3. *The Action of Acidic Reagents on Ethylene Oxide Anhydro Sugars. Part I. The Action of Acid Reagents on* 4 : 6-*Benzylidene* 2 : 3-*Anhydro* α-*Methylalloside.*

By F. H. Newth, W. G. Overend, and L. F. Wiggins.

The action of hydrochloric and hydrobromic acids on 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside has been studied, and each reagent has been found to produce two distinct halogeno α-methylhexosides. Hydrobromic acid gave 2-bromo α-methylaltroside and 3-bromo α-methylglucoside; hydrochloric acid gave 2-chloro α-methylaltroside and 3-chloro α-methylglucoside. The constitution of each of these substances has been established.

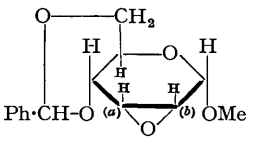
It has been observed that by the action of acid reagents on the 2 : 3-anhydro alloside the main product is a glucose derivative, whereas it has been shown previously that, by the action of alkaline reagents on the same anhydro sugar, the main product is an altrose derivative. Experiments using sulphuric and oxalic acids as the acidic reagents on the 2 : 3-anhydro alloside have shown that these substances produce a similar effect to that of the halogen acids.

Extensive work has been done in the past on the scission of ethylene oxide anhydro rings with alkaline reagents. Thus, Peat and Wiggins (*J.*, 1938, 1810) studied the behaviour of 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside (I) towards alkaline reagents and discovered that two products were formed, namely, a derivative of glucose and a derivative of altrose with the latter predominating. When ammonia was the effective reagent 2-amino 4 : 6-benzylidene α-methylaltroside (II) was obtained in 80% yield accompanied by 3-amino 4 : 6-benzylidene α-methylglucoside (III) in 10% yield, both compounds being isolated as their acetates. Similarly, Richtmyer and Hudson (*J. Amer. Chem. Soc.*, 1941, **63**, 1727) obtained 4 : 6-benzylidene α-methylaltroside and 4 : 6-benzylidene α-methylglucoside in 84% and 7% yield respectively by the action of potassium hydroxide on the alloside (I).

Again, in the ring scission of 4 : 6-benzylidene 2 : 3-anhydro β-methyltaloside (IV) with sodium methoxide (Wiggins, *J.*, 1944, 522) two products were obtained, which were 4 : 6-benzylidene 3-methyl β-methylidoside (V) and 4 : 6-benzylidene 2-methyl β-methylgalactoside (VI), with the former largely in excess. It will be observed that Walden inversion is concomitant with ring scission and accompanies the scission in both directions.

It is of interest that in the anhydro taloside (IV) it is the bond (*c*) furthest from the glycosidic group that breaks to the largest extent, giving rise to a derivative of idose, whereas in the alloside (I) it is the bond (*b*) nearest to the glycosidic group that predominantly breaks. Ring scission of 4 : 6-benzylidene 2 : 3-anhydro α-methylmannoside (VII) with sodium methoxide (Robertson and Griffith, *J.*, 1935, 1193) proceeds in accordance with the above observations, since the main product is 4 : 6-benzylidene 3-methyl α-methylaltroside (VIII).

It appears therefore that, in the ring opening of 2 : 3-ethylene oxide anhydro rings, if the ring lies above the plane of the sugar ring then the C–O bond furthest from the glycosidic group suffers the most extensive scission, whereas if the anhydro ring lies below the plane of the sugar ring, then it is the C–O bond nearest to the glycosidic group which breaks to the greater extent. Although these facts seem to hold for all cases of the ring scission of 2 : 3-anhydro methylhexosides so far studied, ring opening seems to proceed in the opposite sense when the reaction is applied to ethylene oxide derivatives of 1 : 6-anhydro sugars. This statement, however, is based only on the one example as yet available. James, Stacey, Smith, and Wiggins (*Nature*, 1945, **156**, 308; *J.*, 1946, 625) in their constitutional synthesis of chondrosamine found that ring fission of 2 : 3-1 : 6-dianhydro β-talose (IX) led mainly, not to an idose derivative (X) which would have been expected had the ring scission proceeded in the same way as with 4 : 6-benzylidene 2 : 3-anhydro β-methyltaloside, but to a derivative of galactose (XI). That is to say, instead of the C–O bond (*e*) breaking to the largest extent, it is bond (*f*) that suffers the greatest rupture. Thus the presence of the 1 : 6-anhydro ring alters the balance of isomers produced on ethylene oxide ring scission. We have now found that acidic reagents have a similar effect, at least in the one case examined, that of 2 : 3-anhydro α-methylalloside (I). Thus with alkaline reagents the C–O bond (*a*) nearest the glycosidic group predominantly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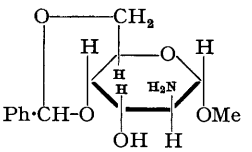
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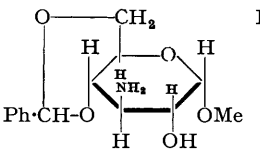
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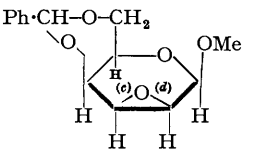
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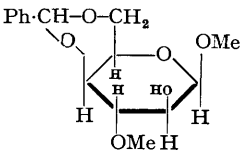
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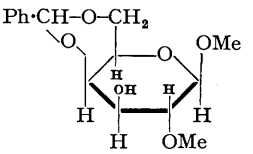
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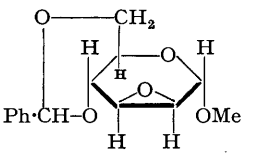
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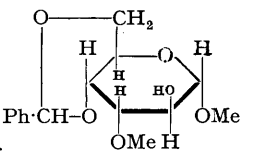
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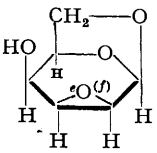
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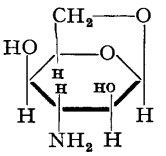
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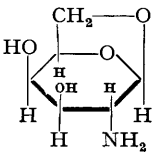
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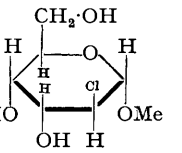
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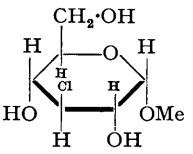
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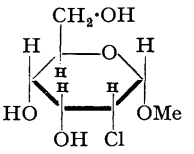
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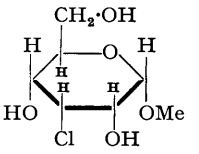
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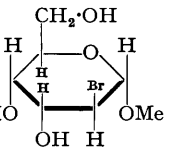
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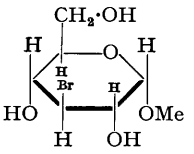
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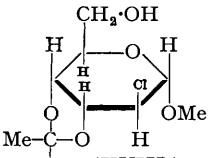
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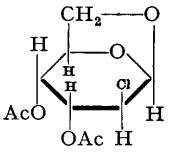
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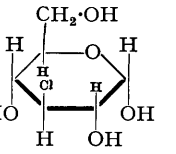
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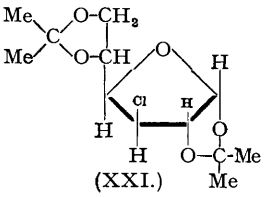
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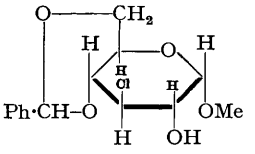
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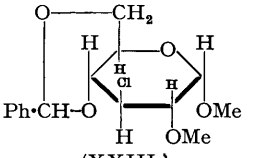
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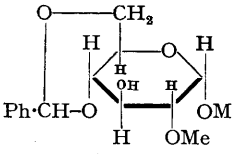
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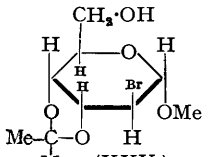
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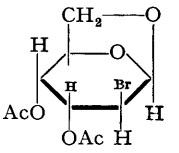
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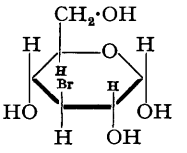
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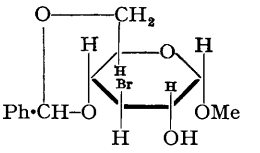
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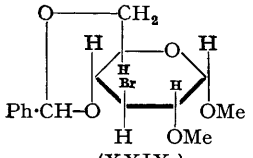
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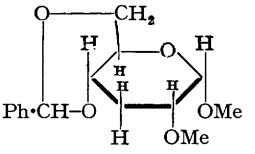
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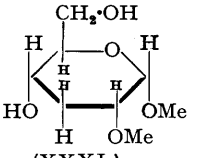
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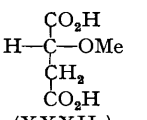
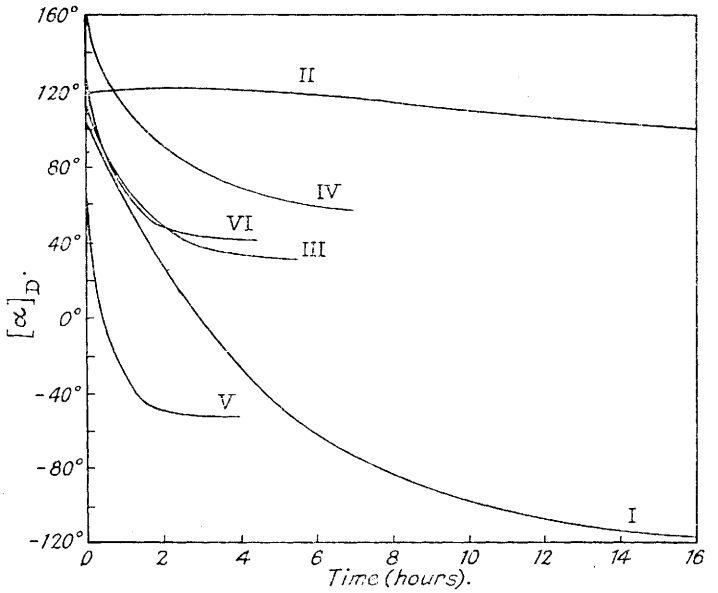

(XXXII.)

breaks, but when acids are used the bond (*b*) furthest from the glycosidic group is ruptured to a greater extent than (*a*).

The alloside (I) on treatment with hydrochloric acid gives two isomers, 2-*chloro* α-*methyl-altroside* (XII) and 3-*chloro* α-*methylglucoside* (XIII), with the latter predominating, although the difference in the amounts of the two isomers is not so pronounced as that observed when alkaline reagents were used to effect ring scission. Similarly, the products obtained by the action of hydrobromic acid were the corresponding bromo derivatives, 3-*bromo* α-*methylglucoside* (XVII) and 2-*bromo* α-*methylaltroside* (XVI), the former being produced to the greater extent.

The chloro hexosides, produced by the action of hydrochloric acid in acetone solution on 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside, were first encountered by Robertson and Dunlop (*J.*, 1938, 472) who did not, however, establish their constitution. The bromo hexosides obtained in the course of this investigation have not been previously described. We have now collected evidence enabling us to state with confidence the structure of these four halohydrins.

When the ethylene oxide ring of the alloside (I) is opened with hydrochloric acid, the formation of four isomeric chlorohydrins (XII, XIII, XIV, and XV) is possible.



Hydrolysis of:

I. 2-*Chloro* α-*methylaltroside with* 5% *sulphuric acid.*
II. 3-*Chloro* α-*methylglucoside with* 15% *sulphuric acid.*
III. 3-*Chloro* α-*methylglucoside with* 25% *sulphuric acid.*
IV. α-*Methylglucoside with* 10% *sulphuric acid.*
V. 2-*Bromo* α-*methylaltroside with* 5% *sulphuric acid.*
VI. 3-*Bromo* α-*methylglucoside with* 25% *sulphuric acid.*

Robertson and Dunlop (*loc. cit.*) found that each of the two chloro compounds isolated was reconverted into the original anhydro sugar by moist silver oxide. Therefore, (XIV) and (XV) are eliminated as possible structures, since we know that anhydro ring formation does not take place unless accompanied by Walden inversion (see Peat, *Ann. Reports*, 1939, **36**, 258).

The two chloro α-methylhexosides must therefore be derivatives of altrose and glucose and may be represented as (XII) and (XIII), the problem being to assign the correct configuration to the two isomers. The solution of this question has been provided by experiments on the hydrolysis of the chloro α-methylhexosides. The products of the reaction of hydrochloric acid with the anhydro alloside (I), which we shall designate as fraction (I) and fraction (II), were obtained in yields of 20% and 40% respectively. Fraction (I) hydrolysed readily with N-sulphuric acid, a change which was accompanied by a rapid and marked alteration in the specific rotation of the compound (see figure). On completion of the hydrolysis the solution was only faintly reducing to Fehling's solution, and a liquid was isolated which after acetylation gave a non-reducing crystalline compound having a very high negative rotation ($[\alpha]_D$ — 212·2°).

This behaviour was strikingly reminiscent of that of crystalline altrose (Hudson and Richtmyer, *J. Amer. Chem. Soc.*, 1935, **57**, 1716; 1940, **62**, 961). The specific rotation of altrose when treated with hot acid solution changes from $[\alpha]_D$ + 34° to − 98°, a change which is accompanied by partial loss in reducing power, this behaviour being ascribed to the formation of 1 : 6-anhydro β-altrose (altrosan). The similarity between these observations and the behaviour of the chloro sugar of fraction (I) was so close as to suggest that, since either fraction (I) or (II) must have the altrose configuration, it must be fraction (I) which did in fact possess this constitution. Further evidence in support of this came from its condensation with acetone. Of the two possible formulæ (XII) and (XIII), clearly only *2-chloro α-methylaltroside* (XII) could form an acetone compound. Condensation of fraction (I) with acetone gave a mono-acetone compound which must therefore be *2-chloro* 3 : 4-*monoacetone α-methylaltroside* (XVIII), and the derivative of altrosan produced by the acid hydrolysis of fraction (I) was *2-chloro* 3 : 4-*diacetyl* 1 : 6-*anhydro* β-*altrose* (XIX). Since we have shown the constitution of fraction (I) to be that of 2-chloro α-methylaltroside, it follows that the second isomer, fraction (II), must possess the only other possible structure, that of 3-chloro α-methylglucoside (XIII). This substance was extremely difficult to hydrolyse by acid, requiring 25% sulphuric acid to effect hydrolysis at a reasonable rate (see figure, in which the hydrolysis of α-methylglucoside is shown for comparison). Here the change in rotation was less marked ($[\alpha]_D$ + 135 ⟶ + 30°) than in the case of fraction (I), and the crystalline product isolated, which strongly reduced Fehling's solution, was *3-chloro glucose* (XX). This condensed with acetone to yield a diacetone derivative which would appear to be *3-chloro* 1 : 2-5 : 6-*diacetone glucofuranose* (XXI). The fact that the chloro sugar does condense with acetone to give a diacetone compound is additional proof of its constitution since atomic models show that 3-chloro glucose, but not 2-chloro altrose, could form a diacetone compound.

Only 3-chloro α-methylglucoside forms a crystalline benzylidene compound, 3-chloro 4 : 6-benzylidene α-methylglucoside (XXII), a compound which by treatment with sodium methoxide can be transformed into the original 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside. The 2-chloro α-methylaltroside gave only a syrupy benzylidene compound, together with some of the original anhydro alloside (I) which had been produced undoubtedly by the action of the sodium carbonate, used in the isolation process, on the syrupy 2-chloro benzylidene α-methylaltroside. The 3-chloro 4 : 6-benzylidene α-methylglucoside (XXII) was easily converted into *3-chloro* 4 : 6-*benzylidene 2-methyl α-methylglucoside* (XXIII), but attempts to remove the halogen atom either by hydrogenation or by alkaline hydrolysis failed. Had the hydrolysis been successful, 4 : 6-benzylidene 2-methyl α-methylglucoside (XXIV) would have been formed. However, the behaviour of this compound was in accordance with our experiences with tosyl esters of sugar derivatives in which anhydro ring formation is not possible, for only when such ring formation can occur does the hydrolysis of tosyl ester occur readily.

On treating 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside with hydrobromic acid in aqueous acetone solution, a mixture of two bromo α-methylhexosides was formed; fraction (A), m. p. 153°, $[\alpha]_D$ + 86·2, was shown to be 2-bromo α-methylaltroside, and fraction (B), m. p. 132—133°, $[\alpha]_D$ + 109·8, was 3-bromo α-methylglucoside. (A) was obtained in 10% and (B) in 40% yield, amounts which are similar to those of the corresponding chloro sugars obtained above. That is to say there has been again a reversal of the balance of the isomers produced by the action of the acid on the anhydro compound when compared with that produced when alkaline reagents were the agents causing ring scission.

The structure of the two bromo α-methylhexosides has been established as follows. The formation of four isomers, analogous to those mentioned in the discussion of the chloro α-methyl-hexosides, is theoretically possible on ring scission of the alloside with hydrobromic acid. The 2-bromo and 3-bromo derivatives of allose are eliminated by virtue of the fact that fraction (A) and fraction (B) have both been converted into the original 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside, so that we are again left with the problem of the allocation of the correct configuration, namely, that of 2-bromo α-methylaltroside (XIV) and 3-bromo α-methyl-glucoside (XV) to fraction (A) and (B). The problem would be solved if the constitution of one only of the isomers could be established, and this we have been able to do unequivocally by the conversion of one of the isomers into a compound of known constitution.

Fraction (B) was converted into crystalline *3-bromo* 4 : 6-*benzylidene α-methylglucoside* (XXVIII) which on methylation with methyl iodide and silver oxide gave *3-bromo* 4 : 6-*benzylidene 2-methyl α-methylglucoside* (XXIX). This, on catalytic hydrogenation over Raney nickel in the presence of alcoholic potash, gave 4 : 6-benzylidene 2-methyl 3-deoxy-α-methyl-glucoside (XXX) identical with the product obtained by Prins (*Helv. Chim. Acta*, 1946, **29**, 1)

from the hydrogenation products of 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside. Prins proved the constitution of (XXX) by hydrolysis to 2-methyl 3-deoxy-α-methylglucoside (XXXI) followed by oxidation to *d*-methoxysuccinic acid (XXXII), which could only be obtained from a compound having the constitution (XXXI). It is clear, therefore, that fraction (B) must be 3-bromo α-methylglucoside (XV) and consequently fraction (A) must possess the only alternative structure, that of 2-bromo α-methylaltroside (XIV).

Additional evidence in support of this contention comes from experiments on the hydrolysis of the two isomers. Fraction (A) undergoes hydrolysis easily with alteration in specific rotation from $[\alpha]_D + 87°$ to $[\alpha]_D - 90°$ (see figure), a change reminiscent of the behaviour of altrose derivatives (Richtmyer and Hudson, *loc. cit.*). The product, which only faintly reduced Fehling's solution, gave on acetylation a liquid product, which probably contained 2-bromo 3 : 4-diacetyl 1 : 6-anhydro β-altrose (XXVI). Moreover, fraction (A) condensed with acetone to yield a crystalline monoacetone compound, and, since only 2-bromo α-methylaltroside could do this, the compound must be 2-*bromo* 3 : 4-*monoacetone* α-*methylaltroside* (XXV). Fraction (B) failed to condense with acetone.

The hydrolysis of fraction (B) took place with difficulty, requiring 25% sulphuric acid to effect a fairly rapid rate of reaction; in this behaviour it was very similar to 3-chloro α-methylglucoside (see figure). The product, which was strongly reducing to Fehling's solution, was isolated as a crystalline bromo sugar, which must be 3-*bromo glucose* (XXVII).

It is clear, therefore, that the ring scission of 2 : 3-anhydro α-methylalloside with hydrobromic and hydrochloric acids follows the same course as when alkaline agents are used to effect ring opening, except that the respective yields of the two isomeric sugar products are reversed. The ring scission with each of the acid agents used is accompanied by a small amount of a third component (not a simple halogeno methylhexoside) which as yet we have not identified, but on which further work is being carried out.

We have used two other acidic reagents, namely, oxalic and sulphuric acids, to effect anhydro ring scission, though with less definite results than those obtained with the halogen acids. Sulphuric acid, after removing the benzylidene residue from 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside, effected partial ring opening giving rise to α-methylglucoside in 15% yield. No other substance, except unchanged 2 : 3-anhydro alloside, isolated as its benzylidene derivative, could, however, be isolated. The fact that α-methylglucoside and not α-methylaltroside is obtained does suggest, however, that sulphuric acid acts in the same way as the halogen acids. In addition, a compound, similar to the third component of the products of the action of halogen acids on the alloside (I), was also isolated by ether extraction of the reaction mixture, but has not yet been identified

During experiments, designed merely to remove the benzylidene residue from 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside, we found that oxalic acid is also effective in opening this particular anhydro ring, the effect being similar to sulphuric acid in so far as we could only isolate α-methylglucoside, in addition to the 2 : 3-anhydro α-methylalloside which remained intact.

Experimental.

Action of Hydrochloric Acid on 4 : 6-*Benzylidene* 2 : 3-*Anhydro* α-*Methylalloside.*—The alloside (12·5 g., prepared according to the method of Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1727) was dissolved in acetone (1 l.) and hydrochloric acid (36 c.c., 2N) added. The solution was boiled under reflux for 4 hours. The acid was neutralised with lead carbonate and the solution filtered. The precipitate was washed with acetone, the combined filtrate and washings were evaporated until free from acetone, and the aqueous solution (A) was extracted with ether to remove benzaldehyde. On evaporation of the ether and subsequent distillation of the benzaldehyde in steam, a syrup remained after evaporation of the water. This was dissolved in ether, evaporation of which gave a low-melting, crystalline substance. It was recrystallised with some difficulty from ether–light petroleum in large prisms, m. p. 59°, $[\alpha]_D^{18°} + 66·2°$ in chloroform (*c*, 1·630). This compound has so far not been identified.

The aqueous solution (A), after ether extraction, was evaporated to dryness under diminished pressure and the residue extracted with boiling ethyl acetate. This extract on being evaporated gave a crystalline solid (8·5 g.). On fractional recrystallisation from ethyl acetate, two fractions were obtained. Fraction (I) had m. p. 160—161°, $[\alpha]_D^{20°} + 111·0°$ in methyl alcohol (*c*, 1·960). Yield, 1·6 g. (Found: C, 40·0; H, 6·1. $C_7H_{13}O_5Cl$ requires C, 39·7; H, 6·1%). Fraction (II) had m. p. 136—138°, $[\alpha]_D^{20°} + 158·5°$ in methyl alcohol (*c*, 0·98). Yield, 2·0 g. (Found: C, 40·1; H, 6·6. $C_7H_{13}O_5Cl$ requires C, 39·7; H, 6·1%). For these two isomeric chloro α-methylhexosides, which are subsequently shown to be 2-*chloro* α-*methylaltroside* and 3-*chloro* α-*methylglucoside* respectively, Robertson and Dunlop (*loc. cit.*) give m. p. 160—162°, $[\alpha]_D^{16°} + 113·1°$ in methyl alcohol, and m. p. 136—138°, $[\alpha]_D^{15°} + 157·2°$ in methyl alcohol.

The syrupy residue which could not be crystallised further was shaken with benzaldehyde (10 c.c.) and zinc chloride (1·5 g.) for 24 hours. The solution was then poured into a mixture of petrol and water, whereupon a crystalline precipitate separated. This crystallised from alcohol in needles, m. p. 165°,

$[\alpha]_D^{20°}$ + 50·9° in chloroform (*c*, 1·37). Yield, 2·5 g. (Found : C, 56·1; H, 6·1; Cl, 12·2. $C_{14}H_{17}O_5Cl$ requires C, 56·0; H, 5·7; Cl, 11·7%).

Condensation of Fraction (II) with Benzaldehyde.—The substance (4·0 g.) was shaken for 24 hours with benzaldehyde (15 c.c.) and zinc chloride (2 g.). The solution was poured into a mixture of petrol and water and the crystalline precipitate which separated recrystallised from alcohol; m. p. 165° (3·2 g.). The benzylidene compound obtained above was therefore the same as that of fraction (II) and was a chloro benzylidene α-methylhexoside, shown to be *3-chloro* 4 : 6-*benzylidene α-methylglucoside.*

The yield of fraction (I) was 18·3% and that of fraction (II) (including the part isolated as the benzylidene derivative) was 38·5%.

In a second experiment, the alloside (13 g.) was dissolved in acetone (1 l.) containing hydrochloric acid (26 c.c., 2N) and the solution heated under reflux for 5½ hours. The acid was then neutralised with lead carbonate, and the precipitate collected and washed with acetone. The combined filtrate and washings were evaporated until free from acetone and the aqueous solution was extracted with ether to remove benzaldehyde. In this experiment, this extract was neglected. The aqueous layer was evaporated to dryness, and the residue extracted with boiling ethyl acetate. This extract deposited crystals.

Fraction (I), m. p. 156—160°, on being recrystallised had m. p. 161° (1·93 g.). The mother liquors were evaporated to dryness and the residue recrystallised from ethyl acetate giving fraction (II), m. p. 136—138° (3·1 g.). A small amount of fraction (I) next separated m. p. 161° (0·55 g.). Total yield of fraction (I) was 2·48 g. The syrupy mother liquors were evaporated to dryness and the residual syrup (2·45 g.) benzylidenated in the manner described above. The crystalline benzylidene compound of fraction (II) was obtained, m. p. 165° [0·95 g. which corresponds to 0·67 g. of fraction (II) itself].

Fraction (I) was obtained in a yield of 23·6%, and fraction (II) (including that obtained as the benzylidene derivative) in a yield of 36%.

Condensation of Fraction (I) with Acetone.—The compound (0·6 g.) was shaken with dry acetone (25 c.c.) containing concentrated sulphuric acid (0·15 c.c.). Solution was complete within one hour. After 24 hours, the solution was neutralised by anhydrous sodium carbonate, the solution filtered, and the residue washed with acetone. The combined filtrate and washings were evaporated, giving a thick colourless liquid (0·66 g.) which slowly crystallised. It crystallised from ethyl acetate–light petroleum in prisms, m. p. 60°, $[\alpha]_D^{20°}$ + 75·9° in chloroform (*c*, 0·80). It was *2-chloro* 3 : 4-*monoacetone α-methylaltroside* (Found : C, 47·2; H, 6·8; Cl, 14·7. $C_{10}H_{17}O_5Cl$ requires C, 47·6; H, 6·7; Cl, 14·1%).

Attempted Condensation of Fraction (II) with Acetone.—The crystalline substance, m. p. 136—138° (1 g.), was shaken with acetone (25 c.c.) containing concentrated sulphuric acid (0·5 g.) for 24 hours. The crystals rapidly dissolved. The acid was neutralised with anhydrous sodium carbonate, the solution filtered, and the inorganic residue washed with acetone. The combined filtrate and washings were evaporated in the presence of a trace of barium carbonate and the residue, which rapidly crystallised, was recrystallised from ethyl acetate; m. p. 136—137° (0·7 g.). It was unchanged starting material (mixed m. p.). This experiment indicated that fraction (II) could not form an acetone compound.

Hydrolysis of 2-Chloro α-Methylaltroside [Fraction (I)] with Sulphuric Acid.—The substance (0·73 g.) was dissolved in sulphuric acid (30 c.c., 0·1N) (*c*, 2·44) and heated at 100°: $[\alpha]_D$ + 14·7° (initial value); + 111·5° (30 mins.); + 109·0° (90 mins.). The reaction was proceeding very slowly, so the strength of the acid was increased tenfold (*c*, 2·38) and the heating continued until constant rotation was reached: $[\alpha]_D$ + 105·1° (initial value); + 56·3° (1 hr.); + 25·2° (2 hrs.); − 18·5° (3·5 hrs.); − 44·5° (5·5 hrs.); − 80·0° (8 hrs.); − 100° (11 hrs.); − 111·8° (13 hrs.); − 115·9° (16 hrs.); − 117·6° (18 hrs.). The solution was neutralised with barium carbonate and filtered, and the precipitate washed with hot water. The combined filtrates, which were only slightly reducing to Fehling's solution, were evaporated to a syrup (0·69 g.) the specific rotation of which was − 99·5° in water (*c*, 6·87). This was boiled with acetic anhydride (20 c.c.) and sodium acetate (2 g.) for 20 minutes, poured into water, neutralised with sodium bicarbonate, extracted with chloroform, and the extract dried ($MgSO_4$). Evaporation of the solvent gave a thick syrup which distilled at 130—150° (bath temp.)/0·01 mm. The distillate set on cooling to a hard glass which partly crystallised on treatment with alcohol. The crystals were collected and recrystallised from alcohol; large prisms, m. p. 90—91°, $[\alpha]_D^{17°}$ − 212 2° in chloroform (*c*, 0·452). Yield, 0·2 g. The compound was *2-chloro* 3 : 4-*diacetyl* 1 : 6-*anhydro β-altrose* (Found : C, 45·9; H, 5·2; Cl, 12·3. $C_{10}H_{13}O_6Cl$ requires C, 45·5; H, 5·0; Cl, 13·5%).

Hydrolysis of 3-Chloro α-Methylglucoside [Fraction (II)].—(a) *With 5% sulphuric acid.* The substance (1·56 g.) was dissolved in sulphuric acid (30 c.c., 5%) (*c*, 5·218) and the solution heated at 100°: $[\alpha]_D$ + 145·3° (initial value); + 145·1° (½ hr.); + 143·5° (1½ hrs.); + 140·0° (5½ hrs.); + 134·6° (8 hrs.); + 128·2° (14½ hrs.); + 127·6° (17 hrs.). These figures show that hydrolysis was slow. The solution, which was reducing to Fehling's solution, was neutralised with barium carbonate, and the precipitate was filtered off and washed with hot water. On evaporation of the combined filtrates, a crystalline product was obtained. This was recrystallised from ethyl acetate; it had m. p. 136—138° (0·5 g.) and was unchanged starting material. It was accompanied by a non-crystalline product.

(b) *With 15% sulphuric acid.* The syrup and crystals from (a) (1·31 g.) were dissolved in sulphuric acid (25 c.c., 15%) (*c*, 5·25) and the solution heated at 100°: $[\alpha]_D$ + 119·3° (initial value); + 120·0° (½ hr.); + 121·2° (2½ hrs.); + 111·9° (9½ hrs.); + 100·2° (16½ hrs.); + 103·0° (20 hrs.). These figures show that the reaction was proceeding still very slowly and on working up the product as before a small amount of the original crystalline substance, m. p. 136°, was recovered (0·2 g.), together with the syrupy material.

(c) *With 25% sulphuric acid.* The crystalline substance, m. p. 136° (4·5 g.), was dissolved in sulphuric acid (75 c.c., 25%) (*c*, 6·0) and the solution boiled under reflux until a constant rotation value was reached: $[\alpha]_D$ + 135° (initial value); + 80·5° (½ hr.); + 66·5° (1 hr.); + 111·2° (2½ hrs.); + 32·2° (4 hrs.); + 30·2° (5·5 hrs.). The solution, reducing to Fehling's solution, was neutralised with barium carbonate, and the precipitate filtered off, and washed with hot water; the combined filtrates were evaporated. The residue was crystalline and on recrystallisation from alcohol gave colourless prisms, m. p. 155—156°;

$[\alpha]_D^{20°}$ + 64·1° in water (*c*, 2·215). It was 3-*chloro glucose*. Yield, 2·5 g. (Found: C, 36·4; H, 5·5 $C_6H_{11}O_5Cl$ requires C, 36·4; H, 5·5%).

Hydrolysis of α-Methylglucoside with 10% *Sulphuric Acid.*—α-Methylglucoside (1 g.) was dissolved in sulphuric acid (25 c.c., 2N) (*c*, 4·0) and heated at 100° until the rotation was constant: $[\alpha]_D$ + 156° (initial value); + 133° (½ hr.); + 119° (1 hr.); + 96° (2 hrs.); + 77° (3 hrs.); + 65° (4 hrs.); + 61° (5 hrs.); + 58° (6 hrs.); + 57° (7 hrs.).

Condensation of 3-*Chloro Glucose with Acetone.*—3-Chloro glucose (0·5 g.) was shaken with acetone (40 c.c.) containing concentrated sulphuric acid (0·2 c.c.). Solution was complete within ½ hour. After 12 hours the acid was neutralised with anhydrous sodium carbonate and the inorganic material filtered off and washed with acetone. The combined filtrates were evaporated and the residue was extracted with chloroform. On evaporation of the solvent, a syrup (0·8 g.) was obtained. This distilled in the presence of barium carbonate as a colourless liquid (0·3 g.), b. p. 155° (bath temp.)/0·02 mm.; $n_D^{22°}$ 1·4612; $[\alpha]_D^{21°}$ — 18·2° in chloroform (*c*, 0·88). It was 3-*chloro diacetone glucose* (Found: C, 52·0; H, 7·2. $C_{12}H_{19}O_5Cl$ requires C, 51·9; H, 6·8%).

Condensation of 2-*Chloro α-Methylaltroside* [*Fraction* (*I*)] *with Benzaldehyde.*—The substance (0·7 g.) was shaken with benzaldehyde (15 c.c.) and zinc chloride (0·5 g.) for 3 days, by which time solution was complete. Sodium carbonate (0·5 g.) dissolved in water was added and the solution steam distilled in a vacuum until all benzaldehyde had been removed. After evaporation to dryness, the residue was extracted with chloroform. On evaporation of the solvent, a residue was obtained which only crystallised to a small extent. The crystalline substance was 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside (20 mg.), m. p. 197—198°, doubtless formed during the process of isolation. The main syrup, however, could not be crystallised. The experiment was repeated with the same result.

Treatment of 3-*Chloro* 4 : 6-*Benzylidene α-Methylglucoside with Sodium Methoxide.*—The substance (40 mg.) was dissolved in chloroform (2 c.c.) and a solution of sodium (3 mg., 1 mol.) in methyl alcohol (2 c.c.) added with cooling. Next day the solution was diluted with an equal volume of water and exhaustively extracted with chloroform. The extract was evaporated after drying ($MgSO_4$), leaving a crystalline residue. This on recrystallisation from alcohol gave 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside (16 mg.), m. p. 199° undepressed in admixture with an authentic specimen.

3-*Chloro* 4 : 6-*Benzylidene* 2-*Methyl α-Methylglucoside.*—3-Chloro 4 : 6-benzylidene α-methylglucoside (1·1 g.) was treated thrice with methyl iodide and dry silver oxide at 45°. After each treatment, the methyl iodide was distilled off and the residue extracted with boiling chloroform. At the conclusion of the third treatment, the *product* was recrystallised from alcohol in needles, m. p. 145—146°; $[\alpha]_D^{20°}$ + 46·4° in acetone (*c*, 0·926). Yield, 0·9 g. (Found: C, 57·5; H, 6·0; Cl, 11·5; OMe, 19·4. $C_8H_{15}O_5Cl$ requires C, 57·3; H, 6·1; Cl, 10·3; OMe, 19·7%).

Attempted Hydrogenation of 3-*Chloro* 4 : 6-*Benzylidene* 2-*Methyl α-Methylglucoside.*—The compound (0·85 g.) suspended in dry methyl alcohol (100 c.c.) containing potassium hydroxide (0·2 g.) was heated with hydrogen in the presence of Raney nickel at 130°/100 atm. for 6 hours. No reaction took place, and the unchanged 3-chloro 4 : 6-benzylidene 2-methyl α-methylglucoside was recovered. The experiment was repeated at 180°/100 atm. for 6 hours but again no reaction took place. A final attempt was made at 220°/125 atm. for 6 hours, but this resulted in complete destruction of the compound.

Attempted Reaction of 3-*Chloro* 4 : 6-*Benzylidene α-Methylglucoside with Sodium Iodide in Acetone.*—The compound (0·43 g.) was dissolved in dry acetone (50 c.c.) containing dry sodium iodide (0·6 g.). The solution was heated in a sealed tube at 100° for 48 hours. No sodium chloride separated and, after the solvent had been removed and the product washed with water and recrystallised from alcohol, starting material was recovered, m. p. 163—165° (0·38 g.). No reaction had occurred.

Treatment of 3-*Chloro* 4 : 6-*Benzylidene* 2-*Methyl α-Methylglucoside with Potassium Hydroxide.*—(*a*) The compound (0·8 g.) was dissolved in acetone (45 c.c.) and water (200 c.c.) containing potassium hydroxide (1·2 g.). The mixture, which was not homogeneous, was boiled under reflux for 9 hours with frequent shaking. It was then diluted with water and extracted with chloroform. The extract, after being dried ($MgSO_4$), was evaporated; the residue on recrystallisation from alcohol had m. p. 143—145° alone or in admixture with the original compound. Yield, 0·7 g.

(*b*) The recovered compound (0·7 g.) was heated with alcoholic potash (1·2 g. KOH in 75 c.c. of alcohol) at 130° in a sealed tube for 48 hours. The product, which was very dark in colour, and had clearly suffered extensive decomposition, was diluted with water and extracted with chloroform. The extract after being dried ($MgSO_4$) and evaporated yielded only starting material, m. p. 141—143° alone or in admixture with the original pure compound. Yield, 0·48 g.

Treatment of 4 : 6-*Benzylidene* 2 : 3-*Anhydro α-Methylalloside with Hydrobromic Acid.*—The alloside (7 g.) was dissolved in acetone (500 c.c.) and hydrobromic acid (20 c.c., 2N) added. The solution was boiled under reflux for 4 hours. The acid was then neutralised with lead carbonate and the inorganic material filtered off and washed with acetone. The aqueous solution was extracted with ether to remove free benzaldehyde. On evaporation of the ether and subsequent steam distillation in a vacuum to remove benzaldehyde and evaporation to dryness, a syrup was obtained. This was dissolved in ether, the solution filtered, and the solvent removed. A low-melting crystalline substance was obtained which was recrystallised with some difficulty from ethyl acetate–light petroleum; it formed prisms, m. p. 65—67°; $[\alpha]_D^{15°}$ + 42·2° in chloroform (*c*, 0·945). This compound has so far not been identified.

The aqueous solution, after ether extraction, was evaporated to dryness under diminished pressure and the residue extracted with boiling ethyl acetate. This extract on being evaporated gave a crystalline residue which was fractionally recrystallised from alcohol. Fraction (A) (0·65 g.) crystallised in prisms, m. p. 153—153·5°; $[\alpha]_D^{17°}$ + 86·2° in alcohol (*c*, 0·487) (Found: C, 32·6; H, 5·1; Br, 29·8. $C_7H_{13}O_5Br$ requires C, 32·7; H, 5·0; Br, 31·1%). Evaporation of the mother liquors and recrystallisation of the residue from ethyl acetate gave fraction (B) (1·9 g.) in needles, m. p. 132—133°; $[\alpha]_D^{15°}$ + 109·8° in alcohol (*c*, 0·437) (Found: C, 32·2; H, 5·2; Br, 31·5%). Fractions (A) and (B) are subsequently shown to be 2-*bromo α-methylaltroside* and 3-*bromo α-methylglucoside* respectively.

On evaporation of the mother liquors a syrupy residue (1·0 g.) was obtained which could not be

crystallised. This was shaken with benzaldehyde (10 c.c.) and zinc chloride (0·5 g.) for 24 hours. Sodium carbonate (0·5 g.) was added and the benzaldehyde removed by steam distillation under reduced pressure. The dry residue was extracted with chloroform; on evaporation of the extract, a crystalline residue was obtained which recrystallised from alcohol in feathery needles, m. p. 174—175°. Yield, 1·1 g. $[\alpha]_D^{16°}$ + 12·8° in chloroform (*c*, 2·336) (Found: C, 49·0; H, 4·8; Br, 24·1. $C_{14}H_{17}O_5Br$ requires C, 48·7; H, 4·9; Br, 23·2%).

Condensation of Fraction (B) with Benzaldehyde.—The crystalline substance, m. p. 132° (6·3 g.), was shaken for 24 hours with benzaldehyde (100 c.c.) and zinc chloride (6·3 g.). Sodium carbonate (8·5 g.) was added, and the benzaldehyde removed by steam distillation under reduced pressure. The dry residue was extracted with chloroform and the extract evaporated. A crystalline residue was obtained which was recrystallised from alcohol giving feathery needles, m. p. 175° undepressed in admixture with the benzylidene compound obtained above; it was 3-*bromo* 4 : 6-*benzylidene* α-*methylglucoside*.

The yield of fraction (A) was 9·6%, and that of fraction (B) (including the part isolated as the benzylidene derivative) was 41%.

Condensation of Fraction (A) with Acetone.—The substance (0·9 g.) was shaken with acetone (40 c.c.) containing concentrated sulphuric acid (0·2 c.c.). Solution took place almost immediately, and after 24 hours the acid was neutralised with anhydrous sodium carbonate. The inorganic material was filtered off and washed with acetone and the combined filtrates were evaporated to a thick syrup. This was distilled in the presence of barium carbonate; b. p. 140° (bath temp.)/0·01 mm. (Found: OMe, 10·4. $C_{10}H_{17}O_5Br$ requires OMe, 10·4%). The distillate subsequently crystallised and was recrystallised from ether–light petroleum in prisms, m. p. 64—66°; $[\alpha]_D^{15°}$ + 43·1° in chloroform (*c*, 1·068) (Found: C, 39·9; H, 5·8. $C_{10}H_{17}O_5Br$ requires C, 40·4; H, 5·7%); it was 2-*bromo* 3 : 4-*monoacetone* α-*methyl-altroside*.

Attempted Condensation of Fraction (B) with Acetone.—The substance (0·3 g.) was shaken with acetone (40 c.c.) containing concentrated sulphuric acid (0·2 c.c.). Solution was complete in 2 hours; after 24 hours the acid was neutralised with anhydrous sodium carbonate and the inorganic material filtered off and washed with acetone. The combined filtrates were evaporated in the presence of sodium carbonate and the residue was extracted with hot ethyl acetate. Evaporation of the solvent gave a syrup which crystallised on trituration with alcohol. It was recrystallised from alcohol; m. p. 130—132° (0·3 g.) undepressed in admixture with the starting material.

Hydrolysis of Fraction (A) with 5% Sulphuric Acid.—The substance (0·29 g.) was dissolved in sulphuric acid (15 c.c. 5%) (*c*, 1·94) and heated at 100° until the rotation was constant. $[\alpha]_D$ + 73·1° (initial value); + 45·4° (5 mins.); + 17·5° (15 mins.); − 28·9° (1 hr.); − 45·4° (1½ hrs.); − 49·5° (2 hrs.); − 55° (3 hrs.); − 55° (4 hrs.).

The sulphuric acid was neutralised with barium carbonate, and the precipitate filtered off and washed with hot water. The filtrate, which was only slightly reducing to Fehling's solution, was evaporated under reduced pressure and the residue extracted with boiling alcohol. Evaporation of the alcohol gave a glassy residue (0·3 g.) which contained barium salts. It was then boiled under reflux with acetic anhydride (10 c.c.) and sodium acetate (0·5 g.) for 10 mins. After being poured into water, the solution was neutralised with sodium bicarbonate and extracted with chloroform. Evaporation of the solvent gave a thick syrup (0·2 g.) which distilled at 160—190° (bath temp.)/0·01 mm. The distillate (0·07 g.) had $[\alpha]_D^{20°}$ − 68·0° in chloroform (*c*, 1·055), and probably contained 2-bromo 3 : 4-diacetyl 1 : 6-anhydro β-altrose (Found: Br, 17·7, 17·1. Calc. for $C_{10}H_{13}O_6Br$: Br, 24·9%).

Hydrolysis of Fraction (B) with Sulphuric Acid.—The substance (1·66 g.) was dissolved in sulphuric acid (25 c.c., 10%) (*c*, 6·652) and the solution boiled under reflux until constant rotation was reached. $[\alpha]_D$ + 116·5° (initial value); + 91° (15 mins.); + 80·5° (30 mins.); + 64·0° (1 hr.); + 46·3° (2 hrs.); + 44·5° (3 hrs.); + 42·5° (4½ hrs.). The solution, which was reducing to Fehling's solution, was neutralised with barium carbonate, and the precipitate filtered off and washed with hot water. On evaporation of the combined filtrates a syrup was obtained (1·55 g.) which crystallised on trituration with alcohol. Recrystallisation from alcohol gave colourless prisms, m. p. 151°; $[\alpha]_D^{20°}$ + 60·9° in water (*c*, 2·530). It was 3-*bromo glucose* (Found: C, 30·0; H, 4·97. $C_6H_{11}O_5Br$ requires C, 29·6; H, 4·54%).

Condensation of Fraction (A) with Benzaldehyde.—The substance (0·5 g.) was shaken for 12 hours with benzaldehyde (10 c.c.) and zinc chloride (0·5 g.). Anhydrous sodium carbonate (0·5 g.) was then added, the excess of benzaldehyde removed by steam distillation under reduced pressure, and the dry residue extracted with hot chloroform. Evaporation of the chloroform gave a semi-crystalline residue (0·3 g.) from which was crystallised 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside, m. p. 198—199° alone or in admixture with an authentic specimen.

Treatment of 3-*Bromo* 4 : 6-*Benzylidene* α-*Methylglucoside with Sodium Methoxide.*—The substance (0·1 g.) was dissolved in chloroform (4 c.c.) and a solution of sodium (8 mg., 1 mol.) in methyl alcohol (4 c.c.) added with cooling. After 12 hours the solution was diluted with water and extracted with chloroform. Evaporation of the solvent after drying ($MgSO_4$) gave a crystalline residue which was recrystallised from alcohol in feathery needles, m. p. 198—199° undepressed in admixture with 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside. Yield, 0·04 g.

3-*Bromo* 4 : 6-*Benzylidene* 2-*Methyl* α-*Methylglucoside.*—3-Bromo 4 : 6-benzylidene α-methylglucoside (7·1 g.) was heated thrice with methyl iodide and dry silver oxide at 45°. After each treatment the methyl iodide was distilled off and the residue extracted with boiling chloroform. After the third treatment, the product was recrystallised from alcohol in feathery needles, m. p. 168—168·5°; $[\alpha]_D^{18°}$ + 7·8° in alcohol (*c*, 0·511). Yield, 6·6 g. (Found: C, 50·3; H, 5·3; Br, 21·3. $C_{15}H_{19}O_5Br$ requires C, 50·1; H, 5·3; Br, 22·3%).

4 : 6-*Benzylidene* 2-*Methyl* 3-*Deoxy*-α-*methylglucoside.*—3-Bromo 4 : 6-benzylidene 2-methyl α-methylglucoside (0·5 g.) was suspended in methyl alcohol (50 c.c.) containing potassium hydroxide (0·25 g.) and shaken with hydrogen over Raney nickel at room temperature. 120 C.c. (N.T.P.) of hydrogen were rapidly absorbed. The catalyst was filtered off and the alcohol evaporated. The residue was washed with water, and recrystallised from alcohol in feathery needles, m. p. 79—80°; $[\alpha]_D^{20°}$ + 81·6°

in alcohol (*c*, 4·54). Yield, 0·3 g. (Found: C, 63·7; H, 7·0. Calc. for $C_{15}H_{20}O_5$: C, 64·3; H, 7·1%). Prins (*loc. cit.*) gives m. p. 79—80°; $[\alpha]_D$ + 83° in chloroform.

Treatment of 4 : 6-*Benzylidene* 2 : 3-*Anhydro* α-*Methylalloside with Sulphuric Acid.*—The alloside (10 g.) was dissolved in acetone (1 l.), sulphuric acid (29 c.c., 2N) added, and the solution boiled under reflux for 4 hours. The acid was then neutralised with barium carbonate and the inorganic precipitate filtered off and washed with acetone. The combined filtrates were evaporated until free from acetone and the aqueous solution was extracted with ether. On evaporation of the ether and subsequent distillation of the benzaldehyde in steam, a syrup (0·5 g.) remained on evaporation to dryness. This rapidly crystallised on addition of alcohol and on recrystallisation from alcohol was obtained in needles, m. p. 146—147°; $[\alpha]_D^{15°}$ + 11·6° in chloroform (*c*, 1·035). This compound has not been identified.

The aqueous solution, after ether extraction, was evaporated to dryness under diminished pressure. The residual syrup (5·5 g.) partially crystallised on addition of alcohol; recrystallisation from alcohol gave α-methylglucoside, m. p. 165° undepressed in admixture with an authentic specimen. Yield, 0·5 g. Evaporation of the mother liquors gave a syrup (4·8 g.), which could not be crystallised. It was shaken with benzaldehyde (50 c.c.) and zinc chloride (4 g.) for 24 hours. The solution was poured into water–light petroleum and the precipitate recrystallised from alcohol; m. p. 197—199° undepressed in admixture with 4 : 6-benzylidene 2 : 3-anhydro α-methylalloside. Yield, 4 g. Evaporation of the mother liquors provided a further 1·4 g. of syrup which could not be crystallised. It was not possible to isolate any of the altrose isomer which may have been formed.

Hydrolysis of 4 : 6-*Benzylidene* 2 : 3-*Anhydro* α-*Methylalloside with Oxalic Acid.*—The procedure adopted was that of Robertson and Dunlop (*loc. cit.*), namely, hydrolysis of the alloside (10 g.) in acetone solution (450 c.c.) containing oxalic acid (15 g. in 50 c.c. of water) by heating under reflux for 24 hours. The acid was removed as insoluble barium oxalate, and the acetone evaporated. Free benzaldehyde was removed by extraction with ether. On evaporation of the aqueous layer, a partly crystalline syrup was obtained; on recrystallisation from alcohol, α-methylglucoside separated, m. p. 164—165°. Yield, 0·8 g. A syrup (2·8 g.) was obtained on evaporation of the mother liquors, but this, which was presumably 2 : 3-anhydro α-methylalloside, could not be crystallised.

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