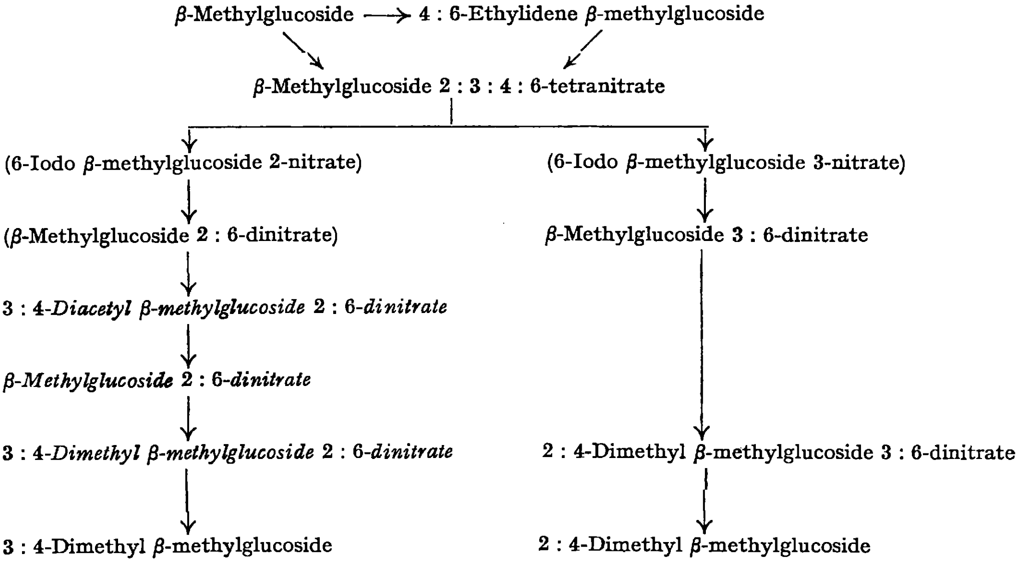
137. *Sugar Nitrates. Part III. 2 : 4-Dimethyl β-Methylglucoside and 3 : 4-Dimethyl β-Methylglucoside from β-Methylglucoside 2 : 3 : 4 : 6-Tetranitrate.*

By John Dewar, Godfrey Fort, and Norman McArthur.

By treating β-methylglucoside 2 : 3 : 4 : 6-tetranitrate successively with sodium iodide (in acetone) and silver nitrate (in acetonitrile), β-methylglucoside 3 : 6- and 2 : 6-dinitrate are obtained, and these can readily be converted into 2 : 4- and 3 : 4-dimethyl β-methylglucoside respectively.

The action of sodium iodide on 4 : 6-ethylidene β-methyglucoside 2 : 3-dinitrate causes the nitrate group in position 2 to be replaced by hydroxyl (Dewar and Fort, this vol., p. 492) and the same reaction applied to 2 : 3-dimethyl β-methylglucoside 4 : 6-dinitrate (Oldham and Rutherford, *J. Amer. Chem. Soc.*, 1932, **54**, 366) leads to the corresponding 6-iodo-4-hydroxy-compound as the principal product. It was thus of interest to examine the effect on a single compound in which nitrate groups occupied all four available positions (*e.g.*, β-methylglucoside 2 : 3 : 4 : 6-tetranitrate) in the expectation that the product would consist largely of the 6-iodo-derivative of the 3-nitrate. Evidence has been obtained that this compound is formed, but is accompanied by a greater proportion of a product derived from the 6-iodo-2-nitrate.



Treatment of a 6-iodo-compound with silver nitrate in acetonitrile yields the corresponding 6-nitrate (Oldham and Rutherford, *loc. cit.*) and it was found better to utilise this reaction than to isolate the iodine derivatives. Fractionation by partition experiments followed, and crystalline β-methylglucoside 3 : 6-dinitrate (cf. Dewar and Fort, *loc. cit.*) was separated. Acetylation of the syrupy residue yielded a crystalline diacetyl dinitrate, for which (on the assumption that one of the nitrate groups occupied position 6) the following were possible structures : (*a*) 2 : 3-diacetyl 4 : 6-dinitrate, (*b*) 2 : 4-diacetyl 3 : 6-dinitrate, (*c*) 3 : 4-diacetyl 2 : 6-dinitrate. For comparison, a sample of (*a*) was prepared (Oldham and Rutherford, *loc. cit.*; Bell and Synge, J., 1937, 1711), and determinations of m. p., mixed m. p., and optical rotation provided conclusive evidence of non-identity. Similarly, structure (*b*) was rejected (cf. Dewar and Fort, *loc. cit.*), and confirmation of (*c*) was obtained by deacetylating, methylating, and then denitrating it to give the known 3 : 4-dimethyl β-methylglucoside (Dewar and Fort, *loc. cit.*). Likewise, methylation and subsequent denitration of β-methylglucoside 3 : 6-dinitrate yielded 2 : 4-dimethyl β-methylglucoside (Dewar and Fort, *loc. cit.*).

It is possible therefore to obtain the 2 : 4-dimethyl and the 3 : 4-dimethyl derivative of β-methylglucoside from this material by these few operations and all but one stage give high yields of products, only the sodium iodide reaction being variable in this respect.

EXPERIMENTAL.

All evaporations were carried out under diminished pressure, and, unless otherwise stated, at below 50°. The light petroleum used in recrystallisations was that of b. p. 60—80°.

β-Methylglucoside 2 : 3 : 4 : 6-*Tetranitrate* (cf. Brough and Dewar, *J. Soc. Chem. Ind.*, 1936, **55**, 207 T; Bell and Synge, *loc. cit.*).—(*a*) To an ice-cold solution of β-methylglucoside (2 g.) in dry chloroform (10 c.c.) was added an ice-cold solution of fuming nitric acid (15 c.c.) in chloroform (15 c.c.); after 15 mins. at 0°, the reaction mixture was poured into ice and water, rapidly shaken, and the chloroform layer separated. This was washed with potassium hydrogen carbonate solution, dried (sodium sulphate), and, on removal of solvent by distillation, a crystalline product (average yield, 69%) was obtained. Recrystallisation from methyl alcohol gave pure nitrate, m. p. 116—117°.

(*b*) Nitration of 4 : 6-ethylidene β-methylglucoside (2 g.) as in (*a*) gave needles (1·4 g.), m. p. 116—117° (*ex* methyl alcohol). A mixture of the products from (*a*) and (*b*) melted sharply at 116—117°. The tetranitrate burned rapidly when heated above its m. p., and exploded violently if confined in a m. p. tube sealed at both ends and heated cautiously.

Treatment of β-Methylglucoside 2 : 3 : 4 : 6-*Tetranitrate with Sodium Iodide in Acetone.*—The following are representative of many different experiments. (*a*) The tetranitrate (2·8 g.), sodium iodide (5·6 g.), and acetone (35 c.c.) were heated for 2 hours in a sealed tube at 100°. Isolation in the standard manner gave a syrup (2·15 g.) from which iodine was evolved on warming a sample with concentrated sulphuric acid. The syrup was dissolved in benzene and extracted four times with water, the last extract being optically inactive. The combined aqueous solutions were saturated with potassium carbonate and extracted four times with acetone, the last extract being without rotation. From the dried benzene solution on evaporation there was obtained a syrup (1·05 g.), which did not crystallise (Found : OMe, 10·2; I, 9·4%). Evaporation of the dried acetone solution gave a syrup (1·06 g.) which did not crystallise (Found :

OMe, 8·6; I, 7·1. Calc. for tri-, di-, and mono-nitrate of 6-iodo β-methylglucoside, respectively: OMe, 7·1, 7·9, 8·9; I, 28·9, 32·2, 36·4%).

(*b*) The tetranitrate (3·4 g.), sodium iodide (6·8 g.), and acetone (30 c.c.) were heated for 14 hours in a sealed tube at 100°; the acetone was distilled off, an almost saturated solution of potassium carbonate added, and the whole extracted 6 times with chloroform. After drying (sodium sulphate), the solvent was distilled off from the combined chloroform solutions, yielding a syrup (2·08 g.). A benzene solution of this was shaken 6 times with water and the combined aqueous solutions, after one wash with benzene, were then extracted 6 times with chloroform. Thereafter, much potassium carbonate was added to the aqueous solution, which was then extracted 6 times with chloroform, and these chloroform extracts, after drying (sodium sulphate), were distilled, giving a syrup (0·933 g.) which would not crystallise. A sample of this syrup (0·885 g.) was treated with silver nitrate (1·08 g.) in acetonitrile (10 c.c.) at 90° for 2 hours. After separation of the precipitated silver iodide, the solvent was distilled off, and the residual syrup extracted several times with boiling chloroform. The solution was decolorised (norit) and then distilled, giving a syrup (0·644 g.) showing a positive test for nitrate and a negative test for iodine (Found: OMe, 12·9%). Partial crystallisation set in after several days. and crystals (0·1 g.) were separated by washing with chloroform, in which the syrupy constituent (X) readily dissolved. The crystals had m. p. 144—146° and did not depress the m. p. of an authentic sample of β-methylglucoside 3 : 6-dinitrate (Dewar and Fort, *loc. cit.*).

The syrup (X) (0·285 g.) on treatment with acetic anhydride (0·56 g.) in pyridine (4 c.c.) for 3 days at room temperature, gave, on isolation in the usual manner, a syrup (0·284 g.), from which, on addition of a small amount of ethyl alcohol, crystals (0·135 g.) separated. Recrystallisation from light petroleum–alcohol gave needles, m. p. 128—129°, of 3 : 4-*diacetyl β-methylglucoside* 2 : 6-*dinitrate* (Found: C, 36·1; H, 4·3; N, 7·5; OMe, 8·7. $C_{11}H_{16}O_{12}N_2$ requires C, 35·9; H, 4·3; N, 7·6; OMe, 8·4%). When admixed with 2 : 3-diacetyl β-methylglucoside 4 : 6-dinitrate, m. p. 120—121°, the m. p. was depressed to 100—108°.

(*c*) The tetranitrate (6·38 g.), sodium iodide (12·8 g.), and acetone (30 c.c.) were heated for 19 hours in a sealed tube at 100°; the solvent was then distilled off and the residue shaken with chloroform and a concentrated solution of potassium carbonate, containing a little sodium thiosulphate. In all, 12 extractions with chloroform were carried out and, after drying (sodium sulphate) and decolorising (norit), the solvent was distilled from the combined chloroform solutions. The resultant syrup (4·14 g.) was now heated at 100° for 2 hours with silver nitrate (4 g.) in acetonitrile (25 c.c.), and then, after filtration, the solvent was removed by distillation. The residue was extracted several times with small volumes of boiling chloroform, and evaporation of these extracts gave a syrup (2·732 g.), which did not contain iodine. To effect a separation, this syrup was shaken with benzene and water, 3 extractions with benzene being carried out. Evaporation of the dried (sodium sulphate) benzene extract gave a syrup (P) (0·323 g.). The aqueous solution from the previous extraction process with benzene was then extracted 3 times with chloroform, and evaporation of the combined, dried (sodium sulphate) solutions gave a syrup (Q) (0·36 g.). Potassium carbonate was now added to the aqueous solution until this was only slightly less dense than chloroform, and 12 extractions were carried out with this solvent. Evaporation of these combined chloroform solutions gave a syrup (R) (1·43 g.).

Residue (R) crystallised partly on addition of chloroform, and the crystalline material was filtered off, washed with chloroform, and recrystallised from chloroform–ethyl alcohol, giving pure β-methylglucoside 3 : 6-dinitrate (0·335 g.), m. p. 145—147°, $[\alpha]_D^{10^\circ}$ − 7·8° (acetone, $l = 2$, $c = 4·7$). Evaporation of the chloroform washings gave a syrup, a sample of which (1·029 g.) was acetylated in the standard manner to give crystals (1·085 g.) {needles (*ex* light petroleum–ethyl alcohol), m. p. 128—129°, $[\alpha]_D^{13^\circ}$ + 5·8° (chloroform, $l = 2$, $c = 5·932$)} of 3 : 4-diacetyl β-methylglucoside 2 : 6-dinitrate.

The syrup (Q) (0·36 g.) on acetylation gave a syrup (0·19 g.) from which by treatment with light petroleum were separated crystals (needles, *ex* light petroleum–ethyl alcohol, m. p. 125—127°) and a syrup from which no definite product could be isolated. No depression of m. p. was observed on mixing the crystalline product with the supposed 3 : 4-diacetyl β-methylglucoside 2 : 6-dinitrate. The syrup (P) did not crystallise and no separation of constituents was effected.

(*d*) In a typical larger-scale repetition of (*c*), 28 g. of starting material gave 5·92 g. of 3 : 4-diacetyl β-methylglucoside 2 : 6-dinitrate and 1·504 g. of β-methylglucoside 3 : 6-dinitrate.

2 : 4-*Dimethyl β-Methylglucoside* 3 : 6-*Dinitrate*.—Methylation of β-methylglucoside 3 : 6-dinitrate (1 g.) gave 1·07 g. of syrup; $n_D^{15^\circ}$ 1·4655, $[\alpha]_D^{15^\circ}$ − 6·9° (chloroform, $l = 2$, $c = 3·50$) (cf. Dewar and Fort, *loc. cit.*).

2 : 4-*Dimethyl β-Methylglucoside*.—Reduction of this dinitrate (0·55 g.) gave a crystalline product (0·39 g.), m. p. 124°, mixed m. p. 124° (cf. Dewar and Fort, *loc. cit.*).

β-Methylglucoside 2 : 6-*Dinitrate*.—3 : 4-Diacetyl β-methylglucoside 2 : 6-dinitrate (6·85 g.) in chloroform (70 c.c.) was treated with methyl alcohol (70 c.c.) in which sodium (0·055 g.) had been dissolved, and the course of the reaction followed polarimetrically. Isolation in the usual way gave the *nitrate* as a syrup (5·048 g.), $n_D^{13^\circ}$ 1·4839, $[\alpha]_D^{13^\circ}$ − 11·6° (chloroform, $l = 2$, $c = 5·03$) (Found: N, 9·7. $C_7H_{12}O_{10}N_2$ requires N, 9·8%).

3 : 4-*Dimethyl β-Methylglucoside* 2 : 6-*Dinitrate*.—The above dinitrate (5 g.) yielded after 2 methylations by Purdie's method a crystalline product (95% yield), which; recrystallised from light petroleum–ethyl alcohol, had m. p. 62—63°, $[\alpha]_D^{11^\circ}$ + 9·7° (chloroform, $l = 2$, $c = 3·707$) (Found: C, 35·1; H, 5·3; N, 8·9. $C_9H_{16}O_{10}N_2$ requires C, 34·6; H, 5·1; N, 8·9%).

3 : 4-*Dimethyl β-Methylglucoside*.—Reduction of the above compound (3·18 g.) in glacial acetic acid (38 c.c.) with zinc and iron powder gave, on isolation in the usual way, a crystalline product (1·967 g.) which was further purified by distillation (b. p. 165—170°/0·9 mm.) and recrystallisation from carbon tetrachloride. It had m. p. 79—81°, unaltered on admixture with 3 : 4-dimethyl β-methylglucoside prepared by another method (Dewar and Fort, *loc. cit.*).

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