41%), m. p. 108°, raised to m. p. 109° by recrystallisation from ether–light petroleum, $[\alpha]_D^{25}$ +57·1° (*c* 1·86 in chloroform) (Found: C, 49·5; H, 6·4. $C_{15}H_{22}O_{10}$ requires C, 49·8; H, 6·1%).

Methyl 4,6-O-*Benzylidene*-α-D-*mannoside*.—Finely powdered methyl α-D-mannoside (40 g.) was dissolved as rapidly as possible in 98—100% formic acid (200 c.c.), and redistilled benzaldehyde (200 c.c.) was immediately added to the solution. After 5 min. the mixture was poured with stirring into light petroleum (b. p. 60—80°; 1600 c.c.) and water (1600 c.c.) containing potassium carbonate (550 g.; anhydrous). Inorganic material separated from the aqueous layer, which was discarded. The upper layer was filtered and the residue washed with light petroleum. Crystallised from chloroform–benzene it gave needles (19 g.), m. p. 140—143°, $[\alpha]_D^{21}$ +61° (*c* 1·84 in chloroform).

Toluene-p-*sulphonates*.—*Methyl* 4,6-O-*benzylidene*-2,3-*di*-O-*toluene*-p-*sulphonyl*-α-D-*mannoside*. Methyl 4,6-*O*-benzylidene-α-D-mannoside (0·5 g.) was treated with toluene-*p*-sulphonyl chloride and pyridine according to Vis and Karrer's method [27] for the corresponding glucoside. After two crystallisations from ethanol–acetone, the *product* (0·6 g., 57%) had m. p. 163—164°, $[\alpha]_D^{20}$ −5·3° (*c* 2·25 in chloroform) (Found: C, 57·2; H, 4·9; S, 10·3. $C_{28}H_{30}O_{10}S_2$ requires C, 56·9; H, 5·1; S, 10·8%).

Methyl 4,6-O-*benzylidene*-3-O-*toluene*-p-*sulphonyl*-α-D-*mannoside*. Methyl 4,6-*O*-benzylidene-α-D-mannoside (15 g.) in pyridine (75 c.c.) was cooled below −10° and treated with toluene-*p*-sulphonyl chloride (11·1 g.) in pyridine (50 c.c.), also cooled to −10°. The mixture was kept at 0° for 24 hr. After 48 hr. at room temperature a few drops of water were added and after 30 min. the mixture was poured into water. The product was isolated by using chloroform, giving a syrup which was crystallised three times from benzene and then from ethanol. The 3-*toluene*-p-*sulphonate* (9 g.) had m. p. 151—153°, $[\alpha]_D^{17}$ +21° (*c* 2·57 in chloroform) (Found: C, 57·9; H, 5·5; S, 6·9. $C_{21}H_{24}O_8S$ requires C, 57·8; H, 5·5; S, 7·3%). The mother-liquors on evaporation and crystallisation from methanol gave the ditoluene-*p*-sulphonate (1·5 g.).

Methyl 3-O-*toluene*-p-*sulphonyl*-α-D-*mannoside*. The above sulphonate (4·12 g.) was dissolved in methanol (38 c.c.) and 0·6N-methanolic hydrogen chloride (2 c.c.) was added. After 14 hr. at room temperature (rotation constant) the solution was neutralised with silver carbonate and filtered. Evaporation gave a syrup which crystallised on trituration with light petroleum. The *sulphonate* (3·4 g.) had m. p. 90—100° and recrystallised from benzene, ethyl acetate–light petroleum, or ether as thin needles (solvates?) which melted below 100° over a wide and variable range [Found (on sample crystallised from ether and dried at 60°): C, 48·6; H, 6·0; S, 8·4. $C_{14}H_{20}O_8S$ requires C, 48·3; H, 5·8; S, 9·2%]. The material was used in subsequent experiments without further purification. No periodate was consumed when the compound was dissolved in 0·1M-sodium periodate and kept for 17 hr.

A syrup, obtained on concentration of an aqueous solution of the toluene-*p*-sulphonate which had been clarified with charcoal, later crystallised spontaneously and recrystallisation from water (*ca.* 5 vol.) yielded prisms, m. p. 120—121·5°, $[\alpha]_D^{17}$ +35° (*c* 2 in water) (Found: C, 48·1; H, 5·8; S, 9·4%). Crystallisation of the prisms from benzene again gave needles having an indefinite m. p.

Methyl 2,4,6-*tri*-O-*acetyl*-3-O-*toluene*-p-*sulphonyl*-α-D-*mannoside*. The above sulphonate

[27] Vis and Karrer, *Helv. Chim. Acta*, 1954, **37**, 378.

(0·28 g.) was set aside overnight with pyridine (1·5 c.c.) and acetic anhydride (0·7 c.c.). The *triacetate*, which separated on addition of water, was crystallised twice from ethanol, to give plates (0·28 g., 73%), m. p. 127·5—128·5°, $[\alpha]_D^{24}$ +26·6° (*c* 1·74 in chloroform) (Found: C, 50·4; H, 5·9; S, 6·3. $C_{20}H_{26}O_{11}S$ requires C, 50·6; H, 5·5; S, 6·75%).

Methyl 2-O-*toluene*-p-*sulphonyl*-6-O-*triphenylmethyl*-α-D-*glucoside*. Methyl 2-*O*-toluene-*p*-sulphonyl-α-D-glucoside (5·72 g.) in pyridine (25 c.c.) was treated with triphenylmethyl chloride (5·0 g.) at room temperature for 4 days. Isolation by means of chloroform gave the *triphenylmethyl ether* which, crystallised from ether–light petroleum (7·4 g., 76%), had m. p. 153—156°. Recrystallised from ethyl acetate–light petroleum it had m. p. 159—160°, $[\alpha]_D^{23}$ +46·1° (*c* 2·02 in chloroform) (Found: C, 66·8; H, 6·2. $C_{33}H_{34}O_8S$ requires C, 67·1; H, 5·8%).

Methyl 3-O-*toluene*-p-*sulphonyl*-6-O-*triphenylmethyl*-α-D-*mannoside*. Methyl 3-*O*-toluene-*p*-sulphonyl-α-D-mannoside (2·1 g.) in pyridine (10 c.c.) was treated with triphenylmethyl chloride (2·0 g., 1·2 mol.) at room temperature for 5 days. The ether was isolated by use of chloroform and crystallised from moist chloroform–light petroleum (b. p. 60—80°) (yield 2·83 g.. 77%; m. p. 98—100°). Recrystallised from aqueous methanol it had m. p. 104°, $[\alpha]_D^{23}$ +29·2° (*c* 2·40 in chloroform) (Found: C, 65·2; H, 6·0; S, 4·9. $C_{33}H_{34}O_8S,H_2O$ requires C, 65·2; H, 5·9; S, 5·3%). The anhydrous compound did not crystallise from anhydrous solvents. The infrared spectrum of the crystalline material showed a hydrate band at 1639 $cm.^{-1}$.

2,3-*Anhydro-mannosides*.—*Methyl* 2,3-*anhydro*-α-D-*mannoside*. (*a*) Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside (5·0 g.) was heated with methanol (30 c.c.) and 0·01N-sulphuric acid (100 c.c.) under reflux until all the solid had dissolved (½ hr.).[8] Methanol was removed by distillation, and the remaining solution extracted with benzene. The aqueous layer was neutralised with barium carbonate, and the filtrate evaporated to dryness. The syrup was dissolved in ethanol and ethyl acetate (100 c.c. of each) and filtered through neutral alumina (20 g.) which was washed with 200 c.c. of the same solvent. The combined filtrates were evaporated to a syrup which crystallised from chloroform–light petroleum, to give the anhydromannoside (2·93 g., 88%), m. p. 81—82°, $[\alpha]_D^{20}$ +108° (*c* 1·40 in chloroform) (Found: C, 47·9; H, 7·1. Calc. for $C_7H_{12}O_5$: C, 47·7; H, 6·9%). Jeanloz and Jeanloz [9] report m. p. 82—83°, $[\alpha]_D$ +108° (in chloroform). The anhydromannoside was not oxidised by 0·1M-sodium metaperiodate during 24 hr. When treated with benzaldehyde and zinc chloride it gave methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside (mixed m. p.).

(*b*) Methyl 3-*O*-toluene-*p*-sulphonyl-α-D-mannoside (0·3 g.) was treated with N-sodium hydroxide (20 c.c.) for 18 hr. at room temperature. The solution was neutralised with N-sulphuric acid and evaporated to small volume. Ethanol was added, solids were removed by filtration, and the filtrate was evaporated to dryness. The residue was extracted with chloroform, and the extract chromatographed on silica gel (30 g.). The column was developed with chloroform–ethanol (24 : 1). Chloroform–ethanol (19 : 1) eluted first methyl 2,3-anhydro-α-D-mannoside (0·07 g., 46%), m. p. 80—81°, followed by a mixture consisting mainly of methyl 3,4-anhydro-α-D-altroside with a little anhydromannoside (total, 0·02 g.).

Methyl 2,3-*anhydro*-6-O-*triphenylmethyl*-α-D-*mannoside*. (*a*) The above anhydro-compound (2·0 g.) was treated with triphenylmethyl chloride (3·5 g., 1·1 mol) in pyridine (15 c.c.) for 42 hr. at room temperature. Isolated by means of benzene, the *triphenylmethyl compound* crystallised on trituration with light petroleum. From ethyl acetate–light petroleum it gave prisms (4·29 g., 90%), m. p. 160—161°, $[\alpha]_D^{23}$ +15·6° (*c* 2·08 in chloroform) (Found: C, 74·5; H, 6·4. $C_{26}H_{26}O_5$ requires C, 74·6; H, 6·3%).

(*b*) Methyl 3,4-anhydro-6-*O*-triphenylmethyl-α-D-altroside (see below) (0·12 g.) was boiled with methanol (10 c.c.) containing sodium methoxide (0·03 g. of sodium) under reflux for 1 hr. After neutralisation by carbon dioxide and evaporation, the residue crystallised from aqueous methanol, giving the anhydromannoside (0·095 g., 79%), m. p. 159—160°, identical with that described in (*a*). The mother-liquors were extracted with chloroform, giving eventually a syrup (0·02 g.) which was examined by paper chromatography in dimethyl sulphoxide–isopropyl ether. The sodium iodide–Methyl Red reagent showed two spots, corresponding to anhydromannoside and anhydroaltroside. The perchloric acid reagent showed, in addition, two weaker spots of lower R_F value, probably methyl ethers.

(*c*) Methyl 2-*O*-toluene-*p*-sulphonyl-6-*O*-triphenylmethyl-α-D-glucoside (4·5 g.) was heated with sodium methoxide (0·6 g. of sodium) in methanol (75 c.c.) under reflux for 3½ hr. An excess of water was added and the mixture extracted with benzene. The benzene extract was washed with water, dried (Na_2SO_4), and evaporated to a brown syrup. A benzene solution

of this was chromatographed on silica gel (100 g.). Benzene–ether (19 : 1) eluted the anhydromannoside (1·39 g.), m. p. 158—160° when crystallised from light petroleum, identical with that described in (*a*).

Methyl 4-O-*acetyl*-2,3-*anhydro*-6-O-*triphenylmethyl*-α-D-*mannoside*. The above triphenylmethyl compound (2·0 g.) was treated with acetic anhydride (2 c.c.) in pyridine (10 c.c.) at room temperature overnight. The *acetate*, m. p. 138—140°, crystallised in quantitative yield on the addition of water. From methanol or light petroleum (b. p. 60—80°) it gave prisms, m. p. 140—141°, $[\alpha]_D^{24}$ +50·4° (*c* 1·57 in chloroform) (Found: C, 72·9; H, 6·3. $C_{28}H_{28}O_6$ requires C, 73·0; H, 6·5%).

3,4-*Anhydroaltrosides*.—*Methyl* 3,4-*anhydro*-α-D-*altroside*. (*a*) A solution of methyl 3-*O*-toluene-*p*-sulphonyl-α-D-mannoside (0·2 g.) and B.D.H. Universal Indicator (1 drop) in water (5 c.c.) was heated to 80°, and 2N-sodium hydroxide was added dropwise, the indicator colour being green before each addition. When the colour became permanently blue the solution was neutralised with dilute sulphuric acid and examined chromatographically in solvent B. A very strong spot of anhydroaltroside and a very faint one of anhydromannoside were formed. The solution was extracted with ethyl acetate to remove any starting material, and then evaporated. The residue was extracted with chloroform, and the extract chromatographed on silica (5 g.). Chloroform–ethanol (19 : 1) eluted first a fraction containing anhydroaltroside and anhydromannoside (0·02 g.), then *anhydroaltroside* (0·08 g., 79%), $[\alpha]_D^{23}$ +97·3°, (*c* 3·61 in water) (Found: C, 43·1; H, 7·0. $C_7H_{12}O_5,H_2O$ requires C, 43·3; H, 7·2%.)

(*b*) A solution of methyl 2,3-anhydro-α-D-mannoside in N-sodium hydroxide showed a 4% decrease in rotation on being kept at room temperature. The half-life of the reaction was ~30 min. After 4 hr. the mixture was neutralised with carbon dioxide, then carefully evaporated, and the residue was extracted with cold ethanol. Paper chromatography of the extract showed a main spot of starting material, together with weak spots of 3,4-anhydroaltroside and methyl α-D-altroside.

Methyl 3,4-*anhydro*-6-O-*triphenylmethyl*-α-D-*altroside*. (*a*) Methyl 3,4-anhydro-α-D-altroside (0·165 g.) was treated with triphenylmethyl chloride (0·25 g., 0·96 mol.) in pyridine (5 c.c.) for 46 hr. at room temperature. Isolation in benzene gave a syrup (0·3 g.) which was dissolved in benzene (20 c.c.) and chromatographed on silica (10 g.). Benzene eluted triphenylmethanol, and benzene–ether (19 : 1) eluted the *ether* (0·08 g.), which, crystallised from ether–light petroleum, had m. p. 104° (Found: C, 74·2; H, 6·6. $C_{26}H_{26}O_5$ requires C, 74·6; H, 6·3%).

(*b*) Methyl 2-*O*-acetyl-3,4-anhydro-6-*O*-triphenylmethyl-α-D-altroside (see below) (0·23 g.) was deacetylated catalytically with sodium methoxide in methanol. Crystallisation from aqueous methanol gave the anhydroaltroside (0·20 g.), m. p. 135—136°, $[\alpha]_D^{20}$ +22·3° (*c* 1·25 in chloroform). It had a different infrared spectrum from the sample of m. p. 104°, and the m. p. of the latter was raised to 135° by nucleation. The spectra were then identical.

Methyl 2-O-*acetyl*-3,4-*anhydro*-6-O-*triphenylmethyl*-α-D-*altroside*. (*a*) The preceding anhydrocompound (0·02 g.) was acetylated with acetic anhydride (0·1 c.c.) in pyridine (0·2 c.c.) at room temperature for 20 hr. Dilution with water gave a solid which crystallised from aqueous methanol, m. p. 143—143·5°.

(*b*) Methyl 3-*O*-toluene-*p*-sulphonyl-6-*O*-triphenylmethyl-α-D-mannoside hydrate (2·5 g.) was treated with sodium methoxide (from 0·15 g. of sodium; 1·6 mol.) in methanol (30 c.c. for 24 hr. at room temperature. A paper chromatogram in solvent D after 23 hr. showed that all starting material had disappeared and that there was more anhydroaltroside than anhydromannoside present. Water was added, and the anhydro-compounds were extracted with chloroform, washed with water, and dried (Na_2SO_4). The syrup obtained by evaporation was treated overnight with acetic anhydride (5 c.c.) in pyridine (10 c.c.), and the acetates were isolated by using benzene. The resulting syrup gave, on crystallisation from methanol or cyclohexane (with appropriate nucleation), the pure *anhydroaltroside* (1·15 g., 61%), m. p. 143—143·5°, $[\alpha]_D^{25}$ +22·4° (*c* 1·02 in chloroform) (Found: C, 73·4; H, 6·2. $C_{28}H_{28}O_6$ requires C, 73·0; H, 6·5%), and also the anhydromannoside (0·27 g., 14%), m. p. 142—143°, identical with an authentic sample.

(*c*) Methyl 2,3-anhydro-6-*O*-triphenylmethyl-α-D-mannoside (5 g.) was heated under reflux with sodium methoxide (0·1 g. of Na) in methanol (30 c.c.) for 1½ hr. The solution was cooled; by crystallisation from aqueous methanol starting material (4·2 g.), m. p. 160—161°, was obtained. Extraction of the aqueous mother-liquors with chloroform gave finally a syrup (0·7 g.) which was chromatographed from benzene solution on neutral silica (50 g.). Benzene–

ether (9 : 1) eluted more starting material (0·05 g.), followed by a syrup (0·4 g.) which on rechromatography and elution with benzene–ether (19 : 1) gave a little starting material followed by the anhydroaltroside. Acetylation of the later fractions gave the anhydro-acetate (0·05 g.), m. p. 143—144° (from methanol), identical with that reported in (*a*).

Comparison of Hydrolysis of Anhydro-sugars by 80% *Acetic Acid.*—The sugars named in Table 1 (5 mg. of hydroxy-compound, 6 mg. of the acetate) were dissolved in warm 80% acetic acid (v/v) (0·1 c.c.), and samples were heated at 100° for periods of 10 min., 30 min., 1 hr., 2 hr., 3 hr., and 4 hr. severally. The samples were examined chromatographically by using the sodium iodide–Methyl Red and sodium periodate–Schiff sprays. The results are shown in Table 1.

Hydrolysis of Methyl 4-O-*Acetyl*-2,3-*anhydro*-6-O-*triphenylmethyl*-α-D-*mannoside with* 80% *Acetic Acid.*—The sugar (0·25 g.) in 80% acetic acid (v/v) (5 c.c.) was heated at 100° for 30 min. Addition of water caused separation of triphenylmethanol (0·14 g., 99%), which was removed. The filtrate was evaporated to dryness and acetylated with acetic anhydride in pyridine overnight. Isolation by using chloroform gave a syrup which crystallised from water on addition of a seed of methyl α-D-altropyranoside tetra-acetate. The acetate (0·13 g., 66%) had m. p. 89—90° and was identical with a sample kindly supplied by Dr. N. K. Richtmyer. The mother-liquors were evaporated to dryness and deacetylated with sodium methoxide in methanol, and the products were examined by paper chromatography. Methyl altroside was by far the major component: traces of altrose and methyl 2,3-anhydro-α-D-mannoside were present. No other compounds were detected.

Hydrolysis of Methyl 2-O-*Acetyl*-3,4-*anhydro*-6-*triphenylmethyl*-α-D-*altroside with* 80% *Acetic Acid.*—The sugar (0·25 g.) was treated as above, but hydrolysis was for 1 hr. Triphenylmethanol (0·135 g., 95%) was obtained. The syrupy acetate mixture crystallised from light petroleum and then from water, to give methyl α-D-mannopyranoside tetra-acetate (0·14 g., 71%), m. p. 63—64°, identical with an authentic sample. The mother-liquors were evaporated and deacetylated catalytically. Methyl α-D-mannoside (12 mg., 11%) crystallised and the methanolic mother-liquors were examined chromatographically in solvent A. No anhydro-compound was present; there was a strong spot of methyl mannoside and a weak one of methyl idoside; a trace of mannose was present and an unidentified compound, of R_F value slightly higher than methyl idoside, giving a yellow colour with the periodate–Schiff reagents.

Hydrolysis of Methyl 3,4-*Anhydro*-6-O-*triphenylmethyl*-α-D-*altroside with* 80% *Acetic Acid.*—The sugar (0·2 g.) was heated with 80% acetic acid (v/v) (5 c.c.) at 100° for 5 hr. Water was added and triphenylmethanol (0·13 g., 100%) filtered off. The filtrate was evaporated to dryness and chromatographed in solvent B on two sheets of Whatman no. 1 paper. Methyl idoside, methyl mannoside, and methyl 3,4-anhydroaltroside were present. The band corresponding to methyl α-D-idoside was extracted with methanol (Soxhlet), and the extract evaporated to a syrup which was treated with acetic anhydride (1 c.c.) and pyridine (5 c.c.) overnight. Isolation in chloroform gave methyl α-D-idoside tetra-acetate, m. p. 108° (from ether–light petroleum), identical with an authentic sample.

Treatment of Methyl 2,3-*Anhydro*-α-D-*mannoside with Alkali at* 100°.—The anhydro-sugar (9 mg.) was heated with N-sodium hydroxide (0·1 c.c.) at 100° for 1 hr. in a sealed tube. The solution was diluted with water, passed through a short column of Dowex 50 (NH_4^+) resin, and evaporated to dryness. The residue was examined by paper chromatography in solvent A Methyl α-D-altroside was by far the major product, together with a trace of methyl idoside. No starting material or methyl 3,6-anhydro-α-D-mannoside was detected; nor was 3,6-anhydro-mannose present in an acid hydrolysate (0·05N-H_2SO_4 at 100° for 1 hr.).

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