162. *β-Methylglucoside 2 : 3 : 6-Trinitrate.*

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β-Methylglucoside 2 : 3 : 6-trinitrate has been synthesised from β-methylglucoside 2 : 3-dinitrate, and its constitution proved by methylation.

Further evidence is brought forward supporting the formulation of the compound described (Bell and Synge, J., 1937, 1711) as 6-acetyl 4-α-acetoxyethyl β-methylglucoside 2 : 3-dinitrate.

Two new crystalline derivatives of β-methylglucoside are described.

In a previous paper (*loc. cit.*) we announced our intention of preparing a glucose derivative substituted in positions 2, 3, and 6 by the nitrate group. We have now succeeded in preparing *β-methylglucoside 2 : 3 : 6-trinitrate*, which we hope will be of use for synthetic work involving substitution of glucose residues at position 4.

The following series of reactions was employed: β-methylglucoside 2 : 3-dinitrate (Bell and Synge, *loc. cit.*) was condensed with triphenylchloromethane to yield its 6-triphenylmethyl ether, which could not be crystallised. Acetylation of this compound gave crystalline *4-acetyl 6-triphenylmethyl β-methylglucoside 2 : 3-dinitrate*, which, on treatment with fuming nitric acid in chloroform (cf. Oldham and Bell, *J. Amer. Chem. Soc.*, 1938, **60**, 323), was converted into crystalline *4-acetyl β-methylglucoside 2 : 3 : 6-trinitrate*. This, on treatment with sodium methoxide, gave a quantitative yield of

β-methylglucoside 2 : 3 : 6-trinitrate as a colourless glass which could not be made to crystallise. The overall yield from β-methylglucoside 2 : 3-dinitrate was about 30%, which corresponds to an overall yield from β-methylglucoside of about 15%.

The constitution of the β-methylglucoside trinitrate was proved by methylation, which, since no case of migration of the nitrate group has yet been reported, we consider to be a valid method. By this means we obtained a syrup having a methoxyl content agreeing with the theoretical for a monomethyl β-methylglucoside trinitrate. Reductive removal of nitrate from this, followed by acetylation, gave a fair yield of crystalline 2 : 3 : 6-triacetyl 4-methyl β-methylglucoside. Our specimen, which, owing to the small quantities with which we were working, could not be completely purified, had m. p. 105—106° and $[\alpha]_D^{20°}$ — 34·9° ($l = 2$, $c = 2·5$ in chloroform). We were unable to obtain a specimen of authentic 2 : 3 : 6-triacetyl 4-methyl β-methylglucoside (Levene and Raymond, *J. Biol. Chem.*, 1932, **97**, 763; Munro and Percival, J., 1935, 873) for a mixed melting point determination, but Professor B. Helferich of Leipzig kindly gave us a specimen of 2 : 3 : 4-triacetyl 6-methyl β-methylglucoside, which depressed the melting point of our compound by more than 20°. The four theoretically possible triacetyl methyl β-methylglucopyranosides are all known, and are tabulated below. Comparison of our compound with those listed leaves no doubt as to its identity.

The triacetyl methyl β-methylglucopyranosides.

Position of Me.	M. p.	$[\alpha]_D$ (chloroform).	Authors.
2	74—75°	+ 6·3°	Brigl and Schinle, *Ber.*, 1929, **62**, 1716.
3	90—90·5	−34·8	Helferich and Lang, *J. pr. Chem.*, 1932, **132**, 321.
4	107—108	−32·8	Levene and Raymond, *loc. cit.*
	106	−34·0	Munro and Percival, *loc. cit.*
6	107—108	−12·4	Helferich and Himmen, *Ber.*, 1929, **62**, 2141; Helferich and Günther, *Ber.*, 1931, **64**, 1276.

The fact that 4-acetyl β-methylglucoside 2 : 3 : 6-trinitrate has quite different properties from the compound formulated by us (Bell and Synge, *loc. cit.*) as 6-acetyl β-methylglucoside 2 : 3 : 4-trinitrate corroborates our proposed structure for the latter compound, and consequently our view that the 1 : 3-dioxan ring of the parent ethylidene compound is opened by acetolysis at C_6 of the glucose chain. An entirely analogous reaction of 4 : 6-ethylidene β-methylglucoside 3-nitrate is described in the preceding paper, and serves as further confirmation.

An attempt to *p*-toluenesulphonylate β-methylglucoside 2 : 3 : 6-trinitrate was unsuccessful. We were previously unable (*loc. cit.*) to *p*-toluenesulphonylate the product of mild acid hydrolysis of 6-acetyl 4-α-acetoxyethyl β-methylglucoside 2 : 3-dinitrate, which probably consists largely of 6-acetyl β-methylglucoside 2 : 3-dinitrate, a compound of similar structure.

Experimental.

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

6-Triphenylmethyl β-Methylglucoside 2 : 3-Dinitrate (I).—5·8 G. of β-methylglucoside 2 : 3-dinitrate and 6·45 g. of freshly prepared triphenylchloromethane were dissolved in the minimum quantity of pyridine which had been dried with phosphoric oxide, and kept for 7 days at 37° in a stoppered flask. The mixture was then poured into water. A gum separated, and was removed by extraction with benzene. The benzene was washed twice with water, dried (sodium sulphate), and evaporated to dryness. Water was repeatedly added to the residue and evaporated, until there was no smell of pyridine; 9·7 g. of syrup were obtained, which could not be crystallised.

4-Acetyl 6-Triphenylmethyl β-Methylglucoside 2 : 3-Dinitrate (II).—The syrup was dissolved in 100 ml. of pyridine–acetic anhydride (1 : 1) and kept at room temperature for 24 hrs., and the mixture then poured into water. The precipitated oil soon became a stiff crystalline mass, which was recrystallised from alcohol, giving 6·1 g. of crystals, m. p. 153—155°, $[\alpha]_D^{18°}$ + 31·8° ($l = 2$, $c = 2$ in chloroform) (Found: C, 59·0; H, 4·75; N, 4·9; OMe, 5·6. $C_{28}H_{28}O_{11}N_2$ requires C, 59·1; H, 4·9; N, 4·85; OMe, 5·45%).

An attempt to shorten the procedure by adding acetic anhydride to the original reaction mixture before (I) had been submitted to benzene extraction led to extensive formation of 4 : 6-diacetyl β-methylglucoside 2 : 3-dinitrate (Bell and Synge, *loc. cit.*), from which (II) could not easily be separated. The procedure finally adopted eliminates all unchanged β-methylglucoside 2 : 3-dinitrate prior to acetylation.

4-Acetyl β-Methylglucoside 2 : 3 : 6-Trinitrate (III).—1 G. of (II) was dissolved in 10 ml. of chloroform, and treated for 10 mins. at 0° with 20 ml. of chloroform–fuming nitric acid (1 : 1). The mixture was poured into excess of ice-water, and the chloroform layer separated, washed with potassium bicarbonate solution, dried (sodium sulphate), and evaporated to dryness. A crystalline mass was obtained, largely a mixture of (III) with triphenylcarbinol. A preliminary experiment with the latter showed that, when dissolved in ether, it is not precipitated by the addition of 3 vols. of hexane. Application of this treatment to a concentrated ethereal solution of the reaction product caused (III) to crystallise immediately in large needles, which could then easily be purified by recrystallisation from alcohol. Crystallisation from alcohol of the material remaining in the ether–hexane solution gave mainly triphenylcarbinol, and when the alcoholic mother-liquors from the crystallisation of this were combined with those from (III), a further yield of (III) could be obtained by repeating the ether–hexane treatment on this mixture. By these means 0·35 g. was obtained, m. p. 94—95°, $[\alpha]_D^{19°}$ + 0·4° ($l = 2$, $c = 3$ in chloroform) (Found: C, 30·45, 31·0; H, 3·5, 3·9; N, 10·65; OMe, 8·75; *M*, cryoscopic in acetic acid, 353. $C_9H_{13}O_{13}N_3$ requires C, 29·1; H, 3·5; N, 11·3; OMe, 8·4%; *M*, 371).

β-Methylglucoside 2 : 3 : 6-Trinitrate (IV).—0·29 G. of (III) was dissolved in 3 ml. of chloroform, and 3 ml. of methyl alcohol, in which 5 mg. of sodium had been dissolved immediately beforehand, were added. After ½ hr., a drop of acetic acid was added, and the mixture evaporated to dryness. The residue was extracted with ether, and the extracts filtered through charcoal and evaporated to dryness. Yield, 0·25 g. of a colourless glass, which could not be crystallised from ether–hexane or from alcohol, or by keeping over phosphoric oxide for a month (Found: OMe, 8·9. $C_7H_{11}O_{12}N_3$ requires OMe, 9·4%).

The *product* (IV), when treated with *p*-toluenesulphonyl chloride in pyridine under the usual conditions, yielded a syrup [only 30% of the weight of (IV) employed] which could not be crystallised.

4-Methyl β-Methylglucoside 2 : 3 : 6-Trinitrate.—0·2 G. of (IV) on double treatment with silver oxide and methyl iodide yielded 0·21 g. of a colourless syrup which could not be crystallised (Found: OMe, 17·9. $C_8H_{13}O_{12}N_3$ requires OMe, 18·1%).

2 : 3 : 6-Triacetyl 4-Methyl β-Methylglucoside.—The above syrup was dissolved in 2 ml. of acetic acid and treated with iron filings and zinc dust over a free flame until no further brown fumes were evolved. Water was added, and then sodium carbonate equivalent to the acetic acid used. The precipitate obtained was washed with water, and the combined filtrate and washings were evaporated to dryness under reduced pressure at 100°. 25 Ml. of acetic anhydride were added and the mixture was heated for a short time on a boiling water-bath and for 5 minutes over a free flame; it was then poured into excess of cold water, and the acetic acid resulting was neutralised with calcium carbonate. The precipitate was collected and washed with chloroform, which was subsequently used for extracting the filtrate. The combined chloroform extracts were dried (sodium sulphate) and evaporated to dryness, giving 0·13 g. of residue, which shortly crystallised in needles. Recrystallisation of this from ether–hexane gave 0·10 g. of crystalline material, which, owing to the small quantity available, was not further recrystallised. The m. p. and rotation are given above (Found: C, 50·7; H, 6·5; OMe, 18·8. Calc. for $C_{14}H_{22}O_9$: C, 50·3; H, 6·6; OMe, 18·6%).

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