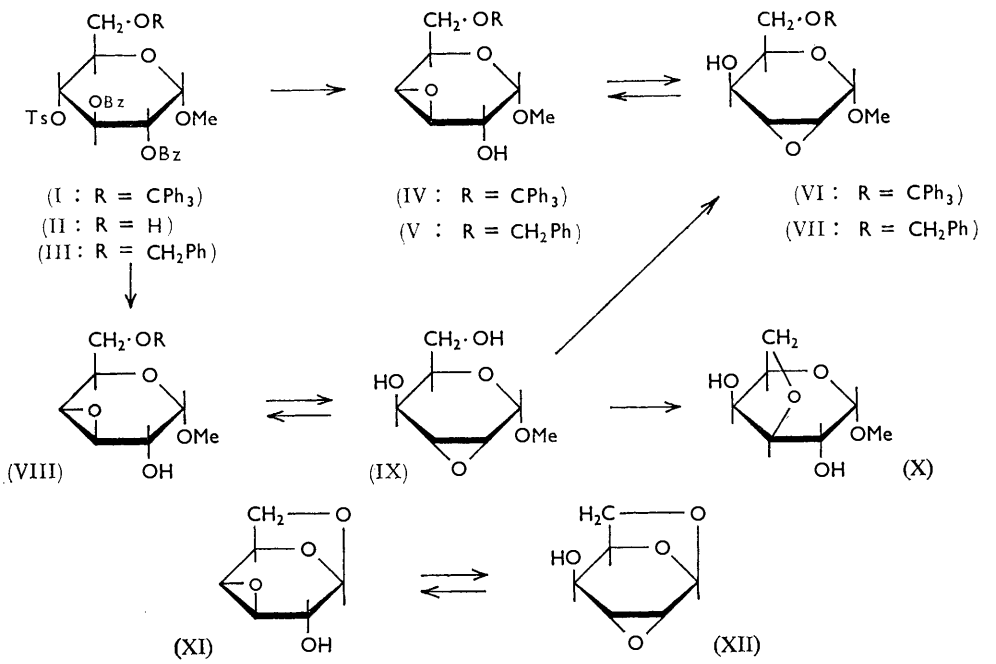
## 1174. *The Behaviour of Derivatives of 3,4-Anhydrogalactose towards Acidic Reagents. Part III* [1]

By J. G. Buchanan and R. Fletcher

Methyl 2,3-anhydro-6-*O*-trityl-α-D-gulopyranoside has been prepared and its equilibration with methyl 3,4-anhydro-6-*O*-trityl-α-D-galactopyranoside under alkaline conditions has been studied. In this case, and in that of the corresponding 6-benzyl ethers, the anhydroguloside isomer predominates slightly at equilibrium.

When methyl 4-*O*-acetyl-2,3-anhydro-6-*O*-trityl-α-D-gulopyranoside is treated with acidic reagents only galactoside isomers can be detected. Methyl 4-*O*-acetyl-α-D-galactoside has been characterised as a primary product which undergoes acetyl migration to the 6-acetate. Final structural details of the products arising from the action of acidic reagents on methyl 2-*O*-acetyl-3,4-anhydro-6-*O*-trityl-α-D-galactopyranoside have been established.

In earlier work it was shown that methyl 2,3-di-*O*-benzoyl-4-*O*-toluene-*p*-sulphonyl-6-*O*-trityl-α-D-glucoside (I) is converted into a mixture of the 3,4-anhydrogalactoside (IV) and 2,3-anhydroguloside (VI) by alkali.[1,2] The evidence was indirect and depended on the behaviour of the mixture of anhydro-sugars and their acetates towards acidic reagents. Only the anhydrogalactoside (IV) and its acetate (XXII) were obtained in crystalline form.[1]




It was necessary to prepare the pure anhydroguloside (VI) in order to study the equilibration of the two anhydro-compounds under alkaline conditions, and to confirm that the acetate (XIII) was converted into methyl 6-*O*-acetyl-3,4-*O*-isopropylidene-α-D-galactoside (XIX) by anhydrous hydrogen chloride in acetone.

[1] Part II, J. G. Buchanan, *J.*, 1958, 2511.
[2] J. G. Buchanan, *J.*, 1958, 995.

The anhydroguloside (IX) was prepared by mild acid hydrolysis [3] of its 4,6-*O*-benzylidene derivative and yielded the crystalline trityl ether (VI), m. p. 174—175°, without difficulty. It is remarkable that this ether had not crystallised previously.[2,4,5] By careful crystallisation each of the anhydro-glycosides, (IV) and (VI), was isolated from the mixture prepared by Oldham and Robertson's method.[4] The combined yield was 80% (42% guloside; 38% galactoside). The two isomers are separable by paper chromatography [6] and by thin-layer chromatography (Kieselgel G). Chromatography on silica gel can be used for the preparative separation of mixtures but care must be taken to avoid hydrolysis of trityl groups on the column (see Experimental section). The reversibility of the reaction was demonstrated by conversion of each isomer into a mixture of the two. On the basis of experiments involving isolation of the products it appeared that the anhydroguloside preponderated to a small extent at equilibrium.

The anhydrogalactoside–anhydroguloside equilibrium has been studied using the 6-benzyl ethers (V) and (VII). The glucoside (II) was benzylated with benzyl bromide and a mixture of silver perchlorate [7] and silver oxide to give the ether (III). Alkali treatment then yielded the crystalline anhydrogalactoside (V). The syrupy anhydroguloside (VII), formed by further alkali treatment of the anhydrogalactoside, afforded a crystalline acetate. At equilibrium there was a small preponderence of the anhydroguloside.

Newth [8,9] has pointed out that in an equilibrium of this kind, provided that the ring conformations are the same, one isomer possesses an equatorial hydroxyl group and the other an axial hydroxyl group. The argument that the isomer with the equatorial hydroxyl should predominate [8-10] holds good in four cases which have been examined in some detail [10-13] and may well hold in another.[14] When acyclic 2,3-epoxy-alcohols are equilibrated, the more highly substituted oxide is preferred.[15,16] Cerny *et al.*[12] described the equilibration of the dianhydrogalactose (XI) and dianhydrogulose (XII). In the case of these 1,6- anhydrides only one chair conformation is possible, and the finding that the dianhydrogulose (XII) is strongly preferred is in full agreement with Newth's hypothesis.[8] In the case of the methyl anhydrohexopyranosides, (IV)—(VII), however, the pyranose ring is flexible and capable of adopting either of the chair modifications, and the system lacks the symmetry of the inositol series. At present we cannot explain the slight preponderance of (VI) over (IV), and of (VII) over (V).

The equilibration of methyl 3,4-anhydro-α-D-galactoside (VIII) and 2,3-anhydro-α-D-guloside (IX) was not studied because of practical difficulties and because of the possibility of irreversible conversion of the latter into the 3,6-anhydrogalactoside (X). A reaction of this kind has been described [17] in connection with configurational studies on sucrose, and it is well known in the 2,3-anhydroalloside series.[18] When the 3,4-anhydrogalactoside (VIII) was treated with 0·1N-sodium hydroxide at 100° the 3,6-anhydrogalactoside (X) was isolated in 71% yield.

When methyl 4-*O*-acetyl-2,3-anhydro-6-*O*-trityl α-D-guloside (XIII) was treated with

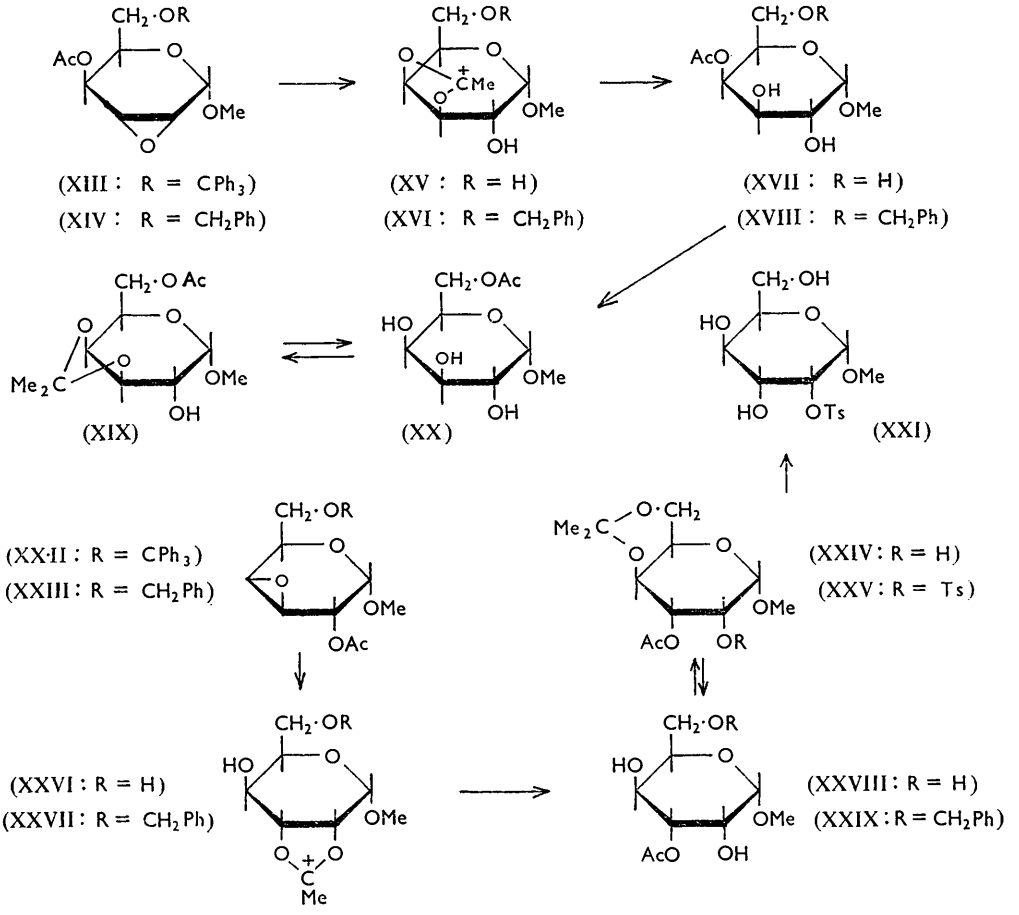
[3] H. R. Bolliger and T. Reichstein, *Helv. Chim. Acta*, 1953, **36**, 302.
[4] J. W. H. Oldham and G. J. Robertson, *J.*, 1935, 685.
[5] V. Labaton and F. H. Newth, *J.*, 1953, 992.
[6] D. A. Applegarth and J. G. Buchanan, *J.*, 1960, 4706.
[7] Cf. M. L. Wolfrom, A. O. Pittet, and I. C. Gillam, *Proc. Nat. Acad. Sci. U.S.A.*, 1961, **47**, 700.
[8] F. H. Newth, *J.*, 1956, 441.
[9] F. H. Newth, *Quart. Rev.*, 1959, **13**, 30.
[10] S. J. Angyal and P. T. Gilham, *J.*, 1957, 3691.
[11] J. G. Buchanan and J. C. P. Schwarz, *J.*, 1962, 4770.
[12] M. Cerny, I. Buben, and J. Pacak, *Coll. Czech. Chem. Comm.*, 1963, **28**, 1569.
[13] M. Cerny, J. Pacak, and J. Stanek, *Coll. Czech. Chem. Comm.*, 1965, **30**, 1151.
[14] W. H. G. Lake and S. Peat, *J.*, 1939, 1069.
[15] E. P. Kohler, N. K. Richtmyer, and W. F. Hester, *J. Amer. Chem. Soc.*, 1931, **53**, 205.
[16] G. B. Payne, *J. Org. Chem.*, 1962, **27**, 3819.
[17] R. U. Lemieux and J. P. Barrette, *J. Amer. Chem. Soc.*, 1958, **80**, 2422.
[18] A. B. Foster, M. Stacey, and S. Vardheim, *Acta Chem. Scand.*, 1958, **12**, 1819, and references cited therein.

hydrogen chloride in anhydrous acetone the major product isolated was methyl 6-*O*-acetyl-3,4-*O*-isopropylidene-α-D-galactoside (XIX) together with the acetate (XX). In accordance with the earlier predictions [1] no gulose derivatives could be detected. The reaction is depicted in the sequence (XIII)⟶(XV)⟶(XVII)⟶(XX)⟶(XIX). Originally it was considered that methyl α-D-galactoside 3,4,6-orthoacetate might be formed from the acetoxonium ion (XV) in order to account for the final location of the acetoxyl group on C-6.[1] Although such an orthoester is sterically feasible we have now shown that the acetoxonium ion (XV) probably yields the 4-acetate (XVII) by way of the 3,4-orthoacetate, and that the 6-acetate (XX) arises by a normal acid-catalysed acetyl migration. Indirect evidence for this comes from the comparable reactions of methyl 4-*O*-acetyl-2,3-anhydro-6-*O*-trityl-α-D-mannoside under acidic conditions;[19] 6-*O*-acetyl-α-D-altroside and its 3,4-*O*-isopropylidene compound are the final products, and in this case the *trans* relationship of the 6-hydroxyl group to the 3- and 4-hydroxyl groups in altropyranose precludes orthotriester formation. More direct evidence has come from a study of the behaviour of the benzyl ether (XIV) towards 80% acetic acid. Whereas the trityl ether (XIII) under these conditions yielded the 6-acetate (XX), the benzyl ether gave a syrupy product, which consumed *ca.* 1 mol. of periodate. This must be the 4-acetate (XVIII), produced from the acetoxonium ion (XVI). Hydrogenolysis yielded crystalline methyl 4-*O*-acetyl-α-D-galactoside (XVII). Treatment of the crude hydrogenolysis product with hot 80% acetic acid yielded only the isomeric 6-acetate (XX). The isomers were distinguishable from each other by their infrared spectra, their $R_F$ values on thin-layer chromatography, and by periodate oxidation. The unsharp melting point of the 4-acetate is probably due to isomerisation to the 6-acetate. The isomerisation occurs very readily, *e.g.*, in ethyl acetate solution at room temperature during several hours. The 4-acetate (XVII) was also obtained when the anhydroguloside (XIII) was subjected to adsorption on a column of silica gel for 21 hr. Subsequent elution gave triphenylmethanol and the 4-acetate. It had previously been found that trityl ethers sometimes decompose during chromatography on silica gel.[11] Furthermore, there are reports [20,21] of the lability to silica chromatography of some epoxides of steroid enol acetates. These compounds rearrange by a mechanism closely related to that operating in the transformation (XIII)⟶(XVII).

In Parts I [2] and II [1] the treatment of the anhydrogalactoside (XXII) with hydrogen chloride in acetone was shown to yield methyl 2(or 3)-*O*-acetyl-4,6-*O*-isopropylidene-α-D-guloside, m. p. 165—167°. The earlier workers had reported m. p. 177—179° for their product,[4,5] and there was a possibility that we had isolated an isomer differing in the location of the acetate group. Through the kindness of Mr. D. M. G. Lloyd and Dr. J. W. H. Oldham we have been able to examine a sample of Oldham and Robertson's " monoacetyl monoacetone α-methyl guloside." In our hands it had m. p. 164—167° and an infrared spectrum identical with that of our compound. By the following series of transformations we have shown the acetyl group to be located as in (XXIV). The isopropylidene group of the toluene-*p*-sulphonate (XXV) [2] was removed by acid hydrolysis and the product deacetylated by alkali treatment to give the crystalline 2-sulphonate (XXI). The structure of the latter was proved by periodate oxidation and by the fact that it was relatively stable to alkali; the 3-sulphonate would not be oxidised by periodate and would yield the anhydrogalactoside (VIII) under alkaline conditions. The acetate (XXIV) was hydrolysed with aqueous acetic acid to give methyl 3-*O*-acetyl-α-D-guloside (XXVIII), which was stable to sodium periodate, showing that no acetyl migration occurs during the hydrolysis. The same acetate (XXVIII) was formed by acetic acid hydrolysis of the triphenylmethyl ether (XXII), presumably by way of the acetoxonium ion (XXVI). Similar acid hydrolysis of the benzyl ether (XXIII) gave, through the acetoxonium ion intermediate (XXVII),

[19] J. G. Buchanan and R. M. Saunders, *J.*, 1964, 1796.
[20] A. H. Soloway, W. J. Considine, D. K. Fukushima, and T. F. Gallagher, *J. Amer. Chem. Soc.*, 1954, **76**, 2941.
[21] N. S. Leeds, D. K. Fukushima, and T. F. Gallagher, *J. Amer. Chem. Soc.*, 1954, **76**, 2943.

the 3-acetate (XXIX) which was hydrogenolysed to the triol (XXVIII). When the anhydrogalactoside (XXII) was treated with hydrogen chloride in acetone [1] the 4,6-ketal (XXIV) probably arose by reaction of the 3-acetate (XXVIII) with acetone (cf. ref. 19). The " methyl mono-*O*-acetyl-α-guloside " referred to in the Experimental section of Part II [1] is the 3-acetate (XXVIII).




## 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. Removal of solvents by distillation was always carried out under reduced pressure.

Adsorption chromatography was carried out using silica gel (Messrs. Hopkin and Williams). Decomposition of trityl ethers during chromatography could be reduced, but not entirely eliminated, by neutralisation of the silica with aqueous ammonia, followed by re-activation.[11] Paper chromatography was carried out on Whatman No. 1 paper with the following solvent systems: (A) butan-1-ol–water (86 : 14 v/v); (B) butan-2-one saturated with water. Vicinal epoxides were detected by sodium iodide and Methyl Red,[11] vicinal glycols by periodate and Schiff's reagent,[22] and reducing sugars with aniline phthalate.[23] Thin-layer chromatography was carried out on Kieselgel G (Merck), carbohydrates being detected with anisaldehyde–sulphuric acid.[24]

[22] J. Baddiley, J. G. Buchanan, R. E. Handschumacher, and J. F. Prescott, *J.*, 1956, 2818.
[23] S. M. Partridge, *Nature*, 1949, **164**, 443.
[24] E. Stahl and U. Kaltenbach, *J. Chromatog.*, 1961, **5**, 351.

Quantitative periodate oxidations were performed using the spectrophotometric method.[25]

*Methyl* 2,3-*Di*-O-*benzoyl*-6-O-*benzyl*-4-O-*toluene*-p-*sulphonyl*-α-D-*glucoside*.—Methyl 2,3-di-*O*-benzoyl-4-*O*-toluene-*p*-sulphonyl-α-D-glucoside [1,5] (20·0 g.) was dissolved in alcohol-free chloroform (100 ml.) and benzene (200 ml.) containing dry silver perchlorate (1·2 g.). The mixture was stirred vigorously at 45°, and Drierite (3 g.) and benzyl bromide (40 ml.) were added. Silver oxide (40 g.) was gradually added to the mixture during 36 hr. with rigorous exclusion of moisture and stirring continued for a further 48 hr. Pyridine (20 ml.) was added and the mixture left overnight. Inorganic salts were removed by filtration, and evaporation of the filtrate left a residue which was extracted with chloroform. The extracts were combined, shaken with water, dried ($Na_2SO_4$), and evaporated to a syrup, which appeared, by thin-layer chromatography in benzene–ether (1 : 1) to be mainly the required ether. The syrup was dissolved in benzene and chromatographed on silica gel (200 g.) Elution with benzene–ether (19 : 1) and crystallisation of the product from chloroform–methanol yielded the *benzyl ether* (18·8 g., 81%), m. p. 149°, $[\alpha]_D^{22}$ +86·7° (*c* 0·24 in chloroform) (Found: C, 64·6; H, 5·6. $C_{33}H_{34}O_{10}S$ requires C, 65·0; H, 5·3%). Benzene–ether (4 : 1) eluted unchanged starting material (3·1 g., 13%).

3,4-*Anhydrogalactosides*.—*Methyl* 3,4-*anhydro*-6-O-*benzyl*-α-D-*galactoside*. Methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-toluene-*p*-sulphonyl-α-D-glucoside (6·5 g.) was dissolved in chloroform (100 ml.), and methanol (40 ml.) containing sodium methoxide [from sodium (0·3 g.)] was added. When thin-layer chromatography (ether) showed the reaction to be complete (11 hr.) the mixture was neutralised with N-hydrochloric acid and the solvent removed by distillation. The residue was extracted with benzene and chromatographed on silica gel (100 g.). Benzene–ether (4 : 1) eluted the *anhydro-compound*, which crystallised from ether and was recrystallised from ether–light petroleum, needles (2·43 g., 86%), m. p. 41—42°, $[\alpha]_D$ +9·3° (*c* 1·75 in chloroform). It could be purified by sublimation (Found: C, 63·3; H, 6·8. $C_{14}H_{18}O_3$ requires C, 63·1; H, 6·8%).

*Methyl* 2-O-*acetyl*-3,4-*anhydro*-6-O-*benzyl*-α-D-*galactoside*. The above anhydro-compound (1·20 g.) was acetylated overnight with acetic anhydride and pyridine. The *acetate* was isolated, by means of chloroform, as a syrup (1·1 g., 79%), $[\alpha]_D^{22}$ +58·9° (*c* 1·47 in chloroform) (Found: C, 61·8; H, 6·8. $C_{16}H_{20}O_4$ requires C, 62·3; H, 6·5%).

2,3-*Anhydrogulosides*.—*Methyl* 2,3-*anhydro*-6-O-*trityl*-α-D-*guloside*. Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-guloside (0·25 g.) was heated under reflux with methanol (1·5 ml.) and 0·01N-sulphuric acid (5 ml.) until a clear solution was obtained (20 min.) (cf. ref. 3.). Water was added and benzaldehyde was removed by extraction with chloroform. The aqueous layer was neutralised [Dowex 3 ($OH^-$) resin], filtered, and evaporated to dryness. The anhydrous syrup was dissolved in pyridine (10 ml.), trityl chloride (0·2 g.) added, and the mixture left at room temperature for 40 hr. Isolation using chloroform, and recrystallisation from light petroleum (b. p. 60—80°), gave the *trityl ether* (0·1 g.), m. p. 174—175°, $[\alpha]_D^{22}$ +21·8° (*c* 1·76 in chloroform) (Found: C, 74·2; H, 6·4. $C_{26}H_{26}O_5$ requires C, 74·6; H, 6·3%).

*Methyl* 4-O-*acetyl*-2,3-*anhydro*-6-O-*trityl*-α-D-*guloside*. The above trityl ether (2·0 g.) was acetylated with acetic anhydride and pyridine. The *acetate* was isolated by addition of water and a seed crystal. Recrystallised from ethanol it gave prisms (2·0 g., 91%), m. p. 104—105°, $[\alpha]_D$ −27·6° (*c* 0·58 in chloroform) (Found: C, 73·1; H, 6·5. $C_{28}H_{28}O_6$ requires C, 73·0; H, 6·5%).

*Methyl* 4-O-*acetyl*-2,3-*anhydro*-6-O-*benzyl*-α-D-*guloside*. Methyl 2,3-anhydro-6-*O*-benzyl-α-D-guloside (1·08 g.; see below) was acetylated with acetic anhyride and pyridine overnight at room temperature. Isolation using chloroform, and recrystallisation from light petroleum, gave the *acetate* (1·10 g., 88%), m. p. 76—78°. Recrystallised from ethanol it had m. p. 77—78°, $[\alpha]_D^{21}$ −0·85° (*c* 0·94 in chloroform) (Found: C, 62·2; H, 6·4. $C_{16}H_{20}O_6$ requires C, 62·3; H, 6·5%).

*Isolation of Anhydrogalactosides and Anhydrogulosides from Mixtures of the Two*.—*The action of alkali on methyl* 2,3-*di*-O-*benzoyl*-4-O-*toluene*-p-*sulphonyl*-6-O-*trityl*-α-D-*glucoside*. The glycoside (20 g.) was heated under reflux for 1 hr. with acetone (180 ml.), 2N-sodium hydroxide (45 ml.), and water (90 ml.). Acetone was removed under reduced pressure and the syrupy material extracted with chloroform. The chloroform solution was washed with water, dried ($Na_2SO_4$), and evaporated to a syrup. Crystallisation from ether gave the anhydroguloside (VI) (3·65 g., 35%), m. p. 174—175°. Careful recrystallisation of the evaporated mother-liquors from dibutyl

[25] G. O. Aspinall and R. J. Ferrier, *Chem. and Ind.*, 1957, 1216.

ether gave the anhydrogalactoside (IV) [1] (3·95 g., 38%), m. p. 140—142°, together with more anhydroguloside (0·77 g., 7%), m. p. 170—173°. Pure samples were obtained in each case by one recrystallisation from ethyl acetate–light petroleum.

*The action of alkali on methyl* 3,4-*anhydro*-6-O-*trityl*-α-D-*galactoside.* The anhydro-compound (0·307 g.) was heated under reflux with sodium methoxide [from sodium (8·4 mg.)] in methanol (7 ml.) for 1 hr. The mixture was neutralised with carbon dioxide, evaporated to dryness, and extracted with benzene. The combined extracts were chromatographed on neutral silica gel (25 g.). Benzene–ether (9 : 1) eluted the anhydrogalactoside (0·115 g.), m. p. 139—141°, recrystallised from light petroleum. Mixed fractions (0·084 g.) followed, and then the anhydroguloside (0·067 g.), m. p. 170—171°, recrystallised from light petroleum and identified by its infrared spectrum.

*The action of alkali on methyl* 2,3-*anhydro*-6-O-*trityl*-α-D-*guloside.* The anhydro-compound (0·516 g.) was heated under reflux with sodium methoxide [from sodium (0·012 g.)] in methanol (10 ml.) for 1¼ hr. Thin-layer chromatography (ether) indicated that equilibrium had been reached within 1 hr. The reaction mixture was neutralised with carbon dioxide and evaporated to dryness. A benzene extract was chromatographed on neutral silica gel (30 g.). Benzene–ether (9 : 1) eluted the 3,4-anhydrogalactoside (0·179 g., 35%), m. p. 137—138° (from light petroleum) raised to 139—140° by recrystallisation. The infrared spectrum was identical with that of an authentic sample. Elution with the same solvent gave a mixture of epoxides (0·023 g., 4·5%), followed by the 2,3-anhydroguloside (0·222 g., 43%), m. p. 170—171° (from light petroleum) raised to m. p. 173—174° by recrystallisation. The infrared spectrum was identical with that of starting material.

*Treatment of methyl* 3,4-*anhydro*-6-O-*benzyl*-α-D-*galactoside with alkali.* The benzyl ether (2·68 g.) was dissolved in methanol (100 ml.) containing sodium methoxide [from sodium (0·13 g.)] and heated under reflux for 1 hr. The solution was neutralised with solid carbon dioxide and solvent removed by distillation. Chloroform extracts of the residue were evaporated to a syrup which was dissolved in benzene and chromatographed on silica gel (140 g.). Benzene–ether (3 : 1) eluted first the anhydrogalactoside which crystallised from light petroleum (0·98 g., 37%), m. p. 39—40° raised to 43—44° by recrystallisation from ether–light petroleum. A mixed fraction (0·125 g., 5%) was eluted next, followed by syrupy *methyl* 2,3-*anhydro*-6-O-*benzyl*-α-D-*guloside* (1·23 g., 46%), $[\alpha]_D^{22}$ +38·1° (*c* 0·88 in chloroform) (Found: C, 63·1; H, 6·75. $C_{14}H_{18}O_5$ requires C, 63·1; H, 6·8%).

*Alkali treatment of methyl* 3,4-*anhydro*-α-D-*galactoside.* The anhydro-compound (0·35 g.) was heated under reflux with 0·1N-sodium hydroxide (11 ml.) for 1 hr. The solution was neutralised with carbon dioxide and evaporated to dryness. The solid was extracted exhaustively with boiling ethyl acetate and the combined extracts were evaporated to small volume. The solution was examined by paper chromatography in solvent A. No vicinal epoxide was present; [11] a strong spot of methyl 3,6-anhydro-α-D-galactoside was detected by periodate and Schiff's reagent (a dark green spot, appearing after 24 hr.), together with traces of methyl α-D-guloside and -idoside. Methyl 3,6-anhydro-α-D-galactoside (0·25 g., 71%), m. p. 140·5°, crystallised from ethyl acetate and was identical with an authentic sample.

*Treatment of* 2,3-*Anhydrogulosides with Acidic Reagents.—Methyl* 4-O-*acetyl*-2,3-*anhydro*-6-O-*trityl*-α-D-*guloside and hydrogen chloride in acetone.* The anhydroguloside (2·0 g.) was treated with acetone (20 ml.) containing dry hydrogen chloride (0·5 g.) for 1 hr. at room temperature, then neutralised with anhydrous sodium carbonate. The filtrate after removal of inorganic solid was evaporated to small volume and treated with water containing a little pyridine. The crystalline triphenylmethanol (1·11 g., 98%) was removed and the filtrate extracted several times with chloroform, leaving an aqueous solution (R). The combined chloroform extracts were dried ($Na_2SO_4$) and evaporated to a syrup; recrystallisation from ether gave methyl 6-*O*-acetyl-3,4-*O*-isopropylidene-α-D-galactoside (0·57 g., 47%), m. p. 101—102°, identical with an authentic sample.[2,4,5] The ethereal mother liquors were evaporated to dryness and the residue deacetylated with sodium methoxide in methanol. After evaporation, the residue was dissolved in water, deionised by means of Dowex 50 ($H^+$) and Dowex 3 ($OH^-$) resins, and the resulting solution, after concentration, examined by paper chromatography in solvent A. Methyl 3,4-*O*-isopropylidene-α-D-galactoside and methyl α-D-galactoside were the major products. Gulose derivatives were entirely absent, but traces of unidentified compounds reacting with aniline phthalate [23] and with periodate and Schiff's reagent [22] were detected. The solution R above was freed from chloride ions with Dowex 3 ($OH^-$) resin and evaporated to dryness. A

sample was dissolved in methanol and examined by paper chromatography before and after deacetylation. A compound corresponding to methyl 6-*O*-acetyl-α-D-galactoside and a trace of methyl α-D-galactoside were present before deacetylation. A greatly increased amount of methyl α-D-galactoside was present after deacetylation. No gulose derivatives were found in either case, although traces of unidentified compounds were detected. The major portion crystallised from ethyl acetate to give slightly impure methyl 6-*O*-acetyl-α-D-galactoside whose infrared spectrum was identical with that of an authentic sample (see below). Paper chromatography showed the presence of a trace of methyl α-D-galactoside, which could not be removed by recrystallisation.

*Methyl* 4-O-*acetyl*-2,3-*anhydro*-6-O-*trityl*-α-D-*guloside and aqueous acetic acid.* The anhydroguloside (0·16 g.) was heated with 80% acetic acid (v/v) (2·7 ml.) for 30 min. at 100°. Evaporation of the solvent left a crystalline solid which crystallised from ethyl acetate to give methyl 6-*O*-acetyl-α-D-galactoside (0·04 g., 49%), m. p. 148°, identical with an authentic sample (see below).

*Methyl* 4-O-*acetyl*-2,3-*anhydro*-6-O-*benzyl*-α-D-*guloside and aqueous acetic acid.* The anhydroguloside (0·61 g.) was heated in 80% acetic acid (v/v) (10 ml.) for 30 min. at 100°. The acetic acid was evaporated under reduced pressure to a syrup which was nearly homogeneous on thin-layer chromatography (ethyl acetate). It consumed sodium periodate (1·12 mol. in 3 days; 1·21 mol. in 5 days). (a) The syrup (0·14 g.) was dissolved in ethyl acetate (7 ml.) containing a few drops of glacial acetic acid and hydrogenated over palladium oxide. The catalyst was filtered off and the filtrate concentrated to small volume. *Methyl* 4-O-*acetyl*-α-D-*galactoside* crystallised as prisms (42 mg., 42%), m. p. 140—145° (softening at 135°), $[\alpha]_D^{25}$ +166° (*c* 0·18 in water) (Found: C, 45·9; H, 6·8. $C_9H_{16}O_7$ requires C, 45·6; H, 6·75%). The m. p. on admixture with the 6-acetate was 130—135°. The infrared spectrum had peaks at 3333 br (OH), 2835 ($OCH_3$), and 1739 cm.$^{-1}$ (ester C=O) but differed otherwise from that of the 6-acetate. On thin-layer chromatography in chloroform–methanol (4 : 1) the 4-acetate had a higher $R_F$ value than the 6-acetate and the two were separable. The 4-acetate consumed periodate as follows: 0·94 mol. (6 hr.); 0·94 mol. (10 hr.); 1·05 mol. (22 hr.). (b) Another portion of syrup (0·44 g.) was hydrogenolysed in the same way as in (a). The product was heated with 80% acetic acid (v/v) (15 ml.) at 100° for 1 hr. Evaporation of the solvent left a syrup which was crystallised from ethyl acetate to give methyl 6-*O*-acetyl-α-D-galactoside (0·13 g., 45%), m. p. 148—150° undepressed on admixture with an authentic sample (see below).

*Adsorption of methyl* 4-O-*acetyl*-2,3-*anhydro*-6-O-*trityl*-α-D-*guloside on silica gel.* The anhydroguloside (0·1 g.) was dissolved in benzene (5 ml.) and adsorbed on a column of silica gel (10 g.). Elution with benzene (50 ml.) did not remove any material. The column was left for 21 hr., and elution with benzene gave triphenylmethanol (52 mg.). Ether–methanol (1 : 1) eluted methyl 4-*O*-acetyl-α-D-galactoside (35 mg.) which crystallised from ethyl acetate. The infrared spectrum was identical with that of the 4-acetate above.

*Methyl* 6-O-*Acetyl*-α-D-*galactoside.*—The above 3,4-*O*-isopropylidene compound (0·70 g.) was heated with 2N-acetic acid at 100° for 1 hr. Evaporation of solvent left a white crystalline solid which crystallised from ethyl acetate to give the *acetate* (0·40 g., 67%), m. p. 149—151°, $[\alpha]_D^{25}$ +148° (*c* 0·37 in water) (Found: C, 45·5; H, 7·0. $C_9H_{16}O_7$ requires C, 45·6; H, 6·75%). In 22 hr. the acetate reduced 2·02 mol. of sodium periodate (constant value) and liberated 1·0 mol. of formic acid. The infrared spectrum showed peaks at 3367, 3268sh, and 3226 (OH), 2841 ($OCH_3$), and 1736 cm.$^{-1}$ (ester C=O).

*Treatment of* 3,4-*Anhydrogalactosides with Acidic Reagents.*—*Methyl* 2-O-*acetyl*-3,4-*anhydro*-6-O-*benzyl*-α-D-*galactoside and aqueous acetic acid.* The anhydrogalactoside (0·16 g.) was heated with 80% acetic acid (v/v) (2·7 ml.) in a sealed tube at 100° for 45 min. Removal of solvent by distillation left a syrup which was chromatographed on silica gel. Chloroform–ethanol (9 : 1) eluted the glycoside as a syrup (0·14 g.) of which part (54 mg.) was dissolved in glacial acetic acid and hydrogenolysed over palladium. Filtration followed by evaporation of the acetic acid left a syrup which crystallised from methanol; it was recrystallised from ethyl acetate, to give *methyl* 3-O-*acetyl*-α-D-*guloside* (29 mg., 71%), m. p. 171°, $[\alpha]_D^{22}$ +108·3° (*c* 0·60 in methanol) (Found: C, 45·9; H, 7·0. $C_9H_{16}O_7$ requires C,45·6; H, 6·75%). The glycoside reduced 0·03 mol. of sodium periodate in 20 days. It could not be detected by periodate and Schiff's reagent after chromatography in solvent A unless the chromatogram had been exposed to ammonia vapour before being sprayed.[1] After deacetylation the product behaved as methyl α-D-guloside in solvent B.

*Methyl* 2-O-*acetyl*-3,4-*anhydro*-6-O-*trityl*-α-D-*galactoside*. The anhydrogalactoside (1·0 g.) was heated with 80% acetic acid (v/v) (16·7 ml.) for 1 hr. at 100°. Addition of water precipitated triphenylmethanol (0·55 g., 100%) which was filtered off. Removal of solvent from the filtrate left a syrup which crystallised twice from ethyl acetate to give methyl α-D-guloside 3-acetate (0·35 g., 65%), m. p. 169—170°, identical with the compound above.

*Methyl* 3-O-*Acetyl*-4,6-O-*isopropylidene*-α-D-*guloside*.—An original sample [4] of Oldham and Robertson's " monoacetyl monoacetone α-methylguloside " had m. p. 164—167° and was identical with the methyl *O*-acetyl-4,6-*O*-isopropylidene-α-D-guloside, m. p. 165—167°, described in Part I.[2]

*Hydrolysis of methyl*-3-O-*acetyl*-4,6-O-*isopropylidene*-α-D-*guloside*. The guloside [2] (0·26 g.) was dissolved in 3N-acetic acid (10 ml.) and heated at 100° for 1 hr. Evaporation of solvent left a syrup which crystallised from methanol to give methyl α-D-guloside 3-acetate (0·19 g., 85%), m. p. 169°, identical with the samples prepared above.

*Methyl* 2-O-*Toluene*-p-*sulphonyl*-α-D-*guloside*.—Methyl 3-*O*-acetyl-4,6-*O*-isopropylidene-2-*O*-toluene-*p*-sulphonyl-α-D-guloside [2] (0·4 g.) was dissolved in 3N-acetic acid (15 ml.) and heated at 100°. After 1 hr. thin-layer chromatography (ethyl acetate) showed the absence of starting material, and the solution was evaporated to dryness. The colourless syrup was treated with methanolic sodium methoxide (0·1 mol.) overnight, neutralised with carbon dioxide, and evaporated to dryness. The residue was dissolved in chloroform and chromatographed on silica gel. Chloroform–ethanol (4 : 1) eluted a syrup which crystallised from ethanol and ethanol–light petroleum to give the *sulphonate* (0·25 g., 77%), m. p. 142°, $[\alpha]_D^{22}$ +38·5 (*c* 0·55 in methanol) (Found: C, 48·0; H, 5·9. $C_{14}H_{20}O_8S$ requires C, 48·3; H, 5·8%). The compound consumed 1·06 mol. of sodium periodate in 3 days (constant value). Treatment with sodium methoxide (2 mol.) for 20 hr. at room temperature did not bring about formation of a vicinal epoxide.

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