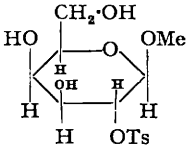
143. *The Conversion of Galactose into Derivatives of* d-*Idose.*

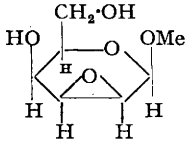
By L. F. Wiggins.

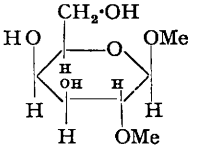
Galactose has been converted into *d*-idose derivatives through the intermediate formation of 4 : 6-benzylidene 2 : 3-anhydro-β-methyltaloside, obtained by alkaline hydrolysis of 2-tosyl 4 : 6-benzylidene β-methylgalactoside. It was observed that 2-tosyl 4 : 6-benzylidene α-methylgalactoside was considerably more stable to alkaline reagents than was the corresponding compound in the β-series. The anhydro-compound suffered ring fission to give 2-methyl 4 : 6-benzylidene β-methylgalactoside and 3-methyl 4 : 6-benzylidene β-methyl-*d*-idoside, the latter greatly predominating. Its formulation as a derivative of *d*-idose is proved by its conversion into the known crystalline tetramethyl δ-idonolactone. Fission of the anhydro-ring with ammonia led to the isolation of 3-acetamido 2-acetyl 4 : 6-benzylidene β-methyl-*d*-idoside but no 2-acetamido 3-acetyl 4 : 6-benzylidene β-methylgalactoside could be separated. Direct treatment of 2-tosyl 3 : 4 : 6-trimethyl β-methylgalactoside with methyl-alcoholic ammonia led to the isolation of a very small amount of a substance believed to be 2-acetamido 3 : 4 : 6-trimethyl β-methylgalactoside.

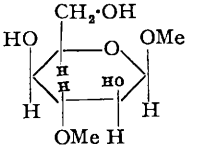
In the course of an investigation designed to elucidate the configuration of the 2-aminohexose, chondrosamine, the synthesis of derivatives of 2-aminogalactose has been attempted by the procedure successfully employed by Haworth, Lake, and Peat (J., 1939, 271) in the determinatlon of the constitution of glucosamine. The application of this method for the preparation of 2-aminogalactose necessitated the fission with ammonia of the ethylene oxide ring of a 2 : 3-anhydro-talose derivative, it having been shown (Peat and Wiggins, J., 1938, 1810) that such ethylene oxide anhydro-rings open in both of the possible directions with the production of two amino-sugars. In the present case 2 : 3-anhydrotalose would be expected to yield 2-aminogalactose and 3-aminoidose. It has been found possible to prepare a derivative of 2 : 3-anhydrotalose and to prove that it has the talose configuration. However, it was not possible to isolate the aminogalactose component of the products of ring scission with ammonia. Nevertheless it is noteworthy that a number of *d*-idose derivatives have been prepared, and evidence obtained which lends further experimental support to the theory of the mechanism of ring closure and ring scission in the anhydro-sugar group (cf. *Ann. Reports*, 1939, **36**, 258).

If this theory is generally applicable, then the following sequence is to be expected: 2-tosyl β-methylgalactoside (I) $\xrightarrow{\text{NaOMe}}$ 2 : 3-*anhydro*-β-*methyltaloside* (II) $\xrightarrow{\text{NaOMe}}$ 2-methyl β-methylgalactoside (III) + 3-*methyl* β-*methylidoside* (IV). Proof has been obtained that the products (III) and (IV) have in fact the configuration


(I.)


(II.)


(III.)


(IV.)

of *d*-galactose and *d*-idose respectively, and in consequence this has provided further support for the hypothesis that Walden inversion accompanies the formation and the scission of ethylene oxide linkages in the sugars.

Crystalline 2 : 3-anhydro-β-methyltaloside was obtained when 2-tosyl β-methylgalactoside was detosylated. Treatment of the anhydro-methyltaloside with benzaldehyde yielded crystalline 4 : 6-*benzylidene* 2 : 3-*anhydro*-β-*methyltaloside* which was also obtained by detosylation of 2-*tosyl* 4 : 6-*benzylidene* β-*methylgalactoside*. When the anhydro-ring of the benzylidene 2 : 3-anhydro-β-methyltaloside was opened with sodium methoxide, two crystalline benzylidene β-methylhexosides, (A) and (B), were isolated. The compound (A), which was present in exceedingly small amount, was shown to be 2-methyl 4 : 6-benzylidene β-methylgalactoside inasmuch as no depression of melting point was observed in admixture with an authentic specimen prepared by Bell and Williamson's method (J., 1938, 1196). The main product (B), obtained in 64% yield, was shown to be 3-*methyl* 4 : 6-*benzylidene* β-*methylidoside*. The benzylidene group was removed from (B) by mild acid hydrolysis (see Robertson and Dunlop, J., 1938, 472), and the liquid monomethyl β-methylhexoside so obtained was methylated to a tetramethyl β-methylhexoside. The constants of this substance agreed closely with those given by Lake and Peat (J., 1939, 1069) for tetramethyl β-methyl-*d*-idoside. Hydrolysis gave a tetramethyl hexose, purified by distillation under high vacuum; subsequent oxidation yielded a crystalline tetramethyl hexonolactone shown to be identical with Lake and Peat's tetramethyl δ-idonolactone (*loc. cit.*). During the distillation of the tetramethyl idose, the octamethyl di-idose isolated by Lake and Peat was not encountered. The substance (B) therefore has the configuration of *d*-idose. It is clear that the methyl group of (B) must be located on either C_2 or C_3. The monomethyl β-methylidoside obtained from (B) was hydrolysed to monomethyl idose which was oxidised to monomethyl idonolactone. These products were non-crystalline. Treatment of the lactone with ammonia, however, yielded an amide which gave a positive Weerman test for α-hydroxyamides. The methyl group is therefore located on C_3, and (B) is correctly described as 3-methyl 4 : 6-benzylidene β-methylidoside, and the anhydro-methylhexoside from which it was derived as 4 : 6-benzylidene 2 : 3-anhydro-β-methyltaloside. Methylation of (B) yielded crystalline 2 : 3-*dimethyl* 4 : 6-*benzylidene* β-*methylidoside*.

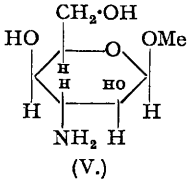
An alternative method of preparation consisted in the hydrolysis, with boiling methyl-alcoholic sodium methoxide, of 2 : 3-ditosyl 4 : 6-benzylidene β-methylgalactoside, prepared by the method of Bacon, Bell,

and Lorber (J., 1940, 1147). A little 4 : 6-benzylidene 2 : 3-anhydro-β-methyltaloside was isolated but, in the main, ring fission occurred and the product (B) was obtained together with a small amount of (A).

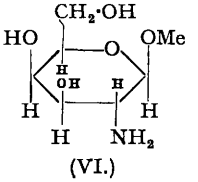
Methylation of 2 : 3-anhydro-β-methyltaloside gave 4 : 6-*dimethyl* 2 : 3-*anhydro*-β-*methyltaloside*, treatment of which with sodium methoxide yielded a trimethyl β-methylhexoside which, by analogy, is described as 3 : 4 : 6-*trimethyl* β-*methylidoside*, containing a trace of 2 : 4 : 6-trimethyl β-methylgalactoside. The product, however, was not crystalline.

An observation of considerable theoretical interest was made when the above series of reactions was carried out with the α-form of 2-tosyl methylgalactoside. Crystalline 2-*tosyl* 4 : 6-*benzylidene* α-*methylgalactoside* was prepared according to the following scheme: 3 : 4-monoacetone α-methylgalactoside ⟶ 6-trityl 3 : 4-monoacetone α-methylgalactoside ⟶ 6-trityl 2-tosyl 3 : 4-monoacetone α-methylgalactoside ⟶ 2-tosyl α-methylgalactoside ⟶ 2-tosyl 4 : 6-benzylidene α-methylgalactoside, the 3-*methyl* derivative of which was readily formed. 2-Tosyl 4 : 6-benzylidene α-methylgalactoside was distinguished by its extreme stability towards alkali: whereas its β-methyl analogue is detosylated by contact with cold sodium methoxide for 10 minutes, yet the α-isomer is not affected by boiling methyl-alcoholic sodium methoxide, and in order to remove the tosyl group it was necessary to heat the α-compound with the alkaline reagent at 120° for 20 hours. Presumably the 2 : 3-anhydrotalose derivative was first formed, but under these drastic conditions the anhydro-ring was immediately opened again and 3-*methyl* 4 : 6-*benzylidene* α-*methylidoside* was the only product obtained. The last compound was easily methylated to the 2 : 3-*dimethyl* homologue. A similar, though not precisely analogous, case was noted by Percival and Percival (J., 1938, 1585), who found that 3-tosyl 2 : 4 : 6-trimethyl α-methylgalactoside, in contrast to the corresponding β-form, was extremely resistant to alkaline hydrolysis.

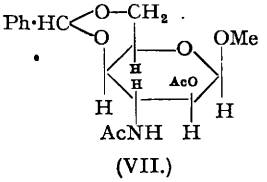
The action of methyl-alcoholic ammonia on 2 : 3-anhydro-β-methyltaloside was next investigated. The main product of this reaction was a crystalline amino-sugar which, by analogy with work on the action of sodium methoxide on the anhydro-compound, was 3-*amino*-β-*methyl*-d-*idoside* (V). It was accompanied by a syrupy product of different specific rotation, which presumably contained 2-amino-β-methylgalactoside (VI): none, however, was isolated in solid form. The 3-amino-β-methylidoside gave crystalline 3-*acetamido* 2 : 4 : 6-*triacetyl* β-*methyl*-d-*idoside* and also 3-*acetamido* β-*methyl*-d-*idoside*.



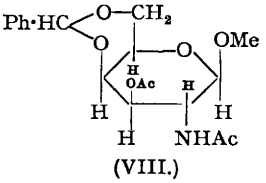
(V.)



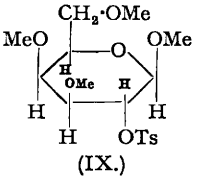
(VI.)



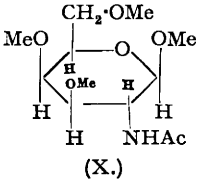
(VII.)



(VIII.)



(IX.)



(X.)

Similarly, only one crystalline compound was isolated by the action of ammonia on 4 : 6-benzylidene 2 : 3-anhydro-β-methyltaloside, followed by acetylation. This was 3-*acetamido* 2-*acetyl* 4 : 6-*benzylidene* β-*methyl*-d-*idoside* (VII). 2-Acetamido 3-acetyl 4 : 6-benzylidene β-methylgalactoside (VIII) should be present in the residual syrups, but so far it has not been possible to crystallise it.

A further attempt was made to obtain a derivative of 2-aminogalactose by treatment of 2-*tosyl* 3 : 4 : 6-*trimethyl* β-*methylgalactoside* (IX) with methyl-alcoholic ammonia, for by this procedure from the corresponding glucose derivative Cutler and Peat (J., 1939, 782) obtained 2-acetamido 3 : 4 : 6-trimethyl β-methylglucoside in very small yield. By adopting this procedure, a very small amount of a crystalline product was isolated, but in insufficient quantity for analyses. By analogy with the work in the glucosamine series, the compound was probably 2-acetamido 3 : 4 : 6-trimethyl β-methylgalactoside (X). It showed m. p. 238°, which is near to the value given for 2-acetyl 3 : 4 : 6-trimethyl β-methylchondrosaminide by Stacey (this vol., p. 274), *viz.*, m. p. 233°. However, on admixture with a sample of this compound prepared from chondrosamine by Dr. M. Stacey of this department, the m. p. was depressed to 226—228°. A parallel experiment with the corresponding compound in the α-series failed altogether to give any crystalline amino-derivative.

It is to be noted that, whereas in the case of ring opening of 4 : 6-benzylidene 2 : 3-anhydro-α-methylalloside with sodium methoxide (Peat and Wiggins, *loc. cit.*) the second product, *viz.*, 3-methyl 4 : 6-benzylidene α-methylglucoside, was isolated quite easily and in 10% yield, in the present case the second product from the sodium methoxide ring fission, *viz.*, 2-methyl 4 : 6-benzylidene β-methylgalactoside, was isolated with the utmost difficulty and in minute yield, a fact which most probably contributes to the lack of success in isolating a corresponding amino-compound by the ring fission with ammonia.

Experimental.

2 : 3-*Anhydro*-β-*methyl*-d-*taloside*.—2-Tosyl β-methylgalactoside (0·6 g.), prepared according to the procedure of Bacon, Bell, and Kosterlitz (J., 1939, 1248), was dissolved in dry methyl alcohol (10 c.c.), and 10% sodium methoxide solution

in methyl alcohol (1·2 c.c.) added. The mixture was kept for 24 hours at room temperature, and the excess sodium methoxide neutralised with N-sulphuric acid. The solution was evaporated to dryness under reduced pressure, and the residue extracted with ethyl acetate. Evaporation of the extract gave a semi-crystalline mass which, recrystallised from ethyl acetate, formed long rods (0·21 g.). There was a residual syrup which could not be crystallised; m. p. 103—104°, $[\alpha]_D^{17°}$ −86·1° in chloroform (*c*, 1·02) (Found: C, 48·1; H, 6·5; OMe, 18·2. $C_7H_{12}O_5$ requires C, 47·7; H, 6·8; OMe, 17·6%).

4 : 6-*Benzylidene* 2 : 3-*Anhydro-β-methyl*-d-*taloside*.—The foregoing 2 : 3-*anhydro-β-methyl*-d-*taloside* (80 mg.) was shaken with freshly distilled benzaldehyde (2 c.c.) and anhydrous zinc chloride (0·5 g.) for 24 hours. Excess of sodium carbonate solution was added, and the excess benzaldehyde removed by distillation with steam. After evaporation to dryness the residue was extracted several times with boiling chloroform. On evaporation of the extract, a crystalline residue was obtained which recrystallised from chloroform–light petroleum, forming long needles (50 mg.), m. p. 242°, $[\alpha]_D^{19°}$ −138·4° in chloroform (*c*, 0·578) (Found: C, 63·2; H, 6·1; OMe, 12·2. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1; OMe, 11·8%).

4 : 6-*Dimethyl* 2 : 3-*Anhydro-β-methyl*-d-*taloside*.—2 : 3-Anhydro-β-methyl-*d*-taloside (0·5 g.) was treated three times with methyl iodide and dry silver oxide at 45°, the product being extracted with boiling chloroform after each treatment. The product finally obtained was recrystallised from ether–light petroleum, forming fine, long needles (0·4 g.), m. p. 72—73°, $[\alpha]_D^{18°}$ −148·4° in chloroform (*c*, 0·89) (Found: C, 53·1; H, 7·8; OMe, 45·6. $C_8H_{16}O_5$ requires C, 52·9; H, 7·8; OMe, 45·6%).

2-*Tosyl* 4 : 6-*Benzylidene β-Methylgalactoside*.—2-Tosyl β-methylgalactoside (7 g.) was shaken with freshly distilled benzaldehyde (30 c.c.) and pulverised anhydrous zinc chloride (10 g.) for 4 hours. The calculated quantity of sodium carbonate, dissolved in water, was added, and the excess benzaldehyde steam-distilled. After evaporation to dryness, the residue was extracted with chloroform. The syrup obtained on evaporation of the extraction liquid crystallised on trituration with alcohol and ether. After recrystallisation from alcohol, 2-*tosyl* 4 : 6-*benzylidene β-methylgalactoside* (6 g.) showed m. p. 164—165°, $[\alpha]_D^{17°}$ −52·8° in chloroform (*c*, 2·388) (Found: C, 57·7; H, 5·7. $C_{21}H_{24}O_8S$ requires C, 57·8; H, 5·5%).

Detosylation of 2-*Tosyl* 4 : 6-*Benzylidene β-Methylgalactoside*.—The galactoside (5·7 g.) was dissolved in chloroform (50 c.c.), and a slight excess of methyl-alcoholic sodium methoxide solution (6 c.c., 1 c.c. = 0·136 g. of sodium methoxide) added. The mixture was vigorously shaken for about 15 minutes, during which the solution became gelatinous and finally a crystalline precipitate consisting of sodium *p*-toluenesulphonate and 4 : 6-benzylidene 2 : 3-anhydro-β-methyl-*d*-taloside separated. The solution was then set aside for 24 hours, filtered, the precipitate washed with water to remove the sodium salt, and recrystallised from chloroform–light petroleum. The product formed large feathery needles (m. p. 242°) and was identical with the 4 : 6-benzylidene 2 : 3-anhydro-β-methyltaloside obtained by benzylidenation of the 2 : 3-anhydro-β-methyl-*d*-taloside. An additional amount was obtained from the initial chloroform filtrate from the crystalline reaction product. The chloroform solution was washed with water, dried over anhydrous magnesium sulphate, filtered, and evaporated to dryness, the residue being recrystallised from chloroform–petrol; m. p. 242°. The total yield of the anhydro-compound was 2·65 g. (78%).

2 : 3-*Ditosyl* 4 : 6-*Benzylidene β-Methylgalactoside*.—4 : 6-Benzylidene β-methylgalactoside (29 g.) was dissolved in pyridine (150 c.c.), and tosyl chloride (42 g.) added with cooling. After the addition was complete, the mixture was warmed at 40° for 4 days, and poured into ice-water; the syrupy precipitate obtained crystallised on trituration with water and alcohol. 2 : 3-Ditosyl 4 : 6-benzylidene β-methylgalactoside separated from ethyl alcohol (28 g.), m. p. 169—171°, $[\alpha]_D^{20°}$ +27·4° in chloroform (*c*, 1·24) (Found: C, 57·3; H, 5·0 Calc. for $C_{28}H_{30}O_{10}S_2$: C, 57·0; H, 5·1%). Bacon, Bell, and Lorber (J., 1940, 1147) give m. p. 168—170°, $[\alpha]_D$ +29·5° in chloroform.

Alkaline Hydrolysis of 2 : 3-*Ditosyl* 4 : 6-*Benzylidene β-Methylgalactoside*.—The galactoside (27 g.) was heated with dry methyl alcohol (120 c.c.) containing sodium (3·6 g., 2 mols.) under reflux for 7 hours, solution then being complete. No crystals separated on cooling, and the solution was diluted with water and exhaustively extracted with chloroform. The extract on evaporation gave a syrup (10·5 g.) which was fractionally crystallised from alcohol. The first fraction (0·5 g.) showed m. p. 242° after recrystallisation and was 4 : 6-benzylidene 2 : 3-anhydro-β-methyl-*d*-taloside. Unchanged galactoside (2·3 g.) was next encountered, and the third fraction (4·4 g.), m. p. 105°, was identical with 3-methyl 4 : 6-benzylidene β-methyl-*d*-taloside (see below). A fourth and last fraction (0·15 g.) showed $[\alpha]_D$ −31·2° in chloroform (*c*, 1·67), m. p. 159—160° unchanged by admixture with 2-methyl 4 : 6-benzylidene β-methylgalactoside, which was described (Bell and Williamson, J., 1938, 1196) as having m. p. 160° and $[\alpha]_D$ −32·8° in chloroform. There was a residual syrup which would not yield any further crystals.

Hydrolysis of 4 : 6-*Benzylidene* 2 : 3-*Anhydro-β-methyl*-d-*taloside with Sodium Methoxide*.—The taloside (1 g.) was heated under reflux for 24 hours with 50 c.c. of dry methyl alcohol and 10 c.c. of 5% methyl-alcoholic sodium methoxide solution. The solution was diluted with water and exhaustively extracted with chloroform. The extract was dried over anhydrous magnesium sulphate, filtered, and evaporated to give a syrup (0·95 g.) which crystallised on trituration with ether. Fractional recrystallisation gave 3-*methyl* 4 : 6-*benzylidene β-methyl*-d-*idoside* (0·71 g.; 64%), m. p. 105°, $[\alpha]_D^{23°}$ −78·5° in chloroform (*c*, 1·325) (Found: C, 60·7; H, 6·7; OMe, 20·5. $C_{15}H_{20}O_6$ requires C, 60·8; H, 6·7; OMe, 20·9%), and a syrupy residue which, with great difficulty, was made to deposit a few crystals of 2-methyl 4 : 6-benzylidene β-methylgalactoside (0·003 g.; 0·27% of the theoretical), m. p. and mixed m. p. with an authentic specimen 159—160°.

2 : 3-*Dimethyl* 4 : 6-*Benzylidene β-Methyl*-d-*idoside*.—3-Methyl 4 : 6-benzylidene β-methyl-*d*-iodside (40 mg.) was methylated by three treatments with methyl iodide and dry silver oxide, the product being extracted after each treatment 6 times with boiling chloroform. The final product was recrystallised from ether–light petroleum and showed m. p. 127°, $[\alpha]_D^{21°}$ −53·2° in chloroform (*c*, 0·601); yield, 30 mg. (Found: C, 61·5; H, 7·1; OMe, 30·4. $C_{16}H_{22}O_6$ requires C, 61·9; H, 7·1; OMe, 30·0%).

Partial Hydrolysis of 3-*Methyl* 4 : 6-*Benzylidene β-Methyl*-d-*idoside*.—3-Methyl 4 : 6-benzylidene β-methyl-*d*-idoside (3·5 g.) was dissolved in acetone (200 c.c.), oxalic acid (10 g.) dissolved in water (35 c.c.) added, and the mixture heated under reflux for 11½ hours. The specific rotation changed from $[\alpha]_D$ −84·8° to −53·4° (constant value) in 8½ hours. The acid was then neutralised with barium carbonate, the solution filtered, and the filtrate and washings evaporated to dryness. The residue was extracted with ethyl acetate, evaporation of which gave a syrup (2·1 g.) (Found: OMe, 28·8. $C_8H_{16}O_6$ requires OMe, 29·8%). The syrup could not be induced to crystallise, but was certainly 3-*methyl β-methyl*-d-*idoside*. A sample (0·2 g.) was rebenzylidenated by treating it with benzaldehyde (3 c.c.) and zinc chloride (0·5 g.) in the usual way. 3-Methyl 4 : 6-benzylidene β-methyl-*d*-idoside (0·17 g.), m. p. 105°, was obtained.

Tetramethyl β-Methyl-d-*idoside*.—3-Methyl β-methyl-*d*-idoside (0·6 g.) was methylated by four treatments with methyl iodide and silver oxide, the product being extracted after each treatment several times with boiling chloroform. The final product was distilled at 90—100°/0·03 mm. (bath temp.) (Found: OMe, 61·2. Calc. for $C_{11}H_{22}O_6$: OMe, 62·0%); yield, 0·5 g., $n_D^{19°}$ 1·4500, $[\alpha]_D^{18°}$ −67·7° in chloroform (*c*, 1·24). Lake and Peat (*loc. cit.*) record $[\alpha]_D$ −68·5° in chloroform, $n_D^{19°}$ 1·4490.

Tetramethyl d-*Idose*.—Tetramethyl β-methyl-*d*-idoside (0·48 g.) was heated in N-sulphuric acid (25 c.c.) at 100° for 5 hours: $[\alpha]_D$ −45·3° (initial value); +13·5° (½ hr.); +19·7° (1½ hrs.); +19·7° (5 hrs.). The acid was neutralised with

barium carbonate, the solution filtered, washed with water, and the combined filtrate and washings evaporated to dryness. The dry residue was repeatedly extracted with boiling chloroform, and on evaporation, the extract gave a syrup which distilled completely at 150—160° (bath temp.)/0·07 mm.; yield, 0·32 g., $n_D^{16°}$ 1·4616, $[\alpha]_D^{13°}$ +18·6° in methyl alcohol (*c*, 1·448) (Found: OMe, 51·6. Calc. for $C_{10}H_{20}O_6$: OMe, 52·5%). Lake and Peat (*loc. cit.*) gave $n_D^{15°}$ 1·4620, $[\alpha]_D$ +21·8° in methyl alcohol. No disaccharide such as that described by Lake and Peat was encountered.

Tetramethyl δ-Idonolactone.—Tetramethyl *d*-idose (0·2 g.) was dissolved in water (3 c.c.), bromine (1 c.c.) added, and the mixture kept at room temperature, with occasional shaking, for a week. The oxidation product was isolated in the usual way, and a syrup (0·13 g.) obtained which crystallised on trituration with ether. Recrystallised from ether, the product formed large prisms, m. p. 88—90°, unchanged in admixture with a specimen obtained by Lake and Peat (*loc. cit.*) and having $[\alpha]_D^{22°}$ −29·7° in water (*c*, 0·672) (no change after 72 hrs.) (Found: C, 51·4; H, 7·5. Calc. for $C_{10}H_{18}O_6$: C, 51·3; H, 7·5%). Lake and Peat (*loc. cit.*) describe tetramethyl δ-idonolactone as showing m. p. 91° and $[\alpha]_D$ −32·0° in water, and no change in rotation on keeping for 72 hours.

3-Methyl d-*Idose.*—3-Methyl β-methylidoside (0·18 g.) was heated with N-sulphuric acid (15 c.c.) for 10 hours at 95°, $[\alpha]_D$ −43·3° (initial value); −1·67° (½ hr.); −26·7° (1½ hrs.); −41·6° (3 hrs.); −56·6° (5½ hrs.); −53·3° (8 hrs.); −54·9° (10 hrs.). The solution, which now reduced Fehling's solution, was neutralised with barium carbonate, filtered, the precipitate washed with hot water, and the filtrate evaporated to dryness. On extracting the residue with absolute alcohol and evaporating the extract, syrupy 3-methyl *d*-idose was obtained (0·13 g.), $[\alpha]_D^{22°}$ −44·5° in water (*c*, 1·241) (Found: OMe, 17·0. Calc. for $C_7H_{14}O_6$: OMe, 16·0%).

3-Methyl d-*Idonamide.*—3-Methyl *d*-idose (0·12 g.) was oxidised with bromine in the usual way, but the resulting lactone would not crystallise. The product, after thorough drying in a vacuum, was dissolved in dry methyl alcohol and the solution saturated with ammonia at 0°. After the mixture had been left for 48 hours at 0° the ammonia and the solvent were removed in a vacuum. The resulting amide slowly crystallised, but could not be recrystallised; it was impure 3-methyl idonamide (Found: N, 4·7. Calc. for $C_7H_{14}O_6N$: N, 6·7%).

Weerman test. The crude 3-methyl idonamide (10 mg.) was dissolved in 2 drops of water, 0·2 c.c. of 1·5N-sodium hypochlorite solution added at 0°, and the mixture kept at 0° for 12 hours. The excess hypochlorite was removed by adding a few crystals of sodium thiosulphate, a little sodium acetate together with a few crystals of semicarbazide hydrochloride were added, and the solution kept overnight at 0°, whereupon 1 mg. of hydrazodicarbonamide (m. p. 258°) separated. A control experiment on gluconamide (10 mg.) carried out in exactly the same way gave 4·5 mg. of hydrazodicarbonamide.

Alkaline Hydrolysis of 4 : 6-*Dimethyl* 2 : 3-*Anhydro-β-methyltaloside.*—The β-methyltaloside (0·385 g.) was dissolved in methyl alcohol (10 c.c.) and heated for 24 hours under reflux with 5% methyl-alcoholic sodium methoxide (10 c.c.). Thereafter the solution was diluted with water and extracted with chloroform. Evaporation of the extract gave a syrup which distilled at 110—120° (bath temp.)/0·03 mm. and showed $n_D^{17°}$ 1·4598, $[\alpha]_D^{17°}$ −70·2° in chloroform (*c*, 1·31) (Found: OMe, 51·8. $C_{10}H_{20}O_6$ requires OMe, 52·5%). This syrup was principally 3 : 4 : 6-*trimethyl β-methyl*-d-*idoside* but probably contained a very small quantity of 2 : 4 : 6-trimethyl β-methylgalactoside. The syrup resisted all attempts to crystallise it.

Conversion of 3 : 4 : 6-*Trimethyl β-Methylidoside into Tetramethyl δ-Idonolactone.*—The syrupy trimethyl β-methyl-*d*-idoside (0·37 g.) was methylated by three treatments with silver oxide and methyl iodide in the usual way to give tetramethyl β-methylidoside, distilling at 95° (bath temp.)/0·03 mm., probably contaminated with a very small amount of tetramethyl β-methylgalactoside. It showed $n_D^{19°}$ 1·4510 and $[\alpha]_D$ −62·8° in chloroform (*c*, 1·625) (Found: OMe, 60·8. Calc. for $C_{11}H_{22}O_6$: OMe, 62·0%). The tetramethyl β-methylidoside was hydrolysed and the product oxidised to the tetramethyl idonolactone by the same procedure as given above for its preparation from 3-methyl β-methylidoside. Crystals were obtained showing m. p. 90° and no depression of m. p. was observed in admixture with authentic tetramethyl δ-idonolactone.

2-Tosyl 4 : 6-*Benzylidene α-Methylgalactoside.*—α-Methylgalactoside (25 g.), after being dried in a vacuum at 110°, was shaken with dry acetone (2 l.) containing concentrated sulphuric acid (10 g.) for 4 days. The solution was neutralised with anhydrous sodium carbonate, filtered, and evaporated to dryness in the presence of sodium carbonate. The syrupy product was distilled at 140° (bath temp.)/0·05 mm. (6·5 g.). This could be crystallised, giving 3 : 4-monoacetone α-methylgalactoside (m. p. 103—104°), but this was wasteful and unnecessary. The distilled syrup (6·5 g.) was tritylated by dissolving it in dry pyridine (30 c.c.), adding trityl chloride (8·5 g.), and heating the mixture at 95° for 1 hour. On pouring into water, an amorphous product was obtained (11·5 g.). This substance, 6-trityl 3 : 4-monoacetone α-methylgalactoside, was converted into syrupy 2-tosyl 6-trityl 3 : 4-monoacetone α-methylgalactoside by treatment with tosyl chloride (5·3 g.) in pyridine at 60° for 3 days. After pouring the mixture into water, the product was isolated by extraction with chloroform, and the resulting syrup (11·2 g.) hydrolysed by heating with acetone (300 c.c.) containing 7 c.c. of N-hydrochloric acid under reflux for 5 hours. The solution was neutralised with barium carbonate, filtered, and evaporated to small volume; addition of water precipitated triphenylcarbinol, which was filtered off, and the filtrate evaporated to dryness. After extraction with ethyl acetate a clear syrup, probably 2-tosyl α-methylgalactoside (3·7 g.), was obtained, but again this could not be crystallised. This syrup was treated with benzaldehyde (20 c.c.) and zinc chloride (6 g.) in the usual way and a crystalline compound was isolated. This was *2-tosyl* 4 : 6-*benzylidene α-methylgalactoside*, m. p. 179—180°, $[\alpha]_D^{18°}$ +117·8° in chloroform (*c*, 0·9) (Found: C, 58·0; H, 5·6; OMe, 7·7. $C_{21}H_{24}O_8S$ requires C, 57·8; H, 5·5; OMe, 7·1%).

2-Tosyl 3-Methyl 4 : 6-*Benzylidene α-Methylgalactoside.*—The foregoing galactoside (5·8 g.) was methylated with silver oxide and methyl iodide by heating at 45° for 10 hours. After 3 treatments a crystalline *compound* was obtained which, recrystallised from alcohol–chloroform–light petroleum, had m. p. 185°, $[\alpha]_D^{18°}$ +164·4° in chloroform (*c*, 1·435) (Found: C, 58·6; H, 5·9. $C_{22}H_{26}O_8S$ requires C, 58·7; H, 5·8%).

2-Tosyl α-Methylgalactoside.—Crystalline 2-tosyl 4 : 6-benzylidene α-methylgalactoside (0·55 g.) was dissolved in acetone (50 c.c.), oxalic acid (2 g.) in water (10 c.c.) added, and the mixture heated under reflux for 12 hours. After neutralisation with barium carbonate, filtration, evaporation of the filtrate, and extraction of the residue with ethyl acetate, syrupy *2-tosyl α-methylgalactoside* was obtained which, even after this preparation through the crystalline benzylidene compound, could not be crystallised. It showed $[\alpha]_D^{18°}$ +83·5° in methyl alcohol (*c*, 4·54) (Found: OMe, 10·0. $C_{14}H_{20}O_8S$ requires OMe, 8·9%).

2-Tosyl 3 : 4 : 6-*Trimethyl α-Methylgalactoside.*—The syrupy 2-tosyl α-methylgalactoside (0·44 g.) was methylated in the usual way by 3 treatments with silver oxide and methyl iodide. The resulting syrup could not be crystallised; yield, 0·4 g., $[\alpha]_D^{18°}$ +74·5° in chloroform (*c*, 3·217) (Found: OMe, 30·7. $C_{17}H_{26}O_8S$ requires OMe, 31·6%).

Action of Alkali on 2-Tosyl 4 : 6-*Benzylidene α-Methylgalactoside.*—(a) *Cold sodium methoxide.* The α-methylgalactoside (7·3 g.) was dissolved in chloroform (50 c.c.), a methyl-alcoholic solution containing sodium methoxide (1·1 g.) added, and the mixture set aside for 24 hours. There was, however, no precipitate of sodium *p*-toluenesulphonate. The mixture was diluted with water and extracted with chloroform; evaporation of the extract gave a crystalline solid, which recrystallised from alcohol (m. p. 180°) and was unchanged 2-tosyl 4 : 6-benzylidene α-methylgalactoside (6·8 g.) (mixed m. p.).

(b) *Hot sodium methoxide.* 2-Tosyl 4 : 6-benzylidene α-methylgalactoside (0·9 g.) was dissolved in methyl alcohol (20 c.c.) containing sodium (0·06 g.; 1 atom), and the mixture boiled for 4 hours; thereafter the solution was diluted with water and extracted with chloroform, the extract dried over anhydrous magnesium sulphate, filtered, and evaporated to dryness. After recrystallisation from alcohol the residue gave crystals (m. p. 180°) which were unchanged galactoside (mixed m. p.); yield 0·75 g.

(c) *Hot sodium methoxide under pressure.* 2-Tosyl 4 : 6-benzylidene α-methylgalactoside (0·7 g.) was heated in methyl-alcoholic solution containing sodium (0·06 g.) at 120° in a sealed tube for 20 hours. The product was isolated by dilution with water and extraction with chloroform as before. On evaporation of the chloroform extract, a residue was obtained which was recrystallised from methyl alcohol (m. p. 134°) and was 3-*methyl* 4 : 6-*benzylidene* α-*methyl*-d-*idoside*; yield 0·3 g., $[\alpha]_D^{17°}$ +66·0° in chloroform (*c*, 1·792) (Found: C, 61·1; H, 6·7. $C_{15}H_{20}O_6$ requires C, 60·8; H, 6·7%). No other crystalline material could be isolated.

2 : 3-*Dimethyl* 4 : 6-*Benzylidene* α-*Methyl*-d-*idoside.*—3-Methyl 4 : 6-benzylidene α-methylidoside (0·12 g.) was methylated by means of three treatments with silver oxide and methyl iodide at 45°. The resulting product, recrystallised from alcohol, formed long needles (0·12 g.), m. p. 152°, $[\alpha]_D^{15°}$ +68·8° in chloroform (*c*, 1·948) (Found: C, 62·2; H, 7·5; OMe, 29·4. $C_{16}H_{22}O_6$ requires C, 61·9; H, 7·1; OMe, 30·0%).

Action of Methyl-alcoholic Ammonia on 2 : 3-*Anhydro-β-methyltaloside.*—2 : 3-Anhydro-β-methyltaloside (0·2 g.) was dissolved in methyl alcohol (50 c.c.), saturated with ammonia gas at 0°, and the solution heated in a sealed tube at 120° for 30 hours. The ammonia and the methyl alcohol were evaporated, and the residue recrystallised from alcohol (0·14 g.); m. p. 192°, $[\alpha]_D^{17°}$ −62·2° in methyl alcohol (*c*, 0·707). It was 3-*amino-β-methylidoside* (Found: N, 7·6. $C_7H_{15}O_5N$ requires N, 7·3%). A residual syrup (B, see below) (0·75 g.) was obtained after evaporation of the mother-liquors from the recrystallisation; this, however, could not be crystallised but showed $[\alpha]_D$ −49·9° in ethyl alcohol (*c*, 1·444).

3-*Acetamido Triacetyl β-Methyl*-d-*idoside.*—3-Amino-β-methyl-*d*-idoside (30 mg.) was boiled with acetic anhydride (3 c.c.) and fused sodium acetate (0·3 g.) for 2 minutes, the product poured into ice–water, neutralised with sodium bicarbonate, and extracted thoroughly with chloroform. The extract was dried over anhydrous magnesium sulphate, filtered, and evaporated to dryness; the residue, recrystallised from acetone–petrol, (30 mg.) had m. p. 178—179°, $[\alpha]_D^{17°}$ −36·0° in chloroform (*c*, 1·39) (Found: C, 49·4; H, 6·3; N, 4·4. $C_{15}H_{23}O_9N$ requires C, 49·8; H, 6·4; N, 3·9%).

Acetylation of Syrup B.—The syrup B (75 mg.) was acetylated by boiling with acetic anhydride (3 c.c.) and fused sodium acetate (0·3 g.) for 2 minutes. The product was isolated as above, and a syrup was obtained which partly crystallised and from which 3-acetamido triacetyl β-methyl-*d*-idoside (30 mg.) (m. p. 178°) was obtained. A residual syrup (30 mg.) which would not crystallise, remained.

3-*Acetamido-β-methyl*-d-*idoside.*—3-Amino-β-methyl-*d*-idoside (45 mg.) was dissolved in dry methyl alcohol (5 c.c.), 3 drops of acetic anhydride added, and the mixture left overnight. Evaporation in a vacuum desiccator over moist potassium hydroxide gave a residue which, recrystallised from alcohol–ether, (35 mg.), had m. p. 202—203°, $[\alpha]_D^{15°}$ −51·4° in methyl alcohol (*c*, 0·935) (Found: C, 45·8; H, 7·3; N, 6·5. $C_9H_{17}O_6N$ requires C, 45·9; H, 7·2; N, 5·9%).

Action of Methyl-alcoholic Ammonia on 4 : 6-*Benzylidene* 2 : 3-*Anhydro-β-methyltaloside.*—The anhydro-compound (1 g.) was dissolved in methyl alcohol (150 c.c.), saturated with ammonia at 0°, and the solution heated in a sealed tube at 125° for 50 hrs. The resulting solution was evaporated to dryness, and the product immediately acetylated by dissolving it in pyridine (30 c.c.), adding acetic anhydride (3 c.c.), and keeping it at 35° for 3 days. The mixture was poured into water, extracted with chloroform, the extract washed successively with 5% sulphuric acid, dilute sodium bicarbonate, and with water, dried over anhydrous magnesium sulphate, and evaporated to dryness. The product rapidly crystallised (crude yield, 0·85 g.). This was recrystallised fractionally (0·65 g.), but each crop of cystals melted at 234°. The mother-liquors finally gave a syrup (0·12 g.) which would not crystallise further. The crystalline material was 3-*acetamido* 2-*acetyl* 4 : 6-*benzylidene β-methyl*-d-*idoside*, $[\alpha]_D$ −13·1° in chloroform (*c*, 0·848) (Found: C, 59·2; H, 6·3; N, 4·5. $C_{18}H_{23}O_7N$ requires C, 59·2; H, 6·2; N, 3·8%). The syrupy residue probably contained 2-acetamido 3-acetyl 4 : 6-benzylidene β-methylgalactoside.

2-*Tosyl* 3 : 4 : 6-*Trimethyl β-Methylgalactoside.*—2-Tosyl β-methylgalactoside (2·3 g.) was treated three times with silver oxide and methyl iodide in the usual way. The product crystallised from ethyl acetate in the form of stout prisms (2·05 g.), m. p. 132°, $[\alpha]_D^{16°}$ −25·1° in chloroform (*c*, 1·356) (Found: C, 52·3; H, 6·8; OMe, 30·7. $C_{17}H_{26}O_8S$ requires C, 52·3; H, 6·7; OMe, 31·7%).

Action of Methyl-alcoholic Ammonia on 2-*Tosyl* 3 : 4 : 6-*Trimethyl β-Methylgalactoside.*—The β-methylgalactoside (1·5 g.) was heated at 200° for 40 hrs. with methyl alcohol (200 c.c.), saturated with ammonia at 0°, in a sealed tube. The product was evaporated to dryness, the residue extracted with chloroform, the chloroform solution evaporated, and the syrup distilled at 140°/0·03 mm. as a very mobile liquid (0·3 g.), $n_D^{20°}$ 1·4496. The distillate was acetylated by dissolving it in methyl alcohol (5 c.c.), adding acetic anhydride (2 drops), and keeping it for 24 hrs. After evaporation in a vacuum desiccator over potassium hydroxide, the syrup was distilled at 90—100°/0·02 mm., leaving a crystalline residue which recrystallised from ethyl acetate and a trace of petrol in small needles (m. p. 238°). The yield was only a few mg. and no analytical figures could be obtained, but by analogy with the experiment of Cutler and Peat (J., 1939, 782) the crystalline product should be 2-acetamido 3 : 4 : 6-trimethyl β-methylgalactoside. On admixture with 2-acetyl 3 : 4 : 6-trimethyl β-methylchondrosaminide (m. p. 233°), prepared by Dr. M. Stacey of this department, there was a depression in m. p. to 226—228°, showing that the two compounds were not identical.

A parallel experiment carried out with syrupy 2-tosyl 3 : 4 : 6-trimethyl α-methylgalactoside failed to give any crystalline material.

The author thanks Professor W. N. Haworth, F.R.S., for his help and interest in this investigation.

The A. E. Hills Laboratories,
The University, Edgbaston, Birmingham.

[*Received, June 5th,* 1944.]