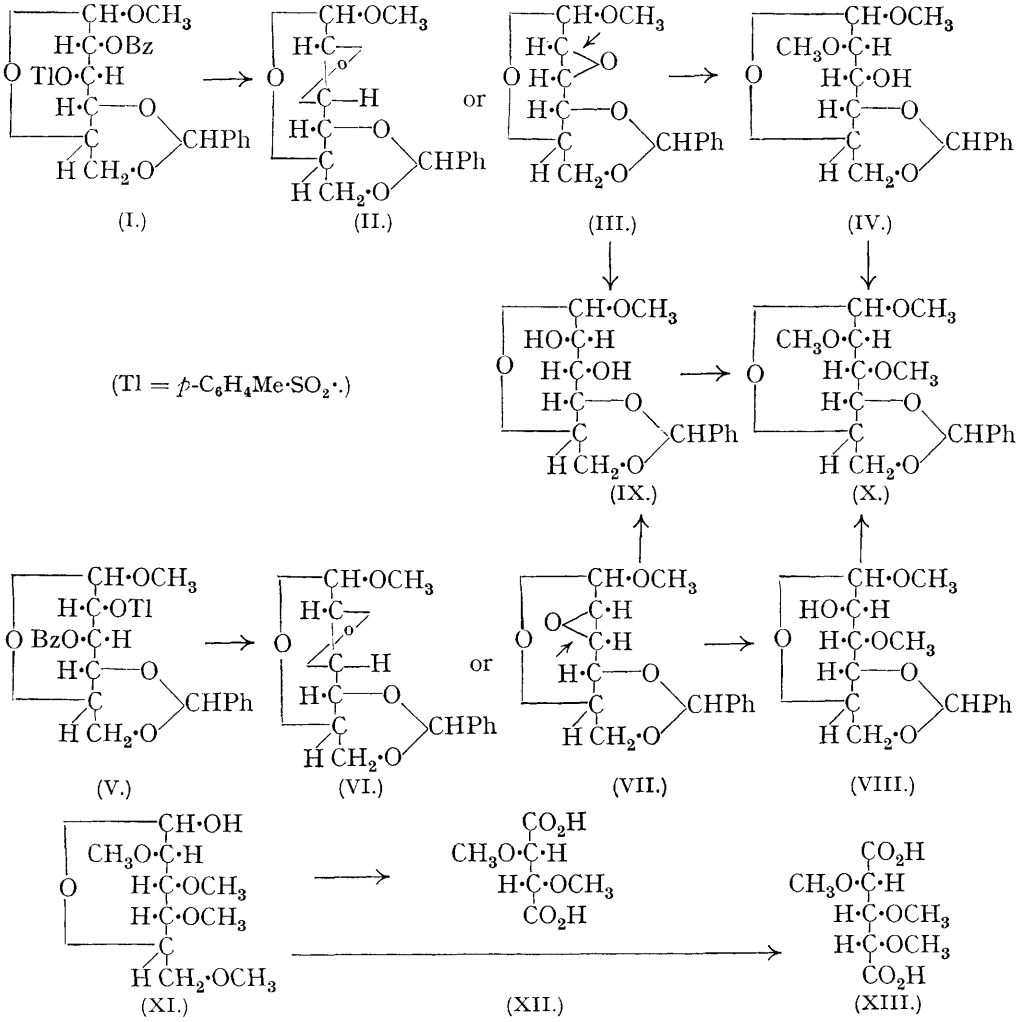
# 283. *The Conversion of Derivatives of Glucose into Derivatives of Altrose by Simple Optical Inversions.*

By George J. Robertson and Charles F. Griffith.



In continuation of our researches on the interconversion of sugars by simple agencies, we now describe a detailed study of the transformation of the glucose configuration into that of altrose. It has recently been shown (Mathers and Robertson, J., 1933, 1076) that the alkaline hydrolysis of 2 : 3-di-*p*-toluenesulphonyl 4 : 6-dimethyl α-methylglucoside follows an unexpected course and leads to the production of a 4 : 6-dimethyl 2 : 3-anhydro-α-methylhexoside along with a 4 : 6-dimethyl α-methylhexoside, which was tentatively described as a derivative of altrose. This result pointed to the idea that an investigation of the analogous reaction with 2 : 3-di-*p*-toluenesulphonyl 4 : 6-benzylidene α-methylglucoside should lead ultimately to the production of altrose in the free condition.

A preliminary research showed that this reaction resulted in the formation of a crystalline 4 : 6-benzylidene 2 : 3-anhydro-α-methylhexoside, m. p. 199—200°, together with a mono-




methyl 4 : 6-benzylidene α-methylhexoside, which was not a derivative of glucose. Moreover, it was significant that, when impure starting material (*i.e.*, a mixture of mono- and

di-*p*-toluenesulphonyl 4 : 6-benzylidene α-methylglucosides) was submitted to similar treatment, a second isomeric 4 : 6-benzylidene 2 : 3-anhydro-α-methylhexoside, m. p. 147°, was also obtained. The formation of two distinct 2 : 3-anhydro-compounds was striking, and it was decided to investigate the behaviour of derivatives substituted with the *p*-toluenesulphonyl residue in the 2- or the 3-position.

2-*Benzoyl* 3-p-*toluenesulphonyl* (I) and 3-*benzoyl* 2-p-*toluenesulphonyl* 4 : 6-*benzylidene* α-*methylglucoside* (V) were accordingly synthesised by a method which depended upon the preferential substitution in position 2 over position 3 (Dr. J. W. H. Oldham, unpublished result). The introduction of a benzoyl group into position 2 in 4 : 6-benzylidene α-methylglucoside without further substitution is difficult to control, and the yields of (I) are poor and variable. It is comparatively easy to introduce a *p*-toluenesulphonyl group into position 2, and the intermediate 2-p-*toluenesulphonyl* 4 : 6-*benzylidene* α-*methylglucoside* may be obtained in a pure condition.

When (I) is submitted to hydrolysis with methyl alcohol containing sodium methoxide, the 4 : 6-benzylidene 2 : 3-anhydro-α-methylhexoside, m. p. 199—200°, is obtained in 92% yield. When (V) is similarly treated, the 4 : 6-benzylidene 2 : 3-anhydro-α-methylhexoside, m. p. 147°, is obtained in 94% yield. It is therefore apparent that the formation of each isomeride is dependent upon the position of the *p*-toluenesulphonyl residue in the parent substance. Moreover, since the two anhydro-compounds are not identical, they may not be represented by structures (II) and (VI), in which the glucose configuration is retained. The formation of non-identical substances in the present instance furnishes, indeed, a strong argument against the possibility of *trans*-linkages in such a position. Ferns and Lapworth (J., 1912, **101**, 273) have shown that the esters of the sulphonic acids are sharply distinguished from those of the carboxylic acids in their mode of reaction with alkali and alkyl oxides. The vulnerable point in each series may be represented simply as follows:

$$R{-}SO_2{-}O{-}\vdots{-}R_1 \qquad\qquad R{-}CO{-}\vdots{-}O{-}R_1$$

When this conception is considered in conjunction with the work of Phillips (J., 1923, **123**, 44; 1925, **127**, 399), who has shown that the hydrolysis of *p*-toluenesulphonyl esters may be accompanied by change in configuration, it becomes clear that in the alkaline hydrolysis of (I) the configuration on carbon atom number 2 remains intact, while inversion is possible on number 3. It follows that the most probable structure for the anhydro-compound, m. p. 199—200°, is represented by (III), and the substance is accordingly described as 4 : 6-*benzylidene* 2 : 3-*anhydro-α-methylalloside*. Similar considerations being applied to the alkaline hydrolysis of (V), the most probable structure for the anhydro-compound, m. p. 147°, is (VII), and it is therefore described as 4 : 6-*benzylidene* 2 : 3-*anhydro-α-methylmannoside*.

The action of sodium methoxide on (III) and (VII) was now investigated, and a striking difference in the stability of the respective ethylene-oxide rings was noted. With (III), boiling with *N*-sodium methoxide solution for 20 hours is sufficient to bring about complete rupture of the ethylene-oxide ring, but with (VII) it is necessary to heat it with 5% sodium methoxide solution in a sealed tube at 100° for 20 hours to achieve a similar result. This may be cited as confirmatory evidence that, in the two substances under discussion, the ethylene-oxide rings lie on opposite sides of the plane of the molecule.

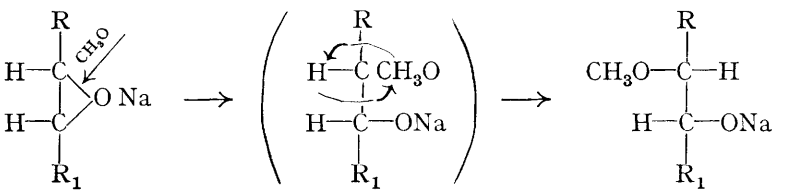
When 4 : 6-benzylidene 2 : 3-anhydro-α-methylalloside (III) is treated with sodium methoxide solution, the opening of the ring is accompanied by partial methylation, and a crystalline monoethyl 4 : 6-benzylidene α-methylhexoside is produced. The resulting substance may possess one of four configurations, *viz.*, those of glucose, mannose, allose, and altrose, depending upon the manner in which the ring is opened. The compound condenses with *p*-toluenesulphonyl chloride, and the derived mono-*p*-toluenesulphonyl compound is not identical with either 2-p-*toluenesulphonyl* 3-*methyl* or 3-*p*-toluenesulphonyl 2-methyl 4 : 6-*benzylidene* α-*methylglucoside* (a sample of the latter was kindly given us by Dr. J. W. H. Oldham). It follows that the new substance is not a derivative of glucose. The methyl group is proved to be in position 2 by the fact that, after the elimination of

the benzylidene residue and also of the methoxyl group in the reducing position, altrosazone, m. p. 164—165°, was derived with the loss of a methoxyl group. This proves the substance to be a derivative of allose or altrose, and the evidence adduced below shows it to be 4 : 6-*benzylidene* 2-*methyl* α-*methylaltroside* (IV). When (IV) is methylated, 4 : 6-*benzylidene* 2 : 3-*dimethyl* α-*methylaltroside*, (X), m. p. 83—85°, is obtained (mixed m. p. with 4 : 6-benzylidene 2 : 3-dimethyl α-methylglucoside of m. p. 122°, 66—110°). 4 : 6-Benzylidene 2 : 3-dimethyl α-methylmannoside is a syrup which shows $[\alpha]_D$ + 62·7°, while (X) has $[\alpha]_D$ + 92·8°.

Similarly, when 4 : 6-benzylidene 2 : 3-anhydro-α-methylmannoside (VII) is treated with sodium methoxide solution, a crystalline 4 : 6-benzylidene monomethyl α-methylhexoside is produced. It is not identical with 4 : 6-benzylidene 2-methyl α-methylaltroside (IV), but on methylation is converted into 4 : 6-benzylidene 2 : 3-dimethyl α-methylaltroside (X). The substance must therefore be 4 : 6-*benzylidene* 3-*methyl* α-*methylaltroside* (VIII). This is confirmed by the fact that, after the elimination of the benzylidene residue and also of the methoxyl group in the reducing position, a 3-methyl osazone is isolated, which is not identical with 3-methyl glucosazone and must therefore be 3-*methyl altrosazone*.

The altrose configuration has been ascribed to the substances (IV), (VIII), and (X), but the accumulated evidence so far described does not serve to discriminate between the allose and the altrose configuration for these compounds. Final proof of the correctness of our view was obtained as follows. The substance (X) was converted successively into 2 : 3-*dimethyl* α-*methylaltroside*, 2 : 3 : 4 : 6-*tetramethyl* α-*methylaltroside*, and 2 : 3 : 4 : 6-*tetramethyl altrose* (XI). The last compound was oxidised with nitric acid as described by Hirst (J., 1926, 353), and the product was a mixture containing *l*-dimethoxysuccinic acid (XII) and *d*-trimethoxyaraboglutaric acid (XIII), the components being identified by the isolation of crystalline *l*-dimethoxysuccindiamide, $[\alpha]_D$ — 89·3°, and crystalline *d*-trimethoxyaraboglutardiamide, $[\alpha]_D$ — 47·9°, respectively. Under similar conditions, tetramethyl allose would yield inactive dimethoxysuccinic acid and inactive trimethoxyriboglutaric acid. The evidence, however, is fundamental, as it furnishes further proof that the glucose and the mannose configuration may be ruled out of consideration. Tetramethyl glucose, under similar conditions, has been shown to yield *d*-dimethoxysuccinic acid and inactive trimethoxyxyloglutaric acid (Hirst, *loc. cit.*), whereas tetramethyl mannose would yield inactive dimethoxysuccinic acid along with an active lyxoglutaric acid.

The conversion of 4 : 6-benzylidene 2 : 3-anhydro-α-methylalloside (III) into 4 : 6-benzylidene 2-methyl α-methylaltroside (IV) involves a Walden inversion on carbon atom number 2, while the analogous conversion of 4 : 6-benzylidene 2 : 3-anhydro-α-methylmannoside (VII) into 4 : 6-benzylidene 3-methyl α-methylaltroside (VIII) involves an inversion on carbon atom number 3. It is thus evident that the ethylene-oxide rings in the isomeric anhydro-compounds open in opposite senses (as indicated by the arrows) under the influence of alkali. The reason for this is obscure, but may be connected with the relative positions of the rings with respect to the plane of the molecule. With regard to the mechanism involved in the opening of the ethylene-oxide rings, it is significant that in each case a methoxyl group is introduced in the position at which Walden inversion occurs. A similar phenomenon has been reported by Ohle and Just (*Ber.*, 1935, **68**, 602) during the conversion of 1 : 2-monoacetone 3 : 4-anhydro-*d*-psicose into 1 : 2-monoacetone 4-methyl *d*-sorbose by the action of sodium methoxide solution. It therefore seems probable that the opening of such a ring system under the above conditions should be formulated as follows :



The action of aqueous caustic potash under pressure on 4 : 6-benzylidene 2 : 3-anhydro-α-methylalloside (III) and 4 : 6-benzylidene 2 : 3-anhydro-α-methylmannoside (VII) has also been investigated. In each case the same substance, 4 : 6-*benzylidene α-methylaltroside* (IX), is produced. It is not identical with 4 : 6-benzylidene α-methylglucoside or with 4 : 6-benzylidene α-methylmannoside, and on methylation is converted into 4 : 6-benzylidene 2 : 3-dimethyl α-methylaltroside (X).

The removal of the benzylidene residue from the substances (IX), (IV), (VIII), and (X) proceeds smoothly in each case with the production of *α-methylaltroside* and its 2- and 3-*methyl* and 2 : 3-*dimethyl* derivatives respectively. On the other hand, the removal of the altrosidic methyl group (by hydrolysis with 4—8% hydrochloric acid) from the above four substances leads in each case to the production of an anhydro-derivative in equilibrium with a small amount of a reducing sugar, instead of to the free sugar, altrose, and its methylated analogues. The following table shows the initial and final specific rotations observed in the above series of hydrolyses. The final values are calculated on the basis of a complete conversion into the respective anhydro-compounds, and the figures in parentheses give the values for the corresponding free sugars.

| | | |
|---|---|---|
| α-Methylaltroside | $[\alpha]_D$ + 104° | ⟶ − 108·4° (− 97·6°) |
| 2-Methyl α-methylaltroside | $[\alpha]_D$ + 103·8° | ⟶ − 116·3° (− 105·5°) |
| 3-Methyl α-methylaltroside | $[\alpha]_D$ + 113·5° | ⟶ − 110·4° (− 99·4°) |
| 2 : 3-Dimethyl α-methylaltroside | $[\alpha]_D$ + 113° | ⟶ − 92·9° (− 84·9°) |

The observed end-points are not comparable with the recorded value for altrose (Austin and Humoller, *J. Amer. Chem. Soc.*, 1934, **56**, 1153, give $[\alpha]_D$ − 32·3° for *l*-altrose at equilibrium) or with the end-point attained in the hydrolysis of tetramethyl *d*-altrose, *viz.*, $[\alpha]_D$ + 51·6°. Although the products of hydrolysis are non-reducing, or almost so, the possibility of systems containing a free reducing group which have no action on Fehling's solution (compare Irvine and Skinner, J., 1926, 1089) has not been overlooked. This is, however, considered improbable in view of the fact that when the supposed anhydro-compounds are boiled with aqueous alkali, there is no pronounced loss in optical activity. The formation of anhydro-compounds during the hydrolysis of a methylaltrosidic group is not without precedent. Fischer, Bergmann, and Schotte (*Ber.*, 1920, **53**, 541) reported that the so-called "methyl epiglucosamine" reduced Fehling's solution only very slightly even after boiling with concentrated hydrochloric acid. This was substantiated by Levene and Meyer (*J. Biol. Chem.*, 1933, **55**, 223), who showed, however, that the failure of the hydrolysis product to reduce Fehling's solution was due, not to the great resistance of the methyl group to acid hydrolysis, but to the fact that hydrolysis was accompanied by the formation of an "anhydro-epiglucosamine." This was followed by the proof (Freudenberg, Burkhart, and Braun, *Ber.*, 1926, **59**, 714) that "methyl epiglucosamine" was, in fact, a 3-aminomethylaltroside. As far as we are aware, there is no other recorded instance of the hydrolysis of a methylaltroside, and it seems likely that this is a property peculiar to altrosides. Nothing very definite can be said regarding the position of the anhydro-linkage in the above compounds, but it seems reasonable to suggest that it must involve position 4 or 6, since only these positions are available in the case of 2 : 3-dimethyl altrose. The investigations are being continued.

## Experimental.

*Alkaline Hydrolysis of* 2 : 3-*Di*-p-*toluenesulphonyl* 4 : 6-*Benzylidene* α-*Methylglucoside*.—A typical experiment is quoted. The material (93 g.), m. p. 148°, was heated on a water-bath with methyl alcohol (400 c.c.) containing sodium (13 g.) for 12 hrs. After standing over-night, the reaction mixture was filtered, and the crystalline residue thoroughly washed with water. This material consisted of long needles (14·5 g.), m. p. 195—198°, and 199—200° after one crystallisation from aqueous acetone. The pure substance showed $[\alpha]_D^{15°}$ + 140·4° in chloroform ($c$ = 2·214) and corresponded with a benzylidene anhydro-α-methylhexoside to which (see p. 1194) the structure 4 : 6-*benzylidene* 2 : 3-*anhydro-α-methylalloside* has been ascribed (Found : OMe, 11·3; C, 63·5; H, 6·1. $C_{14}H_{16}O_5$ requires OMe, 11·7; C, 63·6; H, 6·1%).

The mother-liquor from the alkaline hydrolysis was well diluted with water, and extracted

four times with chloroform; the united extracts were dried (sodium sulphate) and evaporated to dryness, giving a hard glass (28·2 g.), which crystallised on rubbing with ether; 21 g., m. p. 94—97°. Recrystallised from aqueous alcohol, it gave a homogeneous substance, large prisms, m. p. 98—99°, $[\alpha]_D^{15°}$ + 102·7° in chloroform ($c$ = 3·221), which corresponded with a monomethyl benzylidene α-methylhexoside and was later shown to be 4 : 6-*benzylidene* 2-*methyl* α-*methyl-altroside* (Found: OMe, 20·9; C, 60·9; H, 6·8. $C_{15}H_{20}O_6$ requires OMe, 20·9; C, 60·8; H, 6·8%).

The yield of crystalline material isolated in this experiment accounts for 85% of the original starting material. In other experiments, in which impure specimens of 2 : 3-di-*p*-toluenesulphonyl 4 : 6-benzylidene α-methylglucoside were used, an isomeric 4 : 6-benzylidene 2 : 3-anhydro-α-methylhexoside, m. p. 146—147°, was sometimes produced (see below).

2-*Benzoyl* 3-p-*Toluenesulphonyl* 4 : 6-*Benzylidene* α-*Methylglucoside*.—The preparation of this substance from 4 : 6-benzylidene α-methylglucoside is dependent upon the preferential substitution of position number 2 over position 3; the reaction is difficult to control, and the yield poor and variable. The material (10 g.) was dissolved in pyridine (10 c.c.) and benzoyl chloride (5·2 c.c., 1·25 mols.) was slowly added. After standing over-night, the product, isolated as usual and crystallised from ethyl alcohol, was found to consist of an inseparable mixture of the mono- and the di-benzoyl derivative. This was treated directly with an excess of *p*-toluenesulphonyl chloride (6 g.) in the minimum amount of pyridine and set aside for 4 days. The product, isolated in the usual manner, was a glass (10·5 g.) which, on boiling for a few seconds with dilute sodium methoxide, deposited a small amount (1·7 g.) of a homogeneous substance, m. p. 184—186°, $[\alpha]_D^{15°}$ + 83·8° in chloroform ($c$ = 4·24) (Found: OMe, 5·5. $C_{28}H_{28}O_9S$ requires OMe, 5·7%). This substance is 2-*benzoyl* 3-p-*toluenesulphonyl* 4 : 6-*benzylidene* α-*methylglucoside*, for it depressed the m. p. (212—213°) of the 3-benzoyl 2-*p*-toluenesulphonyl isomeride to 130—140°.

*Alkaline Hydrolysis of* 2-*Benzoyl* 3-p-*Toluenesulphonyl* 4 : 6-*Benzylidene* α-*Methylglucoside*.—The material (3·86 g.), m. p. 184—186°, was dissolved in methyl alcohol (100 c.c.) containing sodium (0·5 g.), and the solution boiled for 1 hr. On cooling, a crystalline precipitate was obtained, and was purified by washing with aqueous methyl alcohol. It (1·61 g.) had m. p. 198—199° and proved to be identical with 4 : 6-benzylidene 2 : 3-anhydro-α-methylalloside, m. p. 199—200°, obtained through the alkaline hydrolysis of 2 : 3-di-*p*-toluenesulphonyl 4 : 6-benzylidene α-methylglucoside. The mother-liquors from the hydrolysis were diluted with water and extracted 4 times with chloroform. The united extracts yielded crystalline material (0·14 g.), m. p. 197—199°, identical with that described above. Total yield of pure anhydro-compound 92·7%.

*Action of Sodium Methoxide Solution on* 4 : 6-*Benzylidene* 2 : 3-*Anhydro*-α-*methylalloside*.—The substance (2·05 g.), m. p. 199—200°, was dissolved by heating with methyl alcohol (40 c.c.) containing sodium (0·92 g.), and the solution boiled on a water-bath for 20 hrs. After cooling and dilution with water, the mixture was extracted 4 times with chloroform; the united extracts were dried (sodium sulphate) and evaporated to dryness, a clear glass (2·24 g.) being obtained, which crystallised on being rubbed with ether; after filtration, the crystals (2·01 g.) were washed with light petroleum and had m. p. 87—94°. Recrystallisation from aqueous ethyl alcohol gave a homogeneous substance (87·4% yield), m. p. 98—99°, identical with 4 : 6-benzylidene 2-methyl α-methylaltroside previously isolated (see above).

For purposes of comparison the following derivatives were made.

3-p-*Toluenesulphonyl* 4 : 6-*benzylidene* 2-*methyl* α-*methylaltroside*, prepared by condensing the above material with *p*-toluenesulphonyl chloride in the usual manner, crystallised from methyl alcohol in needles, m. p. 166—167°, $[\alpha]_D^{15°}$ + 57·1° in chloroform ($c$ = 0·963) (Found: OMe, 13·1. $C_{22}H_{26}O_8S$ requires OMe, 13·7%). On admixture with the corresponding α-methylglucoside, m. p. 156—157° (for a sample of which we are indebted to Dr. J. W. H. Oldham), the m. p. was depressed to 130°; and on admixture with 2-*p*-toluenesulphonyl 4 : 6-benzylidene 3-methyl α-methylglucoside, m. p. 151—152° (described below), it was depressed to 130°.

3-*Benzoyl* 4 : 6-*benzylidene* 2-*methyl* α-*methylaltroside*, prepared in the usual manner, crystallised from absolute alcohol–light petroleum; m. p. 135—136°, $[\alpha]_D^{15°}$ + 133·3° in chloroform ($c$ = 2·302) (Found: OMe, 15·2; $C_6H_5$·CO, 28·2; $C_{22}H_{24}O_7$ requires OMe, 15·5; $C_6H_5$·CO, 26·2%).

4 : 6-*Benzylidene* 2 : 3-*dimethyl* α-*methylaltroside* was prepared by methylating the 2-monomethyl compound with Purdie's reagents, but repeated treatment was necessary to effect complete methylation. The pure substance crystallised from light petroleum in prisms, m. p. 83—85°, $[\alpha]_D^{15°}$ + 92·8° in chloroform ($c$ = 1·324) (Found: OMe, 28·4. $C_{16}H_{22}O_6$ requires

OMe, 30·0%). When mixed with the analogous α-methylglucoside, m. p. 121—122°, the m. p. was depressed to 60—110°. The α-methylmannoside analogue is a syrup.

*Partial Hydrolysis of* 4 : 6-*Benzylidene* 2-*Methyl* α-*Methylaltroside.*—The substance (7·9 g.), m. p. 97—98°, was dissolved in a mixture of acetone (50 c.c.), water (40 c.c.), and *N*-hydrochloric acid (10 c.c.), and the solution boiled on a water-bath until the rotation was constant (1½ hrs.), $[\alpha]_D^{15°}$ + 113·1°, allowance being made for change in concentration. After neutralisation with barium carbonate and filtration, the acetone was evaporated. The aqueous solution was extracted with chloroform, to remove benzaldehyde, and evaporated to dryness, the residue being extracted 3 times with boiling acetone. The united extracts were evaporated to dryness, and a colourless syrup (4·88 g.), $n_D^{15°}$ 1·4891, was obtained. On being rubbed under acetone–ether, the syrup crystallised, and subsequent recrystallisation from propyl acetate gave pure 2-*methyl* α-*methylaltroside* (4·0 g.), prisms, m. p. 81—83°, $[\alpha]_D^{15°}$ + 111·6° in chloroform ($c$ = 0·909) (Found: OMe, 29·6. $C_8H_{16}O_6$ requires OMe, 29·8%).

2-p-*Toluenesulphonyl* 4 : 6-*Benzylidene* α-*Methylglucoside.*—The preferential substitution of position 2 with the *p*-toluenesulphonyl residue took place more readily than in the case of the analogous benzoyl compound, and it was possible to isolate the above substance in the pure condition. Benzylidene α-methylglucoside (18 g.) was treated gradually with *p*-toluenesulphonyl chloride (9 g.), each being dissolved in 10 c.c. of pyridine. After 24 hrs., a little water and benzene (20 c.c.) were added to the mixture, and a crystalline precipitate (8·7 g.) was obtained. This proved to be a mixture of mono- and di-*p*-toluenesulphonyl derivatives. The filtered benzene solution was washed 3 times with dilute hydrochloric acid and once with dilute alkali, after which more crystalline material (5·1 g.) separated; crystallised from methyl alcohol, this proved to be 2-p-*toluenesulphonyl* 4 : 6-*benzylidene* α-*methylglucoside*, m. p. 153—154°, $[\alpha]_D^{15°}$ + 64·2° in chloroform ($c$ = 4·93) (Found: OMe, 7·2. $C_{21}H_{24}O_8S$ requires OMe, 7·1%). The position of the *p*-toluenesulphonyl group was proved by methylation. 2-*p*-Toluenesulphonyl 4 : 6-benzylidene 3-methyl α-methylglucoside, derived from the above, had m. p. 151—152°, and when mixed with the 3-*p*-toluenesulphonyl 2-methyl compound, m. p. 156—157° (synthesised from 4 : 6-benzylidene 2-methyl α-methylglucoside; Oldham, unpublished result), the m. p. was depressed to 130—140°. The m. p. of a mixture of the original and the fully methylated material was depressed to 128—145°.

3-*Benzoyl* 2-p-*Toluenesulphonyl* 4 : 6-*Benzylidene* α-*Methylglucoside.*—This was prepared in good yield by the direct benzoylation of 2-*p*-toluenesulphonyl 4 : 6-benzylidene α-methylglucoside; prisms, m. p. 212—213°, $[\alpha]_D^{15°}$ + 51·6° in chloroform ($c$ = 2·876) (Found: OMe, 5·3. $C_{28}H_{28}O_9S$ requires OMe, 5·7%).

*Alkaline Hydrolysis of* 3-*Benzoyl* 2-p-*Toluenesulphonyl* 4 : 6-*Benzylidene* α-*Methylglucoside.*—The material (5 g.), m. p. 212—213°, was dissolved in methyl alcohol (125 c.c.) containing sodium (2·9 g.), and the solution boiled for 2 hrs. After cooling and dilution with water, long needles (2·1 g.), m. p. 145—147°, separated on standing; recrystallisation from aqueous alcohol raised the m. p. to 146—147°. This compound, 4 : 6-*benzylidene* 2 : 3-*anhydro*-α-*methylmannoside* (see p. 1194), had $[\alpha]_D^{15°}$ + 107·4° in chloroform ($c$ = 1·614) (Found: OMe, 11·4; C, 63·5; H, 6·0. $C_{14}H_{16}O_5$ requires OMe, 11·7; C, 63·6; H, 6·1%).

*Action of Sodium Methoxide Solution on* 4 : 6-*Benzylidene* 2 : 3-*Anhydro*-α-*methylmannoside.*—The material (2 g.), m. p. 146—147°, was heated in a sealed tube with methyl alcohol (40 c.c.) containing sodium (2 g.) for 24 hrs. at 100°, and the product was worked up as described on p. 1197, being obtained as a clear yellow glass (2·2 g.) which crystallised spontaneously. It was recrystallised from aqueous ethyl alcohol (yield 77·7%), and was 4 : 6-*benzylidene* 3-*methyl* α-*methylaltroside*, m. p. 131—133° (Found: OMe, 20·8; C, 60·89; H, 6·77. $C_{15}H_{20}O_6$ requires OMe, 20·9; C, 60·8; H, 6·75%), $[\alpha]_D^{15°}$ + 103·4° in chloroform ($c$ = 3·612); mixed with the 2-methyl compound, m. p. 97—98°, its m. p. was depressed to 81—90°.

Its constitution was established by methylation, for after 1 g. of it had been treated by Purdie's reagents, the crude product (0·93 g.) ultimately crystallised from light petroleum containing a little absolute alcohol in prisms (0·6 g.), m. p. 80—82°, of 4 : 6-benzylidene 2 : 3-dimethyl α-methylaltroside, m. p. 83—85°, described above.

*Partial Hydrolysis of* 4 : 6-*Benzylidene* 3-*Methyl* α-*Methylaltroside.*—The material (2·11 g.), m. p. 133°, was dissolved in a mixture of acetone (66 c.c.), water (29 c.c.), and *N*-hydrochloric acid (5 c.c.), and the solution boiled until of constant rotation (2 hrs.), $[\alpha]_D^{15°}$ + 153°, after allowance for change in concentration. The 3-*methyl* α-*methylaltroside* extracted in the manner already described for the 2-methyl compound, was a glass (1·32 g., 89%), which could not be obtained crystalline and did not reduce Fehling's solution; $[\alpha]_D^{15°}$ + 140·3° in chloroform ($c$ = 2·45) (Found: OMe, 26·5. $C_8H_{16}O_6$ requires OMe, 29·8%).

*Action of Aqueous Caustic Potash on* 4 : 6-*Benzylidene* 2 : 3-*Anhydro*-α-*methylalloside*.—The material (9 g.), m. p. 199°, was heated in a pressure bottle with 5% aqueous caustic potash (250 c.c.) for 60 hrs. at 100°, and the mixture filtered from unchanged material (6·7 g.). The filtrate was extracted with chloroform, the extract was dried (sodium sulphate), and evaporated to dryness. The residue (1·55 g.) crystallised, m. p. 160—165°. Recrystallisation from methyl alcohol gave a homogeneous substance, m. p. 169—170°, $[\alpha]_D^{15°}$ + 126·8° in chloroform ($c$ = 0·567) (Found : OMe, 11·3; C, 59·35; H, 6·48. $C_{14}H_{18}O_6$ requires OMe, 11·0; C, 59·58; H, 6·38%), which was shown to be 4 : 6-*benzylidene* α-*methylaltroside* by methylation with the Purdie reagents whereby it was converted into 4 : 6-benzylidene 2 : 3-dimethyl α-methylaltroside described above.

*Action of Aqueous Caustic Potash on* 4 : 6-*Benzylidene* 2 : 3-*Anhydro*-α-*methylmannoside*.—The substance (1 g.), m. p. 147°, was heated in a sealed tube with 5% aqueous caustic potash (40 c.c.) for 60 hrs. at 100°. The contents of the tube were filtered, and a small residue (0·06 g.) was found to consist of unchanged material. The filtrate was treated as in the previous experiment, and a crystalline product (0·73 g.), m. p. 165—169°, obtained. Recrystallisation from methyl alcohol raised the m. p. to 169—170°, undepressed when mixed with 4 : 6-benzylidene α-methylaltroside.

*Partial Hydrolysis of* 4 : 6-*Benzylidene* α-*Methylaltroside*.—The substance (1·48 g.), m. p. 169—170°, was dissolved in a mixture of acetone (25 c.c.) and $N$/10-hydrochloric acid (23·5 c.c.) and boiled until the rotation, $[\alpha]_D^{15°}$ + 114·7°, had risen to a constant value (2 hrs.) of $[\alpha]_D^{15°}$ + 140·9°, with allowance for change in concentration. By the same procedure as in preceding cases, α-*methylaltroside* was obtained as a glass in theoretical yield (1·01 g.), which could not be crystallised from any of the usual solvents. It did not reduce Fehling's solution, and showed $[\alpha]_D^{15°}$ + 125·6° in methyl alcohol ($c$ = 1·011) (Found : OMe, 16·1. $C_7H_{14}O_6$ requires OMe, 16·0%).

*Partial Hydrolysis of* 4 : 6-*Benzylidene* 2 : 3-*Dimethyl* α-*Methylaltroside*.—The altroside (9 g.), m. p. 82—84°, was dissolved in a mixture of acetone (132 c.c.), water (58 c.c.), and $N$-hydrochloric acid (10 c.c.), and the solution boiled until the rotation became constant (2 hrs.) : $[\alpha]_D^{15°}$ + 94·4° ⟶ $[\alpha]_D^{15°}$ + 125°, after allowance for change in concentration. The product was isolated in the manner already described, 2 : 3-dimethyl α-methylaltroside being obtained as a syrup (yield 89·8%, 5·78 g.), $n_D^{15°}$ 1·4769. It showed the usual solubilities of a trimethyl hexose in organic solvents.

*Methylation of* 2 : 3-*Dimethyl* α-*Methylaltroside*.—Five treatments of the altroside (4·97 g.) by Purdie's reagents were necessary for complete methylation; *tetramethyl* α-*methylaltroside* was obtained as a syrup (5·37 g.), $n_D^{15°}$ 1·4500, $[\alpha]_D^{15°}$ + 128·3 in chloroform ($c$ = 0·931) (Found : OMe, 60·6. $C_{11}H_{22}O_6$ requires OMe, 62%).

*Hydrolysis of Tetramethyl* α-*Methylaltroside*.—The foregoing substance (5·16 g.) was dissolved in 2$N$-hydrochloric acid (100 c.c.) and boiled until the rotation became constant, $[\alpha]_D^{15°}$ + 51·6°, allowing for change in concentration. After the usual procedure, tetramethyl altrose was obtained * as a syrup (4·22 g.), which reduced Fehling's solution strongly.

*Oxidation of Tetramethyl Altrose with Nitric Acid* (cf. Hirst, J., 1926, 353).—The altrose (4·17 g.), dissolved in nitric acid (40 c.c.; $d$ 1·42), was gradually heated on a water-bath; reaction began at 55°, and the temperature was gradually raised (35 mins.) to 90° and maintained thereat for 1¾ hrs. The reaction mixture was diluted with water (100 c.c.), and the solution evaporated at constant volume and 40°/10 mm. for 8 hrs. Methyl alcohol was gradually added in place of water over a further 4 hrs., and the solution was then evaporated to dryness. The residue, an almost colourless syrup, was dissolved in methyl alcohol containing 2% of dry hydrogen chloride, and boiled for 1½ hrs.; the cooled mixture was neutralised with silver carbonate, filtered, and evaporated to dryness at 40°/10 mm. In order to remove silver nitrate the residue was extracted with chloroform, and the extract on evaporation yielded a syrup (3·65 g.), which distilled as a colourless syrup (3·46 g.), b. p. 150—155° (bath temp.)/8 mm., $n_D^{15°}$ 1·4370, $[\alpha]_D^{15°}$ − 40·1° in methyl alcohol ($c$ = 0·97). These physical constants and the analysis (Found : OMe, 59·6. Calc. for $C_8H_{14}O_6$ : OMe, 60·2%. Calc. for $C_{10}H_{18}O_7$ : OMe, 62%) are in keeping with the idea that the product was a mixture of dimethyl $l$-dimethoxysuccinate and $d$-trimethoxyaraboglutarate (cf. Hirst, *loc. cit.*).

Direct confirmation was obtained by the isolation of crystalline diamides of the two acids by the action of methyl-alcoholic ammonia on the mixed esters. The syrup (1·38 g.) was dis-

* This result throws doubt upon the identity of the substance tentatively described as 2 : 3 : 4 : 6-tetramethyl altrose (Mathers and Robertson, J., 1933, 1080).

solved in methyl alcohol (12 c.c.) saturated with dry ammonia. The solution immediately turned yellow, but no further colour change took place. After 20 hrs. crystalline material which had separated was filtered off, washed with methyl alcohol and ether, and dried (*A*). After 48 hrs. a second crop (*B*), and after 5 days a third crop (*C*), of crystals were obtained.

Fraction (*A*) (0·09 g.) consisted of needles, and was identified as *l*-dimethoxysuccindiamide. It had no distinct m. p. but darkened at 240° and began to decompose about 270°. It showed $[\alpha]_D^{15°}$ — 89·3° in water ($c$ = 0·22) (cf. Purdie and Irvine, J., 1901, **79**, 957; Hirst, *loc. cit.*) (Found : C, 40·95; H, 6·74; N, 15·9. Calc. for $C_6H_{12}O_4N_2$ : C, 40·9; H, 6·82; N, 15·9%).

Fraction (*B*) (0·07 g.) was obviously a mixture of (*A*) and (*C*) and was not further examined.

Fraction (*C*) (0·22 g.) was obtained as small prisms, identified as *d*-trimethoxyaraboglutardiamide; m. p. (crude) 223—225°, raised by one recrystallisation to 229°. It showed $[\alpha]_D^{15°}$ — 47·9° in water ($c$ = 0·731) (cf. Hirst and Robertson, J., 1925, **127**, 363) (Found : C, 43·63; H, 7·07; N, 13·4. Calc. for $C_8H_{16}O_5N_2$ : C, 43·64; H, 7·27; N, 12·73%).

*Hydrolysis of α-Methylaltroside.*—The glass (0·86 g.) was dissolved in 8% hydrochloric acid (19·2 c.c.), and the solution boiled until of constant rotation : an initial rotation $[\alpha]_D^{15°}$ + 104·5° became strongly lævorotatory after 15 mins., increasing finally (75 mins.) to $[\alpha]_D^{15°}$ — 108·4° (calc. on anhydrohexose). At this point the solution reduced Fehling's solution only very slightly. The product has not yet been examined.

*Hydrolysis of 2-Methyl α-Methylaltroside.*—The altroside (1 g.), m. p. 81—83°, was dissolved in 2*N*-hydrochloric acid (20 c.c.) and boiled in the presence of norit until of constant rotation (2½ hrs.) : $[\alpha]_D^{15°}$ + 103·8° ⟶ — 105·5° (calc. for a 2-methyl hexose) or — 116·3° (calc. for a 2-methyl anhydrohexose). At this point the solution reduced Fehling's solution fairly strongly. After neutralisation with lead carbonate and evaporation of the filtered solution to dryness, the residue was extracted with methyl alcohol. The extract did not reduce Fehling's solution, and on evaporation to dryness afforded a syrup which showed no signs of crystallising (0·75 g. 80%); when boiled with alkali it showed very little colour, and the optical rotation was not appreciably altered (Found : OMe, 16·9. Calc. for $C_7H_{12}O_5$ : OMe, 17·6%. Calc. for $C_7H_{14}O_6$ : OMe, 16%).

Attempts to form an osazone directly from the above product failed. The above hydrolysis was therefore repeated with 2 g. of material, and when equilibrium had been attained (the solution was reducing), potassium acetate (3 g.) and phenylhydrazine acetate (5 g.) in glacial acid (5 c.c.) were added, and the mixture heated at 60° for 2 hrs. and at 100° for ½ hr.; a yellow crystalline mass was deposited on cooling, but as it was contaminated with large amounts of acetylphenylhydrazine, it was dissolved in methyl alcohol containing a little sodium hydroxide solution and boiled. After addition of water, the cooled solution was filtered, and the residue crystallised from very dilute alcohol. Altrosazone, m. p. 164—165° (0·1 g.), was obtained (cf. Austin and Humoller, *loc. cit.*); mixed m. p. with glucosazone (m. p. 204°) 148—152° (Found : N, 15·76. Calc. for $C_{18}H_{22}O_4N_4$ : N, 15·64%).

*Hydrolysis of 3-Methyl α-Methylaltroside.*—The syrupy altroside (1·09 g.) was dissolved in 4% hydrochloric acid (20 c.c.) and treated as in the preceding case : in 3 hrs., $[\alpha]_D^{15°}$ + 113·5° ⟶ $[\alpha]_D^{15°}$ — 99·9° (calc. for a 3-methyl hexose) or — 110·4° (calc. for a 3-methyl anhydrohexose); the solution then reduced Fehling's solution. The reaction product was isolated as in the previous experiment, and consisted of a syrup (0·5 g.) which showed only a faint reaction with Fehling's solution; on being boiled with alkali, it developed very little colour, and its rotation was not appreciably altered (Found : OMe, 15·75. Calc. for $C_7H_{12}O_5$ : OMe, 17·6%). This product appeared to be contaminated with traces of inorganic material.

For the preparation of an osazone, the hydrolysis was repeated with 1·6 g. of material, and a procedure similar to that in the previous experiment was adopted; *3-methyl altrosazone* (0·56 g.) separated free from acetylphenylhydrazine. After being washed with ether, the crystals had m. p. 168—169°, depressed on admixture with 3-methyl glucosazone, m. p. 171—173°, to 143—146° (Found : OMe, 7·2; N, 14·5. $C_{19}H_{24}O_4N_4$ requires OMe, 8·3; N, 15·05%).

*Hydrolysis of 2 : 3-Dimethyl α-Methylaltroside.*—The altroside (0·79 g.) was dissolved in *N*-hydrochloric acid (40 c.c.), and the solution was boiled, etc., as before (2 hrs.) : $[\alpha]_D^{15°}$ + 113° ⟶ $[\alpha]_D^{15°}$ — 84·9° (calc. for 2 : 3-dimethylaltrose). At this point, however, the solution only reduced Fehling's solution very faintly; moreover, the end-point is not comparable with that attained in the hydrolysis of tetramethyl α-methylaltroside ($[\alpha]_D^{15°}$ + 51·6°). It again seemed probable that anhydro-formation had taken place subsequent to the removal of the methyl group, and on this basis the end value for the hydrolysis becomes $[\alpha]_D^{15°}$ — 92·9°. As in previous cases, boiling with alkali was attended by only slight development of colour and loss in optical

activity. The product of hydrolysis was isolated in the usual way as a syrup which did not reduce Fehling's solution.

The authors acknowledge their indebtedness to The Carnegie Trust for the grant of a Scholarship which enabled one of them (C. F. G.) to take part in the research, and to Principal Sir James C. Irvine, C.B.E., F.R.S., for his kindly interest in the work.

THE UNIVERSITY, ST. ANDREWS. [*Received, June 12th,* 1935.]