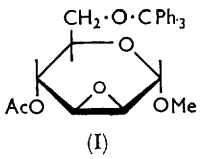
350. *Methyl 2,3-Anhydro-α-D-mannoside and 3,4-Anhydro-α-D-altroside and their Derivatives. Part III.*[1]

By J. G. Buchanan and R. M. Saunders.

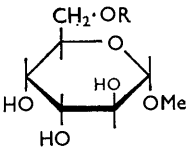
When methyl 4-*O*-acetyl-2,3-anhydro-6-*O*-trityl-α-D-mannoside is treated with aqueous sulphuric acid in acetone, the products are methyl α-D-altroside and its 6-acetate together with methyl 3,4-*O*-isopropylidene-α-D-altroside and its 6-acetate. The preparation of the 3,4- and 4,6-*O*-isopropylidene derivatives of methyl α-D-altroside is described. Methyl 4,6-*O*-isopropylidene-α-D-galactoside is formed in appreciable quantity, together with the well known 3,4-ketal, when methyl α-D-galactoside is treated with acetone and sulphuric acid or zinc chloride. Suggestions are made regarding the role of zinc chloride as a catalyst in cyclic ketal formation.

It has been shown that, when methyl 4-*O*-acetyl-2,3-anhydro-6-*O*-trityl-α-D-mannoside (I) is treated with 80% acetic acid, a derivative of methyl α-D-altroside (II) is produced in high yield.[2] The reaction between the anhydromannoside (I) and aqueous sulphuric acid in acetone was also investigated, but difficulties were encountered. We now describe some of the points of chemical interest which have emerged from this study.

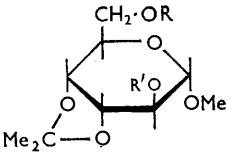
Many anhydro-sugars have been studied with respect to reaction with aqueous mineral acid. In several cases the solvent was aqueous acetone,[3-9] and this can be traced back to the work of Robertson and Dunlop.[3] In the case of the anhydromannoside (I), it was expected that aqueous sulphuric acid in acetone would cause removal of the trityl group and ring-cleavage of the epoxide, to yield monoacetates of methyl α-D-altroside. Acetylation of the crude product did yield methyl α-D-altroside tetra-acetate, and also a syrupy



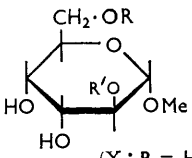
(I)



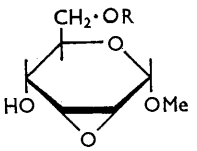
(II: R = H)
(III: R = Ac)



(IV: R = Ac, R' = H)
(V: R = R' = H)
(VI: R = CPh₃, R' = H)
(VII: R = R' = CPh₃)
(VIII: R = CPh₃, R' = Me)
(IX: R = Ac, R' = Ts)



(X: R = H, R' = Me)
(XI: R = Ac, R' = Ts)



(XII)

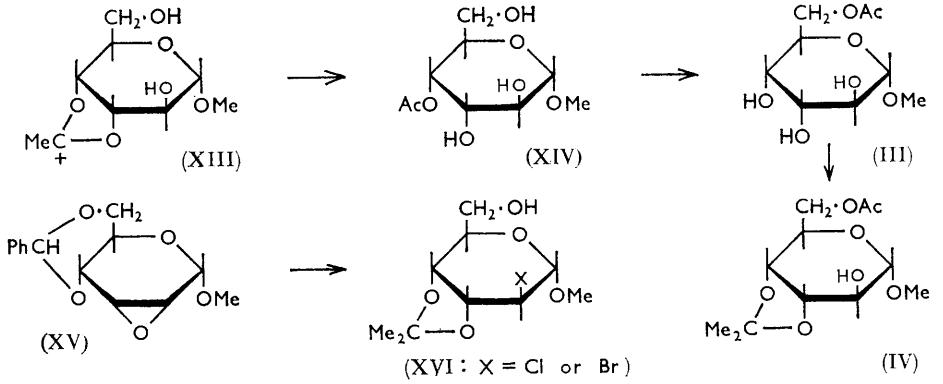
compound. When the crude hydrolysis product was examined in detail, four compounds were detected by paper chromatography, and these have all been identified. Methyl α-D-altroside (II) and its 6-acetate (III) were shown to be present; the location of the *O*-acetyl group in the latter was determined by periodate oxidation. The two other products could be detected on paper chromatograms by periodic acid–Schiff's reagent [10]

[1] Part II, preceding paper.
[2] Buchanan and Schwarz, *J.*, 1962, 4770.
[3] Robertson and Dunlop, *J.*, 1938, 472.
[4] Newth, Overend, and Wiggins, *J.*, 1947, 10.
[5] Mukherjee and Srivastava, *Proc. Indian Acad. Sci.*, 1952, **35**, 178.
[6] Newth and Homer, *J.*, 1953, 989.
[7] Labaton and Newth, *J.*, 1953, 992.
[8] Buchanan, *J.*, 1958, 995.
[9] Buchanan, *J.*, 1958, 2511.
[10] Buchanan, Dekker, and Long, *J.*, 1950, 3162.

but not by sodium periodate–Schiff's reagent;[10,11] this was the first indication, together with the high R_F values of the spots, that *O*-isopropylidene compounds were present. Each of the *O*-isopropylidene compounds was isolated in crystalline form, one directly from a chloroform extract of an aqueous solution of the crude mixture, and the other after chromatography on silica. The former compound was methyl 6-*O*-acetyl-3,4-*O*-isopropylidene-α-D-altroside (IV), and the latter its deacetylated derivative, methyl 3,4-*O*-isopropylidene-α-D-altroside (V). The structure of compound (V) was shown by the following sequence: tritylation gave the mono (VI) and di-ether (VII), both crystalline; methylation of the monotrityl compound gave a crystalline methyl ether (VIII), and subsequent acid hydrolysis yielded methyl 2-*O*-methyl-α-D-altroside (X).[12] It may be argued that this evidence does not eliminate a 4,6-structure for the ketal, since secondary hydroxyl groups are known to react slowly with trityl chloride.[13] However, as will be shown later, the 4,6-isomer has been prepared by an unambiguous route, and the 3,4-structure assigned to the present compound can be considered proved.

The structure of the acetate (IV) followed from its deacetylation to the diol (V); the acetyl group must therefore occupy the 2- or the 6-position. Toluene-*p*-sulphonylation gave the syrupy ester (IX) which, on mild acid treatment, yielded crystalline methyl 6-*O*-acetyl-2-*O*-toluene-*p*-sulphonyl-α-D-altroside (XI); treatment of this ester with alkali gave methyl 2,3-anhydro-α-D-alloside (XII).[3] Had the original acetyl group been on the 2-position the final product would have been methyl 2,6-anhydro-α-D-altroside.[14]

From the earlier work on the anhydromannoside (I) [2] it is probable that the carbonium ion (XIII) is an intermediate in the acid hydrolysis. This gives the 4-acetate (XIV) by way of the ortho-ester, and the acetyl group then migrates (presumably *via* an ortho-ester) to give the 6-acetate (III). The *O*-isopropylidene compound (IV) is then formed in the usual way. Acyl migrations under acidic conditions are not uncommon,[15,16] although most work has been done on alkali-catalysed migrations (see ref. 17 for a list of references). Presumably the C-4 ⟶ C-6 migration occurs while the sugar is in the Cl conformation.

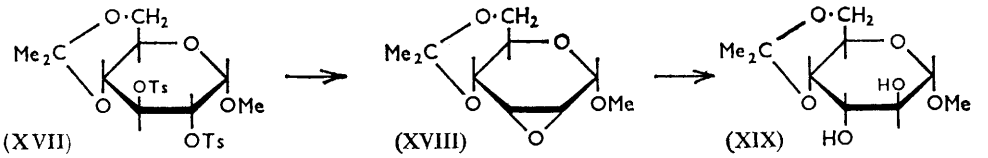


The formation of isopropylidene compounds is not altogether surprising considering the reaction medium. In this light, it is probable that two unidentified compounds arising from the action of hydrochloric and hydrobromic acid, respectively, on methyl-2,3-anhydro-4,6-*O*-benzylidene-α-D-alloside (XV) in acetone are methyl 2-deoxy-2-halogeno-3,4-*O*-isopropylidene-α-D-altrosides (XVI).[4] The results of analysis, by periodate

[11] Baddiley, Buchanan, Handschumacher, and Prescott, *J.*, 1956, 2818.
[12] Robertson and Griffith, *J.*, 1935, 1193.
[13] Helferich, *Adv. Carbohydrate Chem.*, 1948, **3**, 79.
[14] Rosenfeld, Richtmyer, and Hudson, *J. Amer. Chem. Soc.*, 1948, **70**, 2201.
[15] Van Lohuizen and Verkade, *Rec. Trav. chim.*, 1960, **79**, 133.
[16] Lemieux and Barrette, *J. Amer. Chem. Soc.*, 1958, **80**, 2243.
[17] Bonner, *J. Org. Chem.*, 1959, **24**, 1388.

oxidation, of chlorohydrin mixtures arising from such reactions [5] must be interpreted with caution.

O-Isopropylidene derivatives of methyl α-D-altroside have not been described hitherto, and we have examined the formation of such compounds from methyl α-D-altroside and acetone, using sulphuric acid or zinc chloride as catalysts. With sulphuric acid the 3,4-*O*-isopropylidene compound (V) was isolated, identical with the product described earlier; when the reaction was prolonged, or a higher acid concentration used, a small quantity of 1,2:5,6-di-*O*-isopropylidene-β-D-altrofuranose was isolated.[18] When zinc chloride was used as catalyst, two isomeric methyl *O*-isopropylidene-α-D-altrosides were isolated. Chromatography of the mixture on silica gave first a new isomer, m. p. 161—163°, $[\alpha]_D$ +112·7°, in 10% yield, then the known isomer, m. p. 61—62°, $[\alpha]_D$ +102°, in 38% yield. The two compounds had different R_F values in the dimethyl sulphoxide–di-isopropyl ether system.[19] The new isomer was shown to be methyl 4,6-*O*-isopropylidene-α-D-altroside (XIX) by rational synthesis. Methyl 4,6-*O*-isopropylidene-2,3-di-*O*-toluene-*p*-sulphonyl-α-D-glucoside (XVII) was prepared by Jones's method.[20] Treatment with sodium methoxide under conditions similar to those employed for the *O*-benzylidene compound [21] yielded a syrupy anhydro-compound, shown to be the *allo*-isomer (XVIII) by mild acid treatment;

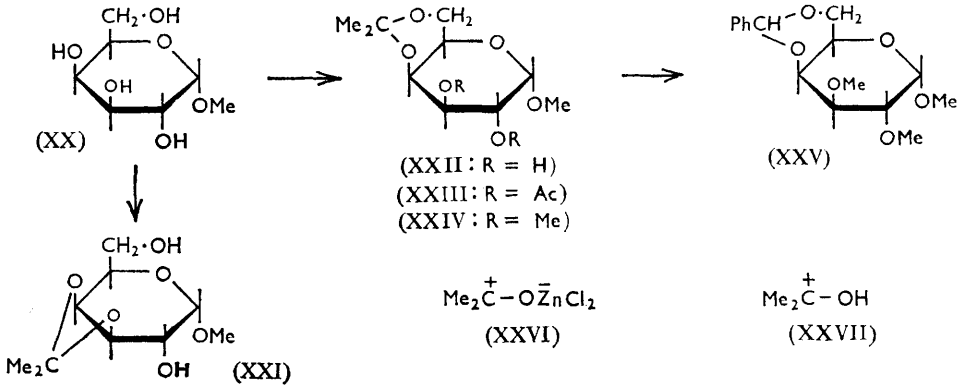


the anhydroalloside (XII) was detected by paper chromatography,[2] and no anhydro-mannoside was present. The formation of only the anhydroalloside (XV) from the disulphonate occurs also in the *O*-benzylidene series.[12,21] When the anhydroalloside (XVIII) was heated with aqueous potassium hydroxide, methyl 4,6-*O*-isopropylidene-α-D-altroside was isolated, clearly differing from the corresponding glucoside which is the only other possible product of alkaline ring-scission. It was indistinguishable from the higher-melting *O*-isopropylidene compound derived from the zinc chloride-catalysed acetonation reaction.

When crude acetonation mixtures were examined by paper chromatography [19] it was found that the sulphuric acid product contained solely the 3,4-isomer, whereas the zinc chloride product contained both isomers. Similarly, the crude mixture obtained from the action of aqueous sulphuric acid in acetone on the anhydromannoside (I) contained no 4,6-isomer. Since the 4,6-isomer was formed only in the zinc chloride-catalysed reaction, the behaviour of methyl α-D-galactoside (XX) towards acetone and sulphuric acid or zinc chloride was investigated. Methyl 3,4-*O*-isopropylidene-α-D-galactoside (XXI) is the well-known product of reaction in the presence of hydrogen chloride,[22] sulphuric acid,[23] anhydrous copper sulphate,[24] and phosphorus pentoxide.[25] The product is usually distilled before crystallisation occurs. In our experiments using sulphuric acid, paper chromatography showed the presence of two products as well as starting material. Column chromatography on neutral silica gel gave the crystalline isomer (XXI) in 47% yield, identified by its physical constants [22–25] and by conversion into the diacetate.[23] The

[18] Newth and Wiggins, *J.*, 1950, 1734.
[19] Wickberg, *Acta Chem. Scand.*, 1958, **12**, 615.
[20] Jones, *Canad. J. Chem.*, 1956, **34**, 840.
[21] Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1727.
[22] Ault, Haworth, and Hirst, *J.*, 1935, 1012.
[23] Foster, Overend, Stacey, and Wiggins, *J.*, 1949, 2542.
[24] Schmidt and Wernicke, *Annalen*, 1947, **558**, 70.
[25] Wolfrom, Shafizadeh, Armstrong, and Shen Han, *J. Amer. Chem. Soc.*, 1959, **81**, 3716.

second product, in 16% yield, was not crystalline but was identified as methyl 4,6-*O*-isopropylidene-α-D-galactoside (XXII) by its subsequent chemical behaviour. It reacted with 1·01 mol. of periodate during 48 hr., and on mild acid hydrolysis gave methyl α-D-galactoside (XX), identified chromatographically. It gave a crystalline diacetate (XXIII) whose properties differed from the acetate of the 3,4-ketal. It also gave, on methylation, a crystalline ether (XXIV); the corresponding ether of the 3,4-isomer is a syrup.[26] Mild



acid hydrolysis of the ether gave syrupy methyl 2,3-di-*O*-methyl-α-D-galactoside, the rotation of which was in agreement with the literature value,[26] and subsequent treatment with benzaldehyde and zinc chloride yielded the crystalline acetal (XXV), identical with an authentic sample.[27]

When zinc chloride was used as catalyst, each isomer, (XXI) and (XXII), was isolated in 28% yield. As in the altroside series, zinc chloride favoured the production of the 4,6-ketal. We believe that the main difference between sulphuric acid and zinc chloride as catalysts is that the zinc chloride reaction is essentially irreversible, the zinc chloride behaving as a dehydrating agent as well as a Lewis acid. This is indicated by the behaviour of methyl α-D-glucoside. Jones [20] was able to prepare the 4,6-*O*-isopropylidene derivative using acetone and zinc chloride, and we have confirmed Ault, Haworth, and Hirst's observation [22] that, with an acid catalyst, no ketal is formed.

Where two isomers are possible, the composition of the mixture will be under kinetic control in the case of zinc chloride; the products of catalysis by strong acid are in a state of equilibrium,[28-30] and the thermodynamically stable isomer prevails. In the case of fructose, zinc chloride [31] and low acid concentrations [32] lead to the same isomer 1,2:4,5-di-*O*-isopropylidene-D-fructose, whereas higher concentrations of strong acid [32] yield 2,3:4,5-di-*O*-isopropylidene-D-fructose; presumably, when low acid concentrations were used the product was isolated before the attainment of equilibrium. It is interesting that, in the case of methyl α-D-altroside and acetone containing sulphuric acid, only the 3,4-ketal is present, probably owing to the presence of axial hydroxyl groups on C-2 and C-3 in the 4,6-ketal.[33,34]

A further point may be made. The acetone–zinc chloride complex (XXVI), which is the most likely intermediate in ketal formation in the presence of zinc chloride, will have

[26] Bell and Williamson, *J.*, 1938, 1196.
[27] Bell and Greville, *J.*, 1955, 1136.
[28] Hann and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 1909.
[29] Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.
[30] Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.
[31] Fischer and Taube, *Ber.*, 1927, **60**, 485.
[32] Ohle and Koller, *Ber.*, 1924, **57**, 1566.
[33] Reeves, *Adv. Carbohydrate Chem.*, 1951, **6**, 107.
[34] Honeyman and Shaw, *J.*, 1959, 2454.

greater steric requirements than the carbonium ion (XXVII), and may show preference for primary hydroxyl groups. Further work is necessary to distinguish these factors.

Experimental

The general methods employed were described in Part I.[2] The following solvent systems were used for paper chromatography: (A) butan-1-ol–water (86 : 14, v/v); (B) dimethyl sulphoxide–di-isopropyl ether.[19] Vicinal epoxides were detected with sodium iodide and Methyl Red,[2] and α-glycols with periodate and Schiff's reagent.[10,11] The detection of *O*-isopropylidene compounds with periodic acid and Schiff's reagent [10] was modified as follows: the chromatogram was sprayed with a solution of sodium periodate (1 g.) in 2N-sulphuric acid (100 c.c.) and left for 7 min. The excess of periodate was destroyed by treatment with gaseous sulphur dioxide, and the chromatogram was sprayed with Schiff's reagent.[11]

Hydrolysis of Methyl 4-O-Acetyl-2,3-anhydro-6-O-trityl-α-D-mannoside with Sulphuric Acid in Acetone.—(*a*) The anhydromannoside (1 g.) was heated under reflux in acetone (50 c.c.) containing aqueous 2N-sulphuric acid (1·5 c.c.) for 4 hr. The solution was cooled, neutralised with barium carbonate, filtered, and the filtrate evaporated to small volume. Water was added and the triphenylmethanol (0·56 g., 99%) filtered off. The resulting filtrate was examined by paper chromatography in solvent A. Neutral periodate–Schiff's reagent showed two spots, R_F 0·25 (methyl α-D-altroside) and 0·47 (methyl *O*-acetyl-α-D-altroside). Acid periodate–Schiff's reagent showed four spots, all dark green in colour, R_F 0·25, 0·47, 0·70 (methyl *O*-isopropylidene-α-D-altroside), and 0·81 (methyl *O*-acetyl-*O*-isopropylidene-α-D-altroside). By treatment with alkali, the compound of R_F 0·47 was converted into that of R_F 0·25 which was itself unaffected; that of R_F 0·81 was converted into that of R_F 0·70. No methyl α-D-glucoside or glucose was detected before or after deacetylation. The above filtrate was evaporated to dryness and acetylated with acetic anhydride and pyridine. The acetates were isolated with chloroform, and chromatographed in benzene–light petroleum (1 : 1) on silica (12 g.). Benzene–ether (19 : 1) eluted the syrupy *O*-isopropylidene compound which was not examined further. Benzene–ether (9 : 1) eluted methyl α-D-altroside tetra-acetate (0·17 g.), indistinguishable from an authentic sample.

(*b*) Methyl 4-*O*-acetyl-2,3-anhydro-6-*O*-trityl-α-D-mannoside (9 g.) was dissolved in acetone (450 c.c.) containing 2N-sulphuric acid (13·5 c.c.), and heated under reflux for 4 hr. The solution was neutralised with barium carbonate, filtered, and concentrated to small volume. Water (150 c.c.) was added, and the precipitated triphenylmethanol filtered off. The filtrate was concentrated to 120 c.c. and extracted thrice with chloroform (30 c.c.). Both phases were retained. The chloroform extracts were dried ($MgSO_4$) and evaporated to dryness, giving *methyl 6-O-acetyl-3,4-O-isopropylidene-α-D-altroside*, prisms (1·42 g., 26%), m. p. 68° (from ether–light petroleum), $[\alpha]_D^{21}$ +84·4° (*c* 2·83 in chloroform) (Found: C, 52·4; H, 7·5. $C_{12}H_{20}O_7$ requires C, 52·2; H, 7·2%).

The aqueous phase (above) was evaporated to dryness, and a portion ($\frac{1}{6}$) of the residue was dissolved in chloroform–ethanol (19 : 1) and chromatographed on neutral silica.[2] The same solvent eluted a mixture of methyl 3,4-*O*-isopropylidene-α-D-altroside and methyl 6-*O*-acetyl-α-D-altroside; chloroform–ethanol (9 : 1) eluted more 6-acetate, and chloroform–ethanol (4 : 1) a trace of 6-acetate together with methyl α-D-altroside. The early fractions were dissolved in benzene and rechromatographed; benzene–ether (2 : 1) eluted the pure isopropylidene compound (0·067 g., 9%), m. p. 61—62° (from ether–light petroleum); it was indistinguishable from the product of reaction between methyl α-D-altroside and acetone containing sulphuric acid (see later). The syrupy *methyl 6-O-acetyl-α-D-altroside* (0·245 g., 33%), $[\alpha]_D^{21}$ +97° (*c* 1·8 in acetone), was chromatographically homogeneous, and on treatment with alkali gave methyl α-D-altroside, identified chromatographically; in 7 days it consumed 2·12 mol. of periodate and liberated 0·96 mol. of formic acid.

Trityl Ethers of Methyl 3,4-O-Isopropylidene-α-D-altroside.—Methyl 3,4-*O*-isopropylidene-α-D-altroside (0·1 g.) was dissolved in pyridine (2·8 c.c.) and treated with trityl chloride (0·14 g., 1·1 mol.) at 37° for 4 days. The product was isolated with chloroform, and was chromatographed in benzene on neutral silica.[2] Benzene eluted the *ditrityl ether*, needles (0·015 g., 5%), m. p. 195—196° (from ether–light petroleum) (Found: C, 80·0; H, 6·5. $C_{48}H_{46}O_6$ requires C, 80·2; H, 6·3%). (Quantitative detritylation with 80% acetic acid gave 95% of 2 mol. of triphenylmethanol, m. p. and mixed m. p. 159—160°.) Benzene–ether (4 : 1) eluted *methyl 3,4-O-isopropylidene-6-O-trityl-α-D-altroside*, crystallising from ether–light petroleum as prisms

(0·12 g., 60%), m. p. 152—153°, $[\alpha]_D^{22}$ +32·8° (*c* 2·1 in chloroform) (Found: C, 73·0; H, 6·9. $C_{29}H_{32}O_6$ requires C, 73·1; H, 6·7%).

Methyl 3,4-O-*Isopropylidene*-2-O-*methyl*-6-O-*trityl*-α-D-*altroside*.—The above monotrityl ether (0·24 g.) was dissolved in dimethylformamide (6·8 c.c.) and stirred with methyl iodide (1 c.c.) and silver oxide (0·99 g.) at room temperature in the dark for 24 hr.[35] The mixture was filtered and the residue washed with dimethylformamide (10 c.c.) and chloroform (15 c.c.). The filtrate and washings were shaken with water (100 c.c.) containing potassium cyanide (1 g.), and extracted with chloroform (5 × 20 c.c.). The combined chloroform extracts were washed with water, dried, and evaporated to a syrup. The *methyl ether* crystallised from ether–light petroleum as prisms (0·14 g., 56%), m. p. 120—121°, $[\alpha]_D^{24}$ +33·3° (*c* 1·75 in chloroform) (Found: C, 73·1; H, 6·9. $C_{30}H_{34}O_6$ requires C, 73·5; H, 6·9%).

Methyl 2-O-*Methyl*-α-D-*altroside*.—The above methyl ether (0·06 g.) was dissolved in 80% acetic acid (2 c.c.) and heated under reflux for 10 min. The solution was evaporated to dryness, water was added, and the triphenylmethanol filtered off. The filtrate was concentrated to a syrup which crystallised under acetone–ether, in the presence of a seed crystal, as needles (0·022 g., 85%), m. p. 80—82°, indistinguishable from an authentic sample.[12]

Deacetylation of Methyl 6-O-*Acetyl*-3,4-O-*isopropylidene*-α-D-*altroside*.—The acetate (0·02 g.) was dissolved in methanol (2 c.c.) containing a little sodium methoxide, and kept at room temperature for 20 hr. Solid carbon dioxide was added, the solution evaporated to dryness, and the residue extracted with hot acetone. The extracts were evaporated to a syrup which crystallised from ether–light petroleum, to give methyl 3,4-*O*-isopropylidene-α-D-altroside, m. p. 61—62°, whose infrared spectrum was identical with that of the 3,4-ketal described above.

Methyl 6-O-*Acetyl*-3,4-O-*isopropylidene*-2-O-*toluene*-p-*sulphonyl*-α-D-*altroside*.—The above 6-acetate (0·51 g.) was dissolved in pyridine (8 c.c.) and treated with toluene-*p*-sulphonyl chloride (1 g.) for 48 hr. at room temperature. The product was isolated with chloroform, giving the *toluene*-p-*sulphonate* as a syrup (0·63 g., 80%), $[\alpha]_D^{22}$ +41·2° (*c* 1·73 in chloroform) (Found: S, 7·87. $C_{19}H_{26}O_9S$ requires S, 7·44%).

Methyl 6-O-*Acetyl*-2-O-*toluene*-p-*sulphonyl*-α-D-*altroside*.—The above sulphonate (0·63 g.) was dissolved in 80% (v/v) acetic acid (18 c.c.) and heated under reflux for 10 min. The solution was evaporated to dryness and chromatographed on neutral silica.[2] Benzene–ether (4 : 1) eluted the *acetate*, which crystallised from ether–light petroleum as prisms (0·34 g., 60%), m. p. 103—104°, $[\alpha]_D^{20}$ +29·8° (*c* 1·49 in chloroform) (Found: C, 49·6; H, 5·7. $C_{16}H_{22}O_9S$ requires C, 49·2; H, 5·6%).

Treatment of Methyl 6-O-*Acetyl*-2-O-*toluene*-p-*sulphonyl*-α-D-*altroside with Alkali*.—The sulphonate (0·1 g.) was dissolved in chloroform (3 c.c.) and treated with sodium methoxide [from sodium (8 mg.)] in methanol (3 c.c.) at 0° for 16 hr. Solid carbon dioxide was added, the solution evaporated to dryness, and the residue extracted with ethyl acetate. The extracts were evaporated to a crystalline residue, which crystallised from ethyl acetate–light petroleum as needles (0·035 g., 78%), m. p. 103—104°, indistinguishable from methyl 2,3-anhydro-α-D-alloside.[3]

Reaction of Acetone with Methyl α-D-*Altroside*.—(*a*) *Sulphuric acid catalyst.* Methyl α-D-altroside (0·44 g.) was dissolved in acetone (15 c.c.) containing concentrated sulphuric acid (0·05 c.c.), and kept at 37° for 1 hr. The solution was poured into an excess of potassium hydrogen carbonate solution, evaporated to dryness, and extracted exhaustively with hot acetone. The extracts were evaporated to dryness; paper chromatography in solvents A and B showed the presence of starting material and one *O*-isopropylidene compound. The residue was dissolved in benzene and chromatographed on neutral silica.[2] Benzene–ether (3 : 1) eluted *methyl* 3,4-O-*isopropylidene*-α-D-*altroside*, prisms (0·23 g., 42%), m. p. 61—62° (from ether–light petroleum), $[\alpha]_D^{22}$ +102° (*c* 1·7 in water) (Found: C, 51·4; H, 7·6. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·7%).

(*b*) *Zinc chloride catalyst.* Methyl α-D-altroside (1 g.) was dissolved in acetone (16 c.c.) and shaken with anhydrous zinc chloride (0·8 g.) at room temperature for 48 hr. The solution was poured into an excess of sodium carbonate, filtered, and evaporated to dryness. The residue was extracted exhaustively with hot acetone, and the extracts concentrated to a syrup. Paper chromatography in solvent B showed the presence of two *O*-isopropylidene compounds; one had the same R_F value as the 3,4-isomer and the other had a higher R_F value (ratio 0·73 : 1);

[35] Kuhn, Trischmann, and Löw, *Angew. Chem.*, 1955, **67**, 32.

solvent A did not separate them (R_F 0·72). The syrup was chromatographed on neutral silica.[2] Chloroform–ethanol (19 : 1) eluted *methyl* 4,6-O-*isopropylidene*-α-D-*altroside*, prisms (0·12 g., 10%), m. p. 161—163° (from ether), $[\alpha]_D^{22}$ +112·7° (*c* 1·80 in water) (Found: C, 50·9; H, 7·4. $C_{10}H_{18}O_7$ requires C, 51·3; H, 7·7%). Further elution with chloroform–ethanol (19 : 1) gave the 3,4-ketal (0·45 g., 38%), indistinguishable from that prepared in (*a*).

Methyl 4,6-O-*Isopropylidene*-2,3-*di*-O-*toluene*-p-*sulphonyl*-α-D-*glucoside*.—This was prepared from methyl 4,6-*O*-isopropylidene-α-D-glucoside,[20] m. p. 0—82°, $[\alpha]_D^{23}$ +92° (*c* 3·7 in water) (lit.,[20] m. p. 84—86°, $[\alpha]_D$ +94°), by toluene-*p*-sulphonylation in pyridine. The sulphonate crystallised from methanol as prisms, m. p. 161—162°, $[\alpha]_D^{24}$ +52·9° (*c* 2·44 in chloroform) (Found: C, 53·1; H, 6·0; S, 11·9. Calc. for $C_{24}H_{30}O_{10}S_2$: C, 53·1; H, 5·5; S, 11·8%). Jones reports m. p. 145°; the corresponding methyl 4,6-*O*-benzylidene-2,3-di-*O*-toluene-*p*-sulphonyl-α-D-glucoside exists in two crystalline forms.[36]

Methyl 2,3-*Anhydro*-4,6-O-*isopropylidene*-α-D-*alloside*.—The preceding disulphonate (1·08 g.) was dissolved in chloroform (15 c.c.) at 0° and treated with sodium methoxide [sodium (0·22 g.) in methanol (5 c.c.)] for 4 days at 0° with occasional shaking. The mixture was kept at room temperature for a further day, water was added, and the product isolated with chloroform. The resulting syrup was treated with ether–light petroleum; some starting matetial, which crystallised, was removed, and the filtrate evaporated, to give the chromatographically pure *anhydro-compound* as a syrup (0·33 g.,76%), $[\alpha]_D^{21}$ +109·7° (*c* 2·59 in chloroform) (Found: C, 55·4; H, 7·4. $C_{10}H_{16}O_5$ requires C, 55·6; H, 7·4%). Mild acid treatment (80% acetic acid) yielded methyl 2,3-anhydro-α-D-alloside, identified by paper chromatography.[2] No 2,3-anhydromannoside could be detected.

Methyl 4,6-O-*Isopropylidene*-α-D-*altroside*.—The foregoing anhydroalloside (0·32 g.) in water (11·5 c.c.) was treated with potassium hydroxide (0·41 g.) and heated under reflux for 44 hr. The homogeneous solution was neutralised with dilute hydrochloric acid, evaporated to dryness, and extracted with hot acetone. The acetone extracts were concentrated, to give a residue which crystallised on standing. It recrystallised from ether to give the 4,6-ketal as prisms (0·23 g., 66%), m. p. 161—163°, indistinguishable from the compound prepared from methyl α-D-altroside and acetone.

Reaction of Acetone with Methyl α-D-*galactoside*.—(*a*) *Sulphuric acid catalyst.* Anhydrous methyl α-D-galactoside (0·53 g.) in acetone (60 c.c.) containing concentrated sulphuric acid (0·24 c.c.) was shaken at 20° for 4 hr. The solution was poured into an excess of aqueous potassium hydrogen carbonate solution. The mixture was evaporated to dryness and extracted with hot acetone. The acetone extracts were evaporated to a syrupy residue which was dissolved in chloroform and filtered through neutral silica gel to remove any starting material. The solution was evaporated, and the residue dissolved in benzene and chromatographed on neutral silica. Benzene–ether (4 : 1) eluted methyl 3,4-*O*-isopropylidene-α-D-galactoside, needles (0·3 g., 47%), m. p. 103—104° (from acetone–light petroleum), $[\alpha]_D^{22}$ +161° (*c* 2·0 in chloroform), R_F 0·68 in solvent A (detected by acid periodate–Schiff's reagent) (lit.,[22] m. p. 101—102°, $[\alpha]_D$ +162°). Continued elution with the same solvent gave a syrupy compound identified as *methyl* 4,6-O-*isopropylidene*-α-D-*galactoside* (0·1 g., 16%), $[\alpha]_D^{21}$ +166° (*c* 1·0 in ethanol), R_F in solvent A (Found: C, 52·0; H, 7·9. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·7%). In 48 hr. it consumed 1·01 mol. of periodate. Hydrolysis in 80% acetic acid at 100° for 10 min. gave methyl galactoside, detected chromatographically.

(*b*) *Zinc chloride catalyst.* Anhydrous methyl α-D-galactoside (0·85 g.) in acetone (16 c.c.) containing anhydrous zinc chloride (0·7 g.) was shaken at 27° for 42 hr. The solution was poured into an excess of aqueous sodium carbonate, filtered, and the filtrate evaporated to dryness. The residue was extracted with hot acetone and the extract treated as in (*a*). Methyl 3,4-*O*-isopropylidene-α-D-galactoside (0·29 g., 28%) and methyl 4,6-*O*-isopropylidene-α-D-galactoside (0·29 g., 28%) were isolated.

Methyl 2,3-*Di*-O-*acetyl*-4,6-O-*isopropylidene*-α-D-*galactoside*.—The above 4,6-ketal (0·1 g.) was treated with pyridine (3 c.c.) and acetic anhydride (1 c.c.) at room temperature for 24 hr. The product was isolated using chloroform, to give the *diacetate*, prisms (0·09 g., 66%), m. p. 97° (from ethanol), $[\alpha]_D^{22}$ +192·5° (*c* 1·59 in chloroform) (Found: C, 53·0; H, 6·9. $C_{14}H_{22}O_8$ requires C, 52·8; H, 6·9%). The infrared spectrum differed from that of the diacetate of the 3,4-ketal,[23] m. p. 116°, which was prepared for comparison.

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

Methyl 4,6-O-*Isopropylidene*-2,3-*di*-O-*methyl*-α-D-*galactoside*.—Syrupy methyl 4,6-*O*-isopropylidene-α-D-galactoside (0·11 g.) in dimethylformamide (2·8 c.c.) was shaken with methyl iodide (0·6 c.c.) and silver oxide (0·2 g.) at room temperature in the dark for 24 hr.[35] Chloroform (15 c.c.) was added, the solution filtered, and the precipitate washed with chloroform (10 c.c.). The chloroform solutions were combined and shaken with water containing potassium cyanide (0·5 g.), then water. The chloroform layer was dried ($MgSO_4$) and evaporated, to give the *dimethyl ether*, needles (0·07 g., 57%), m. p. 130° (from ether–light petroleum), $[\alpha]_D^{25}$ +189° (*c* 1·24 in chloroform) (Found: C, 55·1; H, 8·3. $C_{12}H_{22}O_6$ requires C, 55·0; H, 8·4%).

Methyl 2,3-*Di*-O-*methyl*-α-D-*galactoside*.—The above dimethyl ether (0·036 g.) in methanol (6 c.c.) and 0·01N-sulphuric acid (10 c.c.) was heated under reflux for 30 min. The solution was neutralised with barium carbonate, filtered, and evaporated to a syrup (0·027 g., 88%), $[\alpha]_D^{23}$ +169° (*c* 1·2 in acetone) {lit.,[27] $[\alpha]_D$ +167° ($CHCl_3$)}.

Methyl 4,6-O-*Benzylidene*-2,3-*di*-O-*methyl*-α-D-*galactoside*.—The above methyl 2,3-di-*O*-methyl-α-D-galactoside (0·025 g.), in benzaldehyde (0·6 c.c.) containing anhydrous zinc chloride (0·01 g.), was shaken at room temperature for 20 hr. The mixture was shaken with water and chloroform (20 c.c. of each), and the chloroform layer washed with water, evaporated to dryness, and steam-distilled in the presence of sodium carbonate solution. The cooled, alkaline solution was extracted with chloroform, and the extracts were dried ($MgSO_4$) and evaporated, to give the acetal (0·025 g., 71%), m. p. 123° (from ether) (lit.,[27] 123—124°); its infrared spectrum was identical with that of an authentic sample.

We thank Mr. D. M. G. Lloyd for a sample of methyl 2-*O*-methyl-α-D-altroside from the late Dr. G. J. Robertson's collection, Dr. F. H. Newth for a sample of 1,2:5,6-di-*O*-isopropylidene-β-D-altrofuranose, and the University of Newcastle upon Tyne for the award of an Associated Lead Studentship to one of us (R. M. S.).

Department of Organic Chemistry,
The University, Newcastle upon Tyne 1. [*Received, September 27th*, 1963.]