360. *A New Reaction of* 4 : 6-*Ethylidene* β-*Methylglucoside Derivatives :* 4 : 6-*Dimethyl Glucose.*

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By the use of a new reaction, crystalline 4 : 6-*dimethyl* α-*glucose* has been obtained from 4 : 6-ethylidene β-methylglucoside 2 : 3-dinitrate as starting material, and its constitution has been proved. The new sugar is shown to be the same as the crystalline dimethyl glucose of unknown constitution obtained by Haworth and Sedgwick (J., 1926, 2573).

This reaction consists in effecting, by acetic anhydride containing 0·1% of sulphuric acid, an opening of the 1 : 3-dioxan ring of the ethylidene β-methylglucoside derivative at C_6 of the glucose chain, giving rise to a derivative of 6-acetyl 4-α-acetoxyethyl β-methylglucoside.

The use of this reaction on 2 : 3-diacetyl 4 : 6-ethylidene β-methylglucoside leads to a rapid and economical preparation of 2 : 3 : 6-triacetyl β-methylglucoside.

The action of fuming nitric acid on some ethylidene β-methylglucoside derivatives has been studied, leading to the preparation of crystalline β-*methylglucoside* 4 : 6-*dinitrate*.

Twelve crystalline derivatives of β-methylglucoside are described for the first time.

This research originated in attempts to prepare a glucose derivative substituted in positions 1, 2, 3 and 6 by some radical, *e.g.*, the nitrate group, which does not display the migratory tendencies of carboxylic acyl groups and, unlike toluenesulphonyl radicals, can be removed without danger of Walden inversion. Our aim has not yet been realised, but we are reporting the discovery of a new reaction of the 4 : 6-ethylidene group in β-methylglucoside derivatives, analogous to that described for the 1 : 2-*iso*propylidene group in glucofuranose derivatives by Brigl and Zerrweck (*Ber.*, 1933, **66**, 936) and by Schlubach, Rauchenberger, and Schultze (*ibid.*, p. 1248). We have also succeeded in an efficient synthesis of crystalline 4 : 6-*dimethyl* α-*glucose*, which has been shown to be identical with the crystalline dimethyl glucose of unknown constitution obtained by Haworth and Sedgwick (J., 1926, 2573). We are indebted to Professor W. N. Haworth, F.R.S., for having the mixed melting point determinations carried out in his laboratory.

The reactions studied in the course of this work are summarised on page 1712, where B signifies β-methylglucoside.

Our investigations commenced with attempts to remove the ethylidene radical from 4 : 6-ethylidene β-methylglucoside 2 : 3-dinitrate, prepared by the method of J. W. H. Oldham (unpublished work from St. Andrews); the method consists in treating 4 : 6-ethylidene β-methylglucoside with a large excess of nitrogen pentoxide in chloroform. By the customary methods of mild acid hydrolysis for splitting acetal linkages, the initial material was largely recovered unchanged. More vigorous treatment with acid removed

the glucosidic methyl group, as did also treatment with acetic anhydride containing 1% of sulphuric acid at room temperature. The use of 0·1% sulphuric acid in this manner,

Section I.

4 : 6-*Ethylidene B* 2 : 3-*dinitrate*

↓

B 2 : 3 : 4 : 6-*tetranitrate*

→ ? 6-*Acetyl* 4-α-*acetoxyethyl B* 2 : 3-*dinitrate*

↓

? 6-*Acetyl B* 2 : 3 : 4-*trinitrate*

B 2 : 3-*dinitrate* ⇄ 4 : 6-*Diacetyl B* 2 : 3-*dinitrate*

↓

4 : 6-*Dimethyl B* 2 : 3-*dinitrate*

↓

4 : 6-*Dimethyl B* ——● 4 : 6-*Dimethyl* α-*glucose*

↓

2 : 3-*Di*-p-*toluenesulphonyl* 4 : 6-*dimethyl B*

↑

(2 : 3-Di-*p*-toluenesulphonyl B)

↑

2 : 3-Di-*p*-toluenesulphonyl 4 : 6-benzylidene B

Section II.

2 : 3-Diacetyl 4 : 6-ethylidene B

↓

2 : 3-Diacetyl B 4 : 6-dinitrate

→ (2 : 3 : 6-Triacetyl-4-α-acetoxyethyl B)

↓

B 4 : 6-*dinitrate*

↓

2 : 3-Dimethyl B 4 : 6-dinitrate

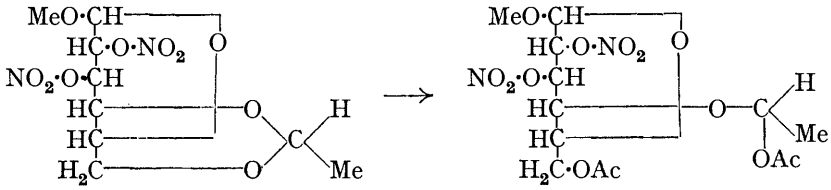
2 : 3 : 6-*Triacetyl B* 4-*nitrate*

↓ ↑

2 : 3 : 6-Triacetyl B

Compounds in parentheses have not been characterised.

however, resulted in the formation of a new crystalline compound in about 60% yield; the rest of the initial material could be recovered unchanged. From the fact that the optical rotation of the mixture attained a constant value after 5 minutes at room temperature, we believe that an equilibrium results during this reaction. We suggest that the new compound is 6-*acetyl* 4-α-*acetoxyethyl* β-*methylglucoside* 2 : 3-*dinitrate*, formed by acetolytic opening of the 1 : 3-dioxan ring at C_6 of the glucose chain :



The proposed structure is supported by (1) the analytical figures, (2) the molecular weight, and the following reactions: (3) Treatment of the compound with sodium methoxide

at room temperature in equal volumes of chloroform and methyl alcohol yields crystalline β-*methylglucoside* 2 : 3-*dinitrate* (see below). (4) On treatment with dilute acid an amorphous product is obtained containing 9·2% OMe (calc. for monoacetyl β-methylglucoside dinitrate, 9·5%). During this treatment the optical rotation tends towards a constant value, and approximately one equivalent of acid per molecule is set free. The product proved very resistant to *p*-toluenesulphonylation by the usual method, with the result that we could not employ this method for proving its constitution. The yield of product, and the fact that it is extracted from water by chloroform, tend to confirm the view that the action of dilute acid is to remove the α-acetoxyethyl group, but further investigation is necessary before detailed information about the structure of the product can be given. (5) Treatment of the compound with fuming nitric acid in chloroform gave a good yield of a crystalline compound having the composition of a monoacetyl β-methylglucoside trinitrate. This substance proved completely resistant to deacetylation by the Zemplén technique. Dilute dimethylamine in alcohol similarly had no effect. More drastic treatment removed nitrate as well as acetate. Owing to this behaviour it was not possible to determine the structure by the usual methods. It was accordingly treated with sodium iodide in acetone under the conditions prescribed by Irvine and Oldham (J., 1925, **127**, 2729) and gave a completely halogen-free product; from this we conclude that in this compound the 6-position of the glucose residue is not occupied by nitrate, since in all known 6-nitrates of glucose derivatives the effect of this treatment is to yield the corresponding iodohydrin (Irvine and Oldham, *loc. cit.*; Oldham, *ibid.*, p. 2840; Oldham and Rutherford, *J. Amer. Chem. Soc.*, 1932, **54**, 366; Irvine and Rutherford *ibid.*, p. 1491). (6) By analogy with the corresponding series of reactions of 2 : 3-diacetyl 4 : 6-ethylidene β-methylglucoside (see below) leading to the formation of 2 : 3 : 6-triacetyl β-methylglucoside 4-nitrate. The action of fuming nitric acid is considered in each case to lead to a direct replacement by nitrate of the α-acetoxyethyl group. (7) A strong smell of acetaldehyde was noticed as a result of treating the compound with dilute acid, sodium methoxide, or fuming nitric acid.

The above reasons suggest that the α-acetoxyethyl group in this compound is situated at position 4 and not at position 6; direct proof has not succeeded, owing to the abnormal reactivities of the two derivatives mentioned above, and until this is achieved, the proposed formula must remain tentative.

β-Methylglucoside 2 : 3-dinitrate [see (3) above] was formed in almost quantitative yield, and on acetylation gave a well-defined *diacetyl* derivative from which the original material could easily be regenerated by treatment with sodium methoxide. Methylation of the 2 : 3-dinitrate with Purdie's reagents gave crystalline 4 : 6-*dimethyl* β-*methylglucoside* 2 : 3-*dinitrate*; this on reductive treatment with sodium sulphide yielded crystalline 4 : 6-*dimethyl* β-*methylglucoside*.

The constitution of the last substance follows from the method of preparation, but additional confirmatory evidence was obtained as below: (1) The substance yielded a crystalline di-*p*-toluenesulphonyl derivative identical with 2 : 3-*di*-p-*toluenesulphonyl* 4 : 6-*dimethyl* β-*methylglucoside* prepared as follows: 2 : 3-di-*p*-toluenesulphonyl 4 : 6-benzylidene β-methylglucoside was prepared by the method of Ohle and Spencker (*Ber.*, 1928, **61**, 2387). The crude material had m. p. 158°, that given by Ohle and Spencker. On recrystallisation, however, the melting point rose to 182—184°, $[\alpha]_D$ in chloroform being − 65·3°, as against the value − 54·7° given by the above authors. After elimination of the benzylidene group (which showed greater stability in the toluenesulphonyl derivative than in the corresponding benzoyl or acetyl compound) by acid hydrolysis, the product was methylated and yielded a crystalline substance which, since there is no evidence that the toluenesulphonyl group is capable of migration, has the constitution suggested above. (2) The ditoluenesulphonyl derivative, treated with sodium iodide and acetone at 100° according to Oldham and Rutherford, was quantitatively recovered, indicating that a toluenesulphonyl group did not occupy position 6 (*J. Amer. Chem. Soc.*, 1932, **54**, 366). (3) The dimethyl β-methylglucoside on acid hydrolysis gave a crystalline dimethyl glucose, m. p. 156—158°, $[\alpha]_D^{17°}$ (water) + 110·2° ($l = 2$, $c = 2·5$) (initial value, extrapolated from readings made in first 10 mins.) reaching + 63·6° in 24 hours, this value remaining unchanged during the next 12 hours; $[\alpha]_D^{23°}$ (pure dry methyl alcohol) ($l = 2$, $c = 1$) + 122° initially,

reaching a final value of + 85·0° in 36 hours (no change during the last 12 hours), which was not altered by the addition of a trace of ammonia. It did not depress the melting point of the dimethyl glucose of Haworth and Sedgwick (*loc. cit.*), for which the properties given were: m. p. 156—157°, $[\alpha]_D$ (in water) + 93·1° initially, falling to + 62·4°, $[\alpha]_D$ (in methyl alcohol) + 110·7°, falling to + 64·7° after catalysis.

On this evidence we suggest that, in spite of the differences in observed rotation, which may be due to differences of solvent, small traces of impurities, etc., our dimethyl glucose and that of Haworth and Sedgwick are the same compound. These authors demonstrated by methylating the compound that it had the structure of a gluco-pyranose, obtaining 2 : 3 : 4 : 6-tetramethyl glucose after hydrolysis of the resulting glucosides.

On treatment with methyl alcohol containing 1% of hydrogen chloride at room temperature, our compound had initially a specific rotation of + 85·2°, reaching + 64·2° after 6½ hours and + 61·3° after 22½ hours, at which value it remained for 3 days. This behaviour contrasts strongly with that of methylated glucoses in which position 4 is unsubstituted, with which condensation to give methylfuranosides can occur. Thus, for example, 2 : 3 : 6-trimethyl glucose, treated in this manner, has a negative rotation within 2 hours.

The above evidence suggests that in our dimethyl glucose and its β-methylglucoside, position 4 is substituted with methyl, while the experiment described in (2) above suggests that the same is true for position 6. We therefore formulate the dimethyl glucose as 4 : 6-dimethyl α-glucose, being the formula anticipated as a result of the method of preparation of the compound and its derivatives.

In order further to explore the action of acetic anhydride containing 0·1% of sulphuric acid on the ethylidene group, we subjected 2 : 3-diacetyl 4 : 6-ethylidene β-methylglucoside to this treatment. The amorphous product was not further examined, since on treatment with fuming nitric acid in chloroform it gave a good yield of crystalline 2 : 3 : 6-triacetyl β-methylglucoside 4-nitrate, identical with the product obtained from 2 : 3 : 6-triacetyl β-methylglucoside by the action of fuming nitric acid (J. W. H. Oldham, unpublished work). The constitution was confirmed by subjecting the new compound to reduction with zinc and iron in acetic acid solution, 2 : 3 : 6-triacetyl β-methylglucoside being obtained in good yield. The overall yield of the latter substance from 4 : 6-ethylidene β-methylglucoside is roughly 40%, and this preparation is therefore, in addition to being more rapid, considerably more economical than either of the previously described methods (Helferich, Bredereck, and Scheidmüller, *Annalen*, 1927, **458**, 111; Levene and Raymond, *J. Biol. Chem.*, 1932, **97**, 763). Our measurement of the rotation in chloroform (— 59·7°) for this compound incidentally confirms the Levene value (— 59·0°) as against the Helferich value (— 64·9°).

As a result of the foregoing experiments, we deduce that the action of acetic anhydride and sulphuric acid on the ethylidene derivative is in the main an acetolytic opening of the 1 : 3-dioxan ring at C_6 of the glucose chain, giving 2 : 3 : 6-triacetyl 4-α-acetoxyethyl β-methylglucoside.

An alternative method for removing the ethylidene group is afforded by the direct action of fuming nitric acid, analogous to a reaction of the benzylidene group employed by Oldham and Rutherford (*J. Amer. Chem. Soc.*, 1932, **54**, 366), but more conveniently carried out, owing to the absence of aromatic by-products. In this way from the ethylidene dinitrate, we obtained crystalline β-methylglucoside 2 : 3 : 4 : 6-tetranitrate, a compound not previously described, but mentioned in an analytical paper by Brough and Dewar (*J. Soc. Chem. Ind.*, 1936, **55**, 207T).

Acting on 2 : 3-diacetyl 4 : 6-ethylidene β-methylglucoside, fuming nitric acid gave a good yield of crystalline 2 : 3-diacetyl β-methylglucoside 4 : 6-dinitrate, the characterisation of which is here described for the first time, although the compound is mentioned in passing by Oldham and Rutherford (*loc. cit.*). Treatment of this with sodium methoxide in chloroform caused β-*methylglucoside* 4 : 6-*dinitrate* to crystallise from the reaction mixture, in which it was only slightly soluble; methylation of this substance gave crystalline 2 : 3-dimethyl β-methylglucoside 4 : 6-dinitrate, identical with that prepared by Oldham and Rutherford (*loc. cit.*).

Experimental.

Unless otherwise stated, all evaporations were carried out under reduced pressure and below 50°. Substances were recrystallised until a constant m. p. was attained.

4 : 6-*Ethylidene* β-*Methylglucoside* 2 : 3-*Dinitrate* (I).—(Instructions for this preparation were afforded us by Dr. Oldham.) A suspension of 2 g. of 4 : 6-ethylidene β-methylglucoside (Helferich and Appel, *Ber.*, 1931, **64**, 1841) in 54 ml. of dry chloroform was cooled with ice, and 18 ml. of a cold solution of 20 g. of nitrogen pentoxide in 100 ml. of dry chloroform added. The mixture was stirred until all had dissolved, kept in ice for 5 minutes, and poured into a large volume of ice-water. The chloroform layer was washed with potassium bicarbonate solution, dried over sodium sulphate, and evaporated to dryness. The colourless syrup obtained crystallised from light petroleum (b. p. 60—80°) or alcohol in stout needles, m. p. 88—89°, $[\alpha]_D^{16°}$ (chloroform) $-$ 21·0° ($l = 2$, $c = 5$) (Found: N, 9·3; OMe, 10·7. Calc. for $C_9H_{14}O_{10}N_2$: N, 9·05; OMe, 10·0%). The yield was 95% of the theoretical; if more than 2 g. of the initial material was used in one batch, the yield was considerably less, *e.g.*, 60% from a batch of 5 g.

6-*Acetyl* 4-α-*Acetoxyethyl* β-*Methylglucoside* 2 : 3-*Dinitrate* (II).—The optical rotation of a 5% solution of (I) in acetic anhydride was negative. If, however, the solution was made up with acetic anhydride containing 0·1% of sulphuric acid, a positive rotation was observed. This had reached a constant value before observation could begin, and remained constant for 24 hours. Investigation of this phenomenon led to the following preparation of (II). A solution of 10 g. of (I) in 200 ml. of acetic anhydride containing 0·2 ml. of sulphuric acid was kept at room temperature for 5 minutes, 5 vols. of ice-water containing a little sodium acetate added, and the mixture stirred until a stiff crystalline mass was obtained. The mixture was extracted with benzene, the extract washed with potassium bicarbonate solution, dried (sodium sulphate), and evaporated to dryness, and the crystalline residue recrystallised from alcohol, giving fine needles, m. p. 113—115°, $[\alpha]_D^{17°}$ (chloroform) $+$ 22·7° ($l = 2$, $c = 3$) (Found: C, 38·2; H, 4·65; N, 6·45; OMe, 8·0; *M*, cryoscopic in acetic acid, 410. $C_{13}H_{20}O_{13}N_2$ requires C, 38·0; H, 4·8; N, 6·8; OMe, 7·5; *M*, 412.

The *substance* (II) was formed in about 60% yield, and more could be obtained by evaporating the mother-liquors (which did not yield another crop of crystals) and repeating the treatment with acetic anhydride and sulphuric acid on the syrup so obtained. This indicates that the reaction does not proceed to completion. This view is confirmed by treating the crude product of the reaction with sodium methoxide, under the conditions detailed below, and subjecting the new product to benzene–water extraction; unchanged (I) can then be obtained crystalline from the benzene layer.

Acid hydrolysis of (II). 1 G. of (II) was dissolved in 27 ml. of acetone and 3 ml. of N-hydrochloric acid. The rotation was observed in a 2 dm. tube: α $+$ 1·57° (initial value), $+$ 0·64° after 40 minutes' refluxing on the water-bath, $+$ 0·02° after 70 mins., $-$ 0·56 after 130 mins., and $-$ 0·63° after 170 mins. During this treatment a strong smell of acetaldehyde was noticed. The mixture was then titrated with N-sodium hydroxide until neutral to phenolphthalein: 5·8 ml. were required, *i.e.*, during hydrolysis 2·8 milliequivs. of acid were liberated, *i.e.*, 1·15 equivs. of acid per molecule. A drop of acetic acid was then added, then excess of potassium bicarbonate solution, and the mixture extracted twice with chloroform; 0·68 g. of a colourless syrup was obtained on evaporation of the chloroform. It could not be crystallised, and on treatment under the usual conditions with *p*-toluenesulphonyl chloride in pyridine gave only 0·3 g. of uncrystallisable product.

6-*Acetyl* β-*Methylglucoside* 2 : 3 : 4-*Trinitrate* (III).—4 G. of (II) were dissolved in 20 ml. of chloroform and cooled to 0°, 20 ml. of fuming nitric acid $+$ 20 ml. of chloroform, also cooled to 0°, were added, and the mixture was kept in ice for 15 minutes and then poured into a large excess of ice-water. The chloroform layer was separated, washed with potassium bicarbonate solution, dried (sodium sulphate), and evaporated; a strong smell of acetaldehyde was observed. The colourless syrup obtained yielded stout, compact crystals (2·2 g.) on treatment with alcohol. A further yield could be obtained by subjecting the material in the mother-liquor to repeated nitric acid treatment. The material, recrystallised from alcohol, had m. p. 104—105°, $[\alpha]_D^{17·5°}$ (chloroform) $-$ 27·0° ($l = 2$, $c = 2·5$) (Found: C, 29·4; H, 3·5; N, 10·7; OMe, 8·5. $C_9H_{13}O_{13}N_3$ requires C, 29·15; H, 3·5; N, 11·3; OMe, 8·4%). The *compound* (III) could be recovered for the most part unchanged after treatment with 0·2 mol. of sodium methoxide in equal vols. of chloroform and methyl alcohol for an hour at room temperature.

1 G. of (III) was heated for 6 hours at 100° in a sealed tube with 1 g. of sodium iodide and 10 ml. of acetone. The product was largely diluted with water containing sodium thiosulphate, and extracted twice with chloroform. On evaporation the chloroform yielded 0·3 g. of a yellow

syrup which could not be crystallised. This gave a negative response to the Lassaigne halogen test after complete removal of the chloroform.

β-*Methylglucoside 2 : 3-Dinitrate* (IV).—10 G. of (II) were dissolved in 100 ml. of chloroform, and 100 ml. of methyl alcohol, in which 0·12 g. of sodium had immediately beforehand been dissolved, were added. The mixture, which gave off a smell of acetaldehyde, was kept at room temperature for ½ hour; 0·4 ml. of acetic acid was then added, and the solution evaporated to dryness. The resulting syrup was dissolved in water and washed with a little benzene, which on separation yielded only 30 mg. of non-volatile matter. The aqueous solution was evaporated in the presence of a little barium carbonate, the product dissolved in ether, and the solution filtered through animal charcoal. On evaporation it yielded a colourless, almost solid glass, which, after standing over phosphoric oxide for 4 days, crystallised in needles; these could be recrystallised from ether–light petroleum (b. p. 50—60°). A quantitative yield was obtained. For further stages of the work, the glass could be used directly, without recrystallisation, as it was evidently very pure. The compound had m. p. 96—98°, $[\alpha]_D^{20°}$ (chloroform containing 5% of acetone, to assist solution) — 20·5° ($l = 2$, $c = 2·5$) (Found: N, 9·8; OMe, 11·2. $C_7H_{12}O_{10}N_2$ requires N, 9·9; OMe, 10·9%).

4 : 6-*Diacetyl* β-*Methylglucoside 2 : 3-Dinitrate* (V).—Acetylation of (IV) by either acetic anhydride and sodium acetate or acetic anhydride and pyridine gave a good yield of this *compound*, which, recrystallised from alcohol, formed stout needles, m. p. 138—140°, $[\alpha]_D^{18°}$ (chloroform) — 5·2° ($l = 2$, $c = 4$) (Found: C, 36·9; H, 4·9; N, 8·0; OMe, 7·8. $C_{11}H_{16}O_{12}N_2$ requires C, 35·85; H, 4·35; N, 7·6; OMe, 8·4%).

4 : 6-*Dimethyl* β-*Methylglucoside 2 : 3-Dinitrate* (VI).—1·6 G. of (IV) was methylated for 4 hours at 45° in excess of methyl iodide in the presence of 4·8 g. of silver oxide. The resulting mixture was taken up in ether, the solution filtered through charcoal, and the filtrate evaporated; the colourless syrup (1·76 g.) obtained shortly crystallised in a high vacuum and on recrystallisation from light petroleum the *product* formed needles, m. p. 54—57°, $[\alpha]_D^{15°}$ (chloroform) — 13·4° ($l = 2$, $c = 3$) (Found: N, 8·6; OMe, 29·8. $C_9H_{16}O_{10}N_2$ requires N, 9·0; OMe, 29·8%).

4 : 6-*Dimethyl* β-*Methylglucoside* (VII).—2 G. of (VI) were dissolved in 10 ml. of alcohol, and 10 ml. of 30% sodium hydroxide solution saturated with hydrogen sulphide were added. After refluxing for ½ hour on the water-bath, the alcohol was removed, potassium carbonate dissolved in the solution until chloroform would just sink, and the solution then extracted nine times with equal volumes of chloroform (cf. Bell, *Biochem. J.*, 1932, **26**, 590). The combined chloroform extracts were dried over sodium sulphate, and evaporated to give a pale yellow syrup. This distilled almost quantitatively at 130—160°/0·4 mm. The distillate crystallised in fine needles (yield, about 70%) and after recrystallisation from ether had m. p. 50—52° and had $[\alpha]_D^{18°}$ (chloroform) — 28·8° ($l = 2$, $c = 3$) (Found: OMe, 41·5. $C_9H_{18}O_6$ requires OMe, 41·8%).

2 : 3-*Di*-p-*toluenesulphonyl* 4 : 6-*Dimethyl* β-*Methylglucoside* (VIII).—(A) A mixture of 0·32 g. of (VII), dissolved in the minimum quantity of pyridine with 0·8 g. of *p*-toluenesulphonyl chloride, was kept at 37° for 48 hours and the product was worked up in the usual manner with benzene and crystallised from alcohol. On recrystallisation, the material had m. p. 146—149°, $[\alpha]_D^{20°}$ (chloroform) — 14·8° ($l = 2$, $c = 3$) (Found: S, 11·8; OMe, 17·3. $C_{23}H_{30}O_{10}S_2$ requires S, 12·1; OMe, 17·55%).

(B) 12 G. of 2 : 3-di-*p*-toluenesulphonyl 4 : 6-benzylidene β-methylglucoside (X), prepared by the method of Ohle and Spencker (*loc. cit.*) (Found: S, 10·8; OMe, 5·4. Calc. for $C_{28}H_{30}O_{10}S_2$: S, 10·85; OMe, 5·3%), were dissolved in 190 ml. of acetone and 10 ml. of 2N-sulphuric acid. The rotation was measured after 2 hours' refluxing (— 7·6°), 2·75 hours (— 3·4°), 3·75 hours (— 3·0°). The mixture was then neutralised with barium carbonate, and evaporated. The benzaldehyde remaining was removed by addition of water and re-evaporation. On addition of alcohol, crystals of unchanged (X) were obtained, so the product was taken up in 200 ml. of acetone and 100 ml. of 0·3N-hydrochloric acid and refluxed again for 7 hours. The benzaldehyde was removed as previously, and the product taken up in chloroform and alcohol and filtered through charcoal. The filtrate on evaporation yielded 10 g. of 2 : 3-di-*p*-toluenesulphonyl β-methylglucoside (IX) as a syrup which could not be crystallised. This was methylated with 15 ml. of methyl iodide and 15 g. of silver oxide; the product gave crystals from alcohol (VIII), m. p. 146—149° (undepressed by specimen A), $[\alpha]_D^{20°}$ (chloroform) — 14·6° ($l = 2$, $c = 5·5$) (Found: S, 12·2; OMe, 17·4%).

4 : 6-*Dimethyl* α-*Glucose* (XI).—2 G. of (VII) were boiled under reflux with 40 ml. of N-hydrochloric acid and the rotation was observed in a 2 dm. tube: 90 mins., + 3·59°; 120 mins., 4·37°; 190 mins., 5·25°; 335 mins., 5·90°. The solution was then cooled, neutralised with excess

of pure lead carbonate, kept in ice for a few minutes, and filtered; the precipitate was washed with alcohol, and the combined filtrate and washings were evaporated under reduced pressure at 100°. The product was extracted four times with boiling ethyl acetate, and the extract filtered hot. On cooling, crystals were immediately deposited. Recrystallised from ethyl acetate, these formed fine needles, m. p. 156—158° (Found: C, 45·5; H, 7·8; OMe, 29·95. $C_8H_{16}O_6$ requires C, 46·15; H, 7·7; OMe, 29·8%). The *compound* did not depress the m. p. of the crystalline dimethyl glucose of Haworth and Sedgwick (*loc. cit.*) (experiment carried out by Prof. Haworth, at Birmingham).

71 Mg. of the compound were dissolved in 5 ml. of methyl alcohol (bench reagent) containing 1% of dry hydrogen chloride. The rotation was measured in a 1 dm. tube at 23°:

Time (hrs.)	0	½	1½	4½	6½	22½
α	+ 1·21°	+ 1·16°	+ 1·07°	+ 0·94°	+ 0·91°	+ 0·87°
$[\alpha]_D$	+85·2°	+81·7°	+75·4°	+66·2°	+64·2°	+61·3°

2 : 3 : 6-*Triacetyl* 4-α-*Acetoxyethyl* β-*Methylglucoside* (XIII).—6·5 G. of 2 : 3-diacetyl 4 : 6-ethylidene β-methylglucoside (XII) (Helferich and Appel, *Ber.*, 1931, **64**, 1841) were dissolved in acetic anhydride (130 ml.) containing 0·1% of sulphuric acid. The rotation observed in a 1 dm. tube was − 3·19° initially (without sulphuric acid), + 0·03° after 5 mins., and + 0·07° after 10 mins. Ice-water (5 vols.) with a little sodium acetate was then added, and the mixture on stirring soon became homogeneous. The solution was neutralised with excess of calcium carbonate and filtered, and the precipitate washed with chloroform, which was subsequently used for extracting the filtrate. The chloroform extracts on drying and evaporation yielded 6·4 g. of a colourless syrup, which did not crystallise (XIII).

2 : 3 : 6-*Triacetyl* β-*Methylglucoside* 4-*Nitrate* (XIV).—(A) 1 G. of (XIII) was treated with fuming nitric acid in chloroform and worked up exactly as described for the preparation of (III); 0·8 g. of a colourless syrup was obtained, which did not crystallise immediately on addition of alcohol, but gave crystals (0·74 g.) on addition of water to the methyl-alcoholic solution to turbidity, followed by a trace of ether. Recrystallisation from methyl alcohol gave a pure *product*, m. p. 112—114°, $[\alpha]_D^{17·5°}$ (chloroform) − 27·0° ($l = 2$, $c = 2·5$) (Found: C, 42·65; H, 5·0; N, 3·5; OMe, 8·1. $C_{13}H_{19}O_{11}N$ requires C, 42·75; H, 5·2; N, 3·8; OMe, 8·5%).

(B) (Oldham's method). 140 Mg. of 2 : 3 : 6-triacetyl β-methylglucoside (XV), prepared by the method of Levene and Raymond (*J. Biol. Chem.*, 1932, **97**, 763), were treated with fuming nitric acid in chloroform exactly as described above, and worked up to give 183 mg. of a colourless syrup, which crystallised from methyl alcohol; m. p. 112—114° (undepressed by A), $[\alpha]_D^{24°}$ (chloroform) − 26·9° ($l = 2$, $c = 1·7$).

2·4 G. of (XIV) were dissolved in 15 ml. of glacial acetic acid and reduced with iron filings and zinc dust until the solution gave no colour with diphenylamine in sulphuric acid. It was then diluted with water, neutralised with excess of barium carbonate, and filtered. The precipitate was washed with chloroform, which was then used for extracting the filtrate. The chloroform extract on evaporation yielded 2·2 g. of a colourless syrup, which crystallised immediately on addition of ether. Recrystallisation was effected by concentrating and cooling an ethereal solution of the material; the product had m. p. 112—115° and did not depress the m. p. of authentic (XV). $[\alpha]_D^{23°}$ (chloroform) − 59·7° ($l = 2$, $c = 3·3$). Levene and Raymond (*loc. cit.*) give m. p. 113·5—114·5° and $[\alpha]_D$ − 59·0°.

β-*Methylglucoside* 2 : 3 : 4 : 6-*Tetranitrate* (XVI) (cf. Brough and Dewar, *loc. cit.*).—2 G. of (I) were treated with fuming nitric acid in chloroform and worked up exactly as described above for the preparation of (III); 2·7 g. of a syrup were obtained, which gave stout needles from alcohol, m. p. 116—118°, $[\alpha]_D^{17°}$ (chloroform) + 9·35° ($l = 2$, $c = 4$) (Found: N, 14·15; OMe, 8·15. Calc. for $C_7H_{10}O_{14}N_4$: N, 15·0; OMe, 8·3%).

2 : 3-*Diacetyl* β-*Methylglucoside* 4 : 6-*Dinitrate* (XVII) (cf. Oldham and Rutherford, *loc. cit.*).—2 G. of (XII) were dissolved in chloroform and treated with fuming nitric acid exactly as described for the preparation of (III). 2·27 G. of a colourless syrup were obtained, which gave fine needles from methyl alcohol, m. p. 118—120°, $[\alpha]_D^{16°}$ (chloroform) − 7·3° ($l = 2$, $c = 5$) (Found: N, 7·15; OMe, 8·4. $C_{11}H_{16}O_{12}N_2$ requires N, 7·6; OMe, 8·4%).

β-*Methylglucoside* 4 : 6-*Dinitrate* (XVIII).—7 G. of (XVII) were dissolved in 70 ml. of chloroform, and to the solution were added 5 ml. of methyl alcohol in which 0·1 g. of sodium had been dissolved immediately beforehand. The mixture was kept at room temperature and after 100 minutes a mat of fine needle-like crystals had separated (yield, 4·3 g.; 80% of the theoretical). The crystals were very slightly soluble in boiling chloroform and extremely soluble in cold alcohol. Recrystallisation was best effected from water; m. p. 147—149°, $[\alpha]_D^{17°}$ (methyl alcohol,

pure B.D.H.) — 5·3° ($l = 2$, $c = 2$) (Found: N, 9·0; OMe, 10·85. $C_7H_{12}O_{10}N_2$ requires N, 9·9; OMe, 10·9%).

This substance, on a single treatment with methyl iodide and silver oxide, yielded a quantitative amount of product crystallising from alcohol; m. p. 98—99°, not lowered by authentic 2 : 3-dimethyl β-methylglucoside 4 : 6-dinitrate of the same m. p.; $[\alpha]_D^{20°}$ (chloroform) — 19·95° ($l = 2$, $c = 1·3$). Oldham and Rutherford (*loc. cit.*) give m. p. 98—99°, $[\alpha]_D$ (chloroform) — 20·8° ($c = 3$).

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