

**103. Sugar Nitrates. Part IV.\*** *Reactions of Nitrates and Sulphonates with Sodium Methoxide in Methanol and Some Sodium Salts.*

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Treatment with sodium methoxide of the 3-nitrate and 3-toluene-*p*-sulphonate of 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose and the 6-nitrate and 6-toluene-*p*-sulphonate of 1 : 2-3 : 4-di-*O*-isopropylidene-D-galactose yielded the corresponding alcohols, although with the nitrates much decomposition occurred. Removal of nitrate groups with sodium nitrite in aqueous ethanol has been studied and the stability of sulphonates towards this reagent has been demonstrated. Methyl 4-*O*-methyl-β-D-glucoside has been obtained by preferential removal of the 4-nitrate group of methyl β-D-glucoside 2 : 3 : 4 : 6-tetranitrate. The stability of nitrate groups towards acids has been confirmed by preparation of methyl 2-*O*-methyl-α-D-glucoside 3-nitrate from its 4 : 6-*O*-benzylidene derivative and by removal of the 5 : 6-cyclohexylidene group from 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose 3-nitrate.

SOME new nitrates have been prepared in the glucose and galactose series by the action of fuming nitric acid in acetic anhydride on the parent alcohol<sup>1</sup> or by treatment of the corresponding 6-deoxy-6-iodo-sugar with silver nitrate in boiling methyl cyanide. The relative stability of nitrate groups to acid hydrolysis is shown by the preparation in good yield of methyl 2-*O*-methyl-α-D-glucoside 3-nitrate from its 4 : 6-*O*-benzylidene derivative, and that of 1 : 2-*O*-cyclohexylidene-D-glucose 3-nitrate from the corresponding 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose 3-nitrate. Selective nitration of methyl 4 : 6-*O*-benzylidene-α-D-glucoside gave the 3-nitrate in 28% yield.

Reaction of 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose 3-toluene-*p*-sulphonate with sodium methoxide in boiling methanol gave 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose (94%). Similar reaction of the corresponding 3-nitrate proceeded with much decomposition to give the same product (69%) together with nitrite ion (34%) and nitrate ion (42%). Sodium (1.49 equivalents) was used in the reaction, and no unsaturated compounds could be detected in the organic products. When 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose was boiled with sodium methoxide in methanol, the amount of sodium methoxide present decreased and cyclohexanone was formed in small amounts.

Removal of the nitrate group from 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose 3-nitrate may occur by (1) nucleophilic attack by methoxide ion on the nitrogen atom, yielding parent alcohol and methyl nitrate, (2) nucleophilic attack by methoxide ion on the carbon atom, giving a methyl ether and nitrate ion, (3) elimination of a β-hydrogen atom with formation of an unsaturated derivative and nitrate ion, or (4) elimination of an α-hydrogen atom, yielding a carbonyl group and nitrite ion. The use of anhydrous methanol in this de-esterification prevents reactions involving hydroxyl ion: formation of an anhydro-ring is not possible in this blocked ester. Only mechanism (1) yields the parent alcohol; our results showed that 69% of the reaction occurred in this way and 31% by other routes. No methyl ethers have been encountered in this or similar work, eliminating mechanism (2), and the absence of unsaturated compounds shows that mechanism (3) does not occur to a measurable extent. That ether formation can occur in such reactions has been shown by the formation of methyl β-D-glucoside from tetra-*O*-acetyl-α-D-glucosyl nitrate,<sup>2</sup> and of 2-ethoxyoctane from 1-methylheptyl nitrate.<sup>3</sup> Only mechanism (4) gives rise to nitrite; the quantity of nitrite present in our reaction mixture was in agreement with the value of

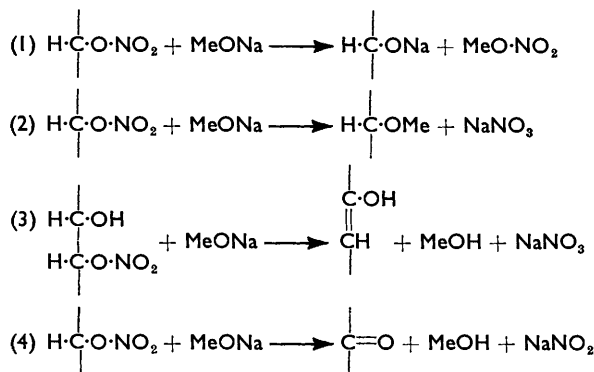
\* Part III, *J.*, 1957, 2278.

<sup>1</sup> Honeyman and Morgan, *Chem. and Ind.*, 1953, 1035.

<sup>2</sup> Gladding and Purves, *J. Amer. Chem. Soc.*, 1944, **66**, 76.

<sup>3</sup> Cristol, Franzus, and Shadan, *ibid.*, 1955, **77**, 2512.

31% suggested for this possibility. No ketonic product was isolated, but the quinoxaline derivative from methyl 4:6-*O*-benzylidene- $\alpha$ -D-glucoside was obtained by adding *o*-phenylenediamine after treatment of the 2:3-dinitrate with sodium methoxide in methanol,<sup>4</sup> proving the formation of ketonic products in these reactions. Nitrate ion could be formed by the alkaline hydrolysis of methyl nitrate. Although the presence of this nitrate was not proved, only 76% of the nitrogen present could be accounted for, and Shepherd<sup>5</sup> observed that in the hydrolysis products of methyl  $\beta$ -D-glucoside 2:3:4:6-tetranitrate at least 0.45 mol. of nitrate was present in non-ionic form. In both mechanisms (1) and (4) nitrogen-oxygen bond fission takes place: inversion at the carbon atom is not observed. It is therefore suggested that the ketonic product is degraded, consuming additional alkali.



Under similar conditions, the 6-nitrate and 6-toluene-*p*-sulphonate of 1:2:3:4-di-*O*-isopropylidene-D-galactose gave the parent alcohol in good yield: no methyl ethers were isolated. Alkaline hydrolysis of 1:2:3:5-di-*O*-isopropylidene-D-glucose 6-toluene-*p*-sulphonate is reported<sup>6</sup> to give some 5:6-didehydro-6-deoxy-1:2:3:5-di-*O*-isopropylidene-D-glucose, but no unsaturated derivatives could be detected in the reactions of the 6-nitrate and 6-toluene-*p*-sulphonate used in the present work. Thus the ester groups were being removed mainly by a mechanism analogous to (1), but the presence of a small quantity of nitrite in the case of the 6-nitrate indicated that some reaction was occurring by a mechanism analogous to (4).

It may be concluded from these and earlier results that a 6-nitrate group is removed from an aldohexose by sodium methoxide with nitrogen-oxygen cleavage only, giving mainly the parent alcohol together with some aldehyde. If formation of an anhydro-ring is possible, however, the reaction proceeds by carbon-oxygen fission only, giving the anhydro-ring. A nitrate group on a secondary carbon atom is removed with nitrogen-oxygen fission unless an anhydro-ring can be formed, in which case the nitrate group may be removed partly by nitrogen-oxygen fission to give the parent alcohol and ketonic products, and partly by carbon-oxygen fission with inversion to give an anhydro-compound. These two types of fission may occur simultaneously in the case of a nitrate group attached to a secondary carbon atom when anhydro-ring formation is possible, but only one type occurs in the case of a similar primary nitrate group. In the first case a ditoluene-*p*-sulphonate gives the anhydro-ring only whereas a diacetate gives the diol, and in this respect the nitrate group is intermediate between an acetate and a sulphonate group. As the nitrate group attracts electrons less strongly than a toluene-*p*-sulphonate group, it is to be expected that it will form anhydro-rings less readily. However, these fundamental reactions of the nitrate group are complicated by conformational effects, and by side

<sup>4</sup> Honeyman and Morgan, *J.*, 1955, 3660.

<sup>5</sup> Shepherd, *J.*, 1953, 3635.

<sup>6</sup> Ohle and von Vargha, *Ber.*, 1929, **62**, 2425.

reactions and degradations which increase with the number of nitrate groups in the molecule and often predominate.

A mechanism was suggested earlier<sup>4</sup> for removal of nitrate groups by sodium iodide. This was confirmed when methyl 4 : 6-*O*-benzylidene-3-deoxy-3-iodo- $\alpha$ -D-glucoside was heated with sodium iodide in acetone for 4 days at 100°. Starting compound was recovered (75%), but when heating was for only 20 hr. the corresponding 3-nitrate was converted in 21% yield into methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside.<sup>4</sup> It follows that the latter reaction is unlikely to proceed through the 3-deoxy-3-iodo-derivative. Newth has reported<sup>7</sup> that methyl 4 : 6-*O*-benzylidene-3-deoxy-3-iodo- $\alpha$ -D-glucoside 2-toluene-*p*-sulphonate gives the corresponding 2 : 3-didehydro-2 : 3-dideoxy-derivative when heated with sodium iodide for only 10 min. This reaction does not occur when the 2-hydroxyl group is unsubstituted, even if the time of heating is increased 500-fold, thus exhibiting a similar effect to that observed by Foster and Overend<sup>8</sup> for 1 : 2-diols. This reagent attacked 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose 3-nitrate slowly, 59% of nitrate being removed in 48 hr. at 100°. The corresponding 3-toluene-*p*-sulphonate and methyl  $\beta$ -L-arabinoside 2 : 3 : 4-tritoluene-*p*-sulphonate were recovered unchanged when treated similarly, confirming the stability of sulphonyl groups attached to secondary carbon atoms in the sugar-ring towards this reagent. Boiling 1 : 2-3 : 4-di-*O*-isopropylidene-D-galactose 6-nitrate with sodium iodide in *isobutyl* methyl ketone for 2 days gave the 6-deoxy-6-iodo-derivative: the prolonged boiling required is another example of the stability of 6-esters of 1 : 2-3 : 4-di-*O*-isopropylidene-D-galactose.<sup>9</sup>

Reduction of a primary toluene-*p*-sulphonate group with lithium aluminium hydride results in a terminal methyl group,<sup>10,11</sup> but similar reduction of 1 : 2-3 : 4-di-*O*-isopropylidene-D-galactose 6-nitrate has now been found to give the parent alcohol as when a nitrate group is attached to a secondary carbon atom.<sup>12</sup> It should be noted that a secondary toluene-*p*-sulphonyloxy-group gives mainly the free hydroxyl group under such conditions (in contrast to a primary sulphonate), but sometimes a deoxy-sugar is obtained.<sup>13,14</sup>

Our study of reactions of sodium nitrite in aqueous ethanol<sup>4,15,16</sup> has been continued. When methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 3-nitrate was boiled with the reagent for 7 days, the products were unchanged compound (52%) and the glucoside (15%), showing the stability of the 3-nitrate group. Treatment of the 2 : 3-dinitrate for only 21 hr. had given<sup>4</sup> the 3-nitrate in 70% yield, so it was possible that in this case the 3-nitrate group was activating that on C<sub>(2)</sub>. Any ester group with a positively charged centre atom, as in the nitrate group, should have a similar activating effect on an adjacent nitrate group, and that this was true for the methanesulphonate group was shown when methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 2-methanesulphonate 3-nitrate was boiled with the reagent for 21 hr.: the 3-nitrate group was removed (42%), giving methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 2-methanesulphonate, together with starting compound (41%). That a 2-nitrate group is stable when not adjacent to another nitrate group was shown by boiling methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 2-nitrate with the reagent for 21 hr., for it was recovered substantially unchanged (51%). When 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose 3-nitrate was boiled with sodium nitrite in aqueous ethanol for 3 days, the nitrate group was removed slowly, to give 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose (31%) and starting compound (48%). The slow removal of the nitrate group by this reagent and by sodium iodide is probably due to the absence of a suitable activating group.

<sup>7</sup> Newth, *J.*, 1956, 471.

<sup>8</sup> Foster and Overend, *J.*, 1951, 2452.

<sup>9</sup> Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 185.

<sup>10</sup> Schmid and Karrer, *Helv. Chim. Acta*, 1949, **32**, 1371.

<sup>11</sup> Karrer and Boettcher, *Chem. Ber.*, 1953, **36**, 571.

<sup>12</sup> Ansell and Honeyman, *J.*, 1952, 2778.

<sup>13</sup> Allerton and Overend, *J.*, 1954, 3629.

<sup>14</sup> Vis and Karrer, *Helv. Chim. Acta*, 1954, **37**, 378.

<sup>15</sup> Ennor, Honeyman, and Stening, *Chem. and Ind.*, 1956, 1308.

<sup>16</sup> Honeyman and Stening, *J.*, 1957, 2278.

Sodium nitrite in aqueous ethanol reacts slowly with a 6-nitrate group, to give the parent alcohol, and in this respect the reaction is different from that with sodium iodide which gives the 6-deoxy-6-iodo-sugar. Methyl 2 : 3 : 4-tri-*O*-acetyl- $\alpha$ -D-glucoside 6-nitrate was recovered (62%) after being boiled with the reagent for 18 hr., and 3 : 5-*O*-benzylidene-1 : 2-*O*-isopropylidene-D-glucose 6-nitrate gave the parent alcohol (34%) and starting compound (52%). Similar treatment of 1 : 2-3 : 4-di-*O*-isopropylidene-D-galactose 6-nitrate for 7 days gave the alcohol (4%) and starting compound (78%), a further example of the stability of such galactose derivatives. The use of this reagent to prepare partially methylated sugars was demonstrated by the preparation of methyl 4-*O*-methyl- $\beta$ -D-glucoside. Methyl  $\beta$ -D-glucoside 2 : 3 : 4 : 6-tetranitrate was boiled with sodium nitrite in aqueous ethanol for 5.5 hr., and the resultant methyl  $\beta$ -D-glucoside 2 : 3 : 6-trinitrate was methylated; reduction of the nitrated methyl ether with zinc and iron dust in glacial acetic acid gave methyl 4-*O*-methyl- $\beta$ -D-glucoside; the overall yield from methyl  $\beta$ -D-glucoside is 24%, and the preparation involves 4 stages, whereas by previous methods<sup>17,18</sup> the compound is obtained in 7% and 12% yield in preparations involving 7 stages. These denitrations are not caused by the weak alkaline solution which results when sodium nitrite is dissolved in water, for high yields of products are obtained, and no inversion or anhydro-ring formation can be detected even after prolonged boiling. Nitrate groups are removed more slowly by sodium nitrite in anhydrous ethanol, owing to the lower solubility of sodium nitrite. Solvent action is negligible, for methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 2 : 3-dinitrate was recovered (75%) after being boiled in aqueous alcohol for 4 days. Sulphonates are stable to the reagent, further evidence that alkaline hydrolysis is not the cause of removal of the nitrate group. The 2 : 3-ditoluene-*p*-sulphonate and 2 : 3-dimethanesulphonate of methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside, methyl 3 : 4-*O*-isopropylidene- $\beta$ -L-arabinoside 2-toluene-*p*-sulphonate, methyl  $\beta$ -L-arabinoside 2 : 3 : 4-tritoluene-*p*-sulphonate, and 1 : 2-3 : 4-di-*O*-isopropylidene-D-galactose 6-toluene-*p*-sulphonate were all recovered in high yield after being boiled with aqueous ethanolic sodium nitrite for 2—5 days, showing the stability of such groups towards the reagent. Methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 2 : 3-diacetate was deacetylated (79%) after similar treatment for 7 days: the diacetate was recovered after being boiled alone in the solvent for a similar period. Hence the deacetylation by sodium nitrite is probably due to the alkaline solution.

Sodium nitrate in boiling aqueous ethanol did not react with methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 2 : 3-dinitrate, but similar treatment of this compound with sodium acetate for 7 days gave unchanged compound (42%) and 3-nitrate (27%). When treated similarly for 5 days, 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose 3-nitrate gave a small quantity of parent alcohol, but starting compound (87%) was recovered. When boiled with sodium carbonate in aqueous ethanol, nitrate groups were removed by alkaline hydrolysis with much decomposition.

#### EXPERIMENTAL

The petroleum used was light petroleum, b. p. 60—80°; chloroform solutions were dried over sodium sulphate before being evaporated under reduced pressure; chromatographic separations were carried out by passing dried solutions through activated alumina, Type H 100/200S mesh, supplied by Messrs. Peter Spence and Sons Ltd.

Where appropriate, identity was established by methods including determination of mixed m. p.s.

Unless otherwise stated  $[\alpha]_D$  are in chloroform.

*Preparation of Nitrates.*—(a) 1 : 2-5 : 6-Di-*O*-isopropylidene-D-glucose 3-nitrate. Acetic anhydride (5 ml.) containing fuming nitric acid (2 ml.) was added to 1 : 2-5 : 6-di-*O*-isopropylidene-D-glucose (4 g.) suspended in acetic anhydride (10 ml.) at 0°, and after 25 min. at room temperature the solution was poured into ice-water containing potassium carbonate. The

<sup>17</sup> McGilvray, *J.*, 1952, 3648.

<sup>18</sup> Hayward and Purves, *Canad. J. Chem.*, 1954, **32**, 19.

symp, washed repeatedly with ice-water, was extracted with chloroform, and the extract was chromatographed. Evaporation of the chloroform eluant gave 1:2-5:6-di-*O*-isopropylidene-*D*-glucose 3-nitrate, a syrup (3.26 g.),  $[\alpha]_D^{21} -40.4^\circ$  (*c* 5.5) (Found: C, 47.1; H, 6.3; N, 4.7.  $C_{12}H_{19}O_8N$  requires C, 47.2; H, 6.3; N, 4.6%).

(b) 1:2-5:6-Di-*O*-cyclohexylidene-*D*-glucose 3-nitrate. Similar treatment of 1:2-5:6-di-*O*-cyclohexylidene-*D*-glucose<sup>19</sup> (8 g.) yielded, when the reaction solution was poured into ice-water, a white solid which, recrystallised from methanol, was 1:2-5:6-di-*O*-cyclohexylidene-*D*-glucose 3-nitrate (6.52 g., 73%), m. p. 83—84°,  $[\alpha]_D^{20} -22.2^\circ$  (*c* 0.9) (Found: C, 56.4; H, 7.1; N, 3.5.  $C_{18}H_{27}O_8N$  requires C, 56.2; H, 7.1; N, 3.6%).

(c) 1:2-3:4-Di-*O*-isopropylidene-*D*-galactose 6-nitrate. Fuming nitric acid (3 ml.) in acetic anhydride (7 ml.) was added at 0° to a solution of 1:2-3:4-di-*O*-isopropylidene-*D*-galactose<sup>20</sup> (14 g.) in acetic anhydride (35 ml.). After 20 min. at room temperature, the mixture, when treated by the procedure described for 1:2-5:6-di-*O*-cyclohexylidene-*D*-glucose 3-nitrate, yielded a product which, recrystallised from aqueous ethanol, was 1:2-3:4-di-*O*-isopropylidene-*D*-galactose 6-nitrate (11.4 g., 69%), m. p. 61°,  $[\alpha]_D^{19.8} -59.8^\circ$  (*c* 2.0) (Found: C, 47.5; H, 6.1; N, 4.3.  $C_{12}H_{19}O_8N$  requires C, 47.2; H, 6.3; N, 4.6%).

(d) 3:5-*O*-Benzylidene-1:2-*O*-isopropylidene-*D*-glucose 6-nitrate. Fuming nitric acid (0.27 ml.) in acetic anhydride (2 ml.) was added to 3:5-*O*-benzylidene-1:2-*O*-isopropylidene-*D*-glucose<sup>21</sup> (1.27 g.) suspended in acetic anhydride (5 ml.) at 0°, and the mixture was left at room temperature for 10 min. The product, precipitated when the mixture was poured into ice-water, recrystallised from methanol as 3:5-*O*-benzylidene-1:2-*O*-isopropylidene-*D*-glucose 6-nitrate (0.95 g., 66%), m. p. 86°,  $[\alpha]_D^{22} +12.1^\circ$  (*c* 0.6) (Found: C, 54.7; H, 5.5.  $C_{18}H_{19}O_8N$  requires C, 54.4; H, 5.4%).

A solution of 3:5-*O*-benzylidene-6-deoxy-6-iodo-1:2-*O*-isopropylidene-*D*-glucose<sup>22</sup> (0.1 g.) and silver nitrate (0.06 g.) in methyl cyanide (5 ml.) was boiled under reflux for 8 hr. The cooled mixture was filtered and evaporated to a syrup which, recrystallised twice from methanol, gave the 6-nitrate (0.075 g., 85%), m. p. 85—86°.

(e) 2:3-5:6-Di-*O*-isopropylidene-*D*-mannose 1-nitrate. The solution obtained by adding fuming nitric acid (1.4 ml.) and acetic anhydride (3.5 ml.) to a suspension of 2:3-5:6-di-*O*-isopropylidene-*D*-mannose (2.61 g.) in acetic anhydride (7 ml.) at 0°, after 40 min. at room temperature, was poured into ice-water. The resulting solid recrystallised from ether (25 ml.), to yield 2:3-5:6-di-*O*-isopropylidene-*D*-mannose 1-nitrate (2.82 g., 90%), m. p. 83.5—84° (Found: C, 46.9; H, 6.3; N, 4.7.  $C_{12}H_{19}O_8N$  requires C, 47.2; H, 6.3; N, 4.6%). The product decomposed with the evolution of brown fumes after 15 days in an airtight bottle.

(f) Methyl 2:3:4-tri-*O*-acetyl- $\alpha$ -*D*-glucoside 6-nitrate. Methyl cyanide (100 ml.) containing methyl 2:3:4-tri-*O*-acetyl-6-deoxy-6-iodo- $\alpha$ -*D*-glucoside<sup>23</sup> (3.3 g.) and silver nitrate (1.9 g.) was boiled under reflux for 4 hr. The mixture was then cooled to 0°, filtered, and evaporated to dryness. The residue was extracted thrice with boiling chloroform, and the combined extracts were evaporated to a solid which, recrystallised from aqueous methanol, was methyl 2:3:4-tri-*O*-acetyl- $\alpha$ -*D*-glucoside 6-nitrate (2.0 g., 70%), m. p. 112.5—113.5°,  $[\alpha]_D^{19} +125.8^\circ$  (*c* 1.2).

(g) Methyl 4:6-*O*-benzylidene- $\alpha$ -*D*-glucoside 3-nitrate. Fuming nitric acid (0.97 ml., 0.022 mole) was added gradually to a solution of methyl 4:6-*O*-benzylidene- $\alpha$ -*D*-glucoside (5.65 g., 0.02 mole) in chloroform (30 ml.) and acetic anhydride (15 ml.) at 0°. After 1 hr. the mixture was neutralised with dilute aqueous potassium carbonate. The chloroform layer was washed twice with water before being evaporated. The resulting syrup was chromatographed in benzene solution. Elution with benzene, followed by evaporation of the solvent, gave an unidentified syrup (0.4 g.). The solid, obtained by elution with chloroform followed by evaporation, recrystallised from chloroform-light petroleum as methyl 4:6-*O*-benzylidene- $\alpha$ -*D*-glucoside 3-nitrate<sup>4</sup> (1.8 g., 28%),  $[\alpha]_D^{20} +112.9^\circ$  (*c* 1.1), m. p. 171—172°.

(h) Methyl 2-*O*-methyl- $\alpha$ -*D*-glucoside 3-nitrate. A suspension of Amberlite IR-120(H) (2.2 g.) was stirred in boiling 80% methanol (50 ml.) containing methyl 4:6-*O*-benzylidene-2-*O*-methyl- $\alpha$ -*D*-glucoside 3-nitrate (1.5 g.) for 4.5 hr. The resin was filtered off and washed with methanol;

<sup>19</sup> Gluzman and Klyushnik, *J. Gen. Chem. (U.S.S.R.)*, 1955, **25**, 2073.

<sup>20</sup> Raymond and Schroeder, *J. Amer. Chem. Soc.*, 1948, **70**, 2785.

<sup>21</sup> Brigl and Gruner, *Ber.*, 1932, **65**, 1428.

<sup>22</sup> Foster, Overend, Stacey, and Wiggins, *J.*, 1949, 2542.

<sup>23</sup> Compton, *J. Amer. Chem. Soc.*, 1938, **60**, 395.

evaporation of the combined washings and filtrate gave a colourless syrup which was chromatographed in benzene. Elution with benzene and with chloroform, followed by evaporation, yielded traces of unidentified syrup. The column was then washed with ethanol; removal of the solvent gave colourless syrup (0.7 g.) which crystallised to give *methyl 2-O-methyl- $\alpha$ -D-glucoside 3-nitrate*, m. p. 89—90° (Found: C, 38.2; H, 6.0.  $C_8H_{15}O_8N$  requires C, 38.0; H, 6.0%).

The product (0.3 g.), powdered anhydrous zinc chloride (0.3 g.), and benzaldehyde (2 ml.) were shaken at room temperature for 24 hr. When the mixture was poured into ice-water, two layers formed. The upper layer was decanted and the other extracted twice with chloroform. The combined extracts were dried, and excess of benzaldehyde and solvent were removed by distillation under reduced pressure. The resultant syrup, recrystallised twice from light petroleum, was *methyl 4 : 6-O-benzylidene-2-O-methyl- $\alpha$ -D-glucoside 3-nitrate* (0.31 g., 75%), m. p. 116°.

(i) 1 : 2-O-cyclohexylidene-D-glucose 3-nitrate. Amberlite IR-120(H) (14 g.) and 1 : 2.5 : 6-di-O-cyclohexylidene-D-glucose 3-nitrate (10 g.) were boiled for 4.5 hr. under reflux in stirred methanol (120 ml.) containing water (30 ml.). After being filtered, the solution was evaporated to a syrup, which was extracted with hot chloroform. Evaporation of the extract yielded a syrup which was shaken with petroleum, then crystallised from carbon tetrachloride and water successively, to give needles of 1 : 2-O-cyclohexylidene-D-glucose 3-nitrate (5.0 g., 63%), m. p. 95°,  $[\alpha]_D^{18} -1.0^\circ$  (*c* 1.0) (Found: C, 47.3; H, 6.3; N, 4.5.  $C_{12}H_{19}O_8N$  requires C, 47.2; H, 6.3; N, 4.6%).

Oxidation of the 3-nitrate with aqueous periodic acid, followed by steam-distillation of the solution, gave formaldehyde, identified as the dimedone derivative, m. p. 188°.

*cycloHexanone* (3 ml.) containing concentrated sulphuric acid (0.145 ml.) and 1 : 2-O-cyclohexylidene-D-glucose 3-nitrate (1.0 g.) was shaken for 5 hr. at room temperature. *n*-Heptane was added to the mixture, which was warmed until two layers were formed. The heptane layer was decanted, shaken with potassium carbonate solution, washed with water, dried ( $Na_2SO_4$ ), and evaporated. The syrup, crystallised from warm methanol, gave 1 : 2.5 : 6-di-O-cyclohexylidene-D-glucose 3-nitrate (0.86 g., 68%), m. p. 81—82°.

*Preparation of Methyl  $\beta$ -L-Arabinoside 2 : 3 : 4-Tritoluene-p-sulphonate*.—Solutions of methyl  $\beta$ -L-arabinoside (10 g.) in pyridine (30 ml.) and toluene-*p*-sulphonyl chloride (54 g.) in pyridine (100 ml.) were mixed at 0°, and the resulting solution was left at room temperature for 8 days. The product, isolated by being precipitated in ice-water and crystallised from ethanol, was *methyl  $\beta$ -L-arabinoside 2 : 3 : 4-tritoluene-p-sulphonate* (28 g., 74%), m. p. 113—114°,  $[\alpha]_D^{20} +95.6^\circ$  (*c* 0.7) (Found: C, 51.8; H, 4.9.  $C_{27}H_{30}O_{11}S_3$  requires C, 51.5; H, 4.8%).

*Reactions of Nitrates and Sulphonates with Sodium Methoxide in Methanol*.—(a) 1 : 2.5 : 6-Di-O-cyclohexylidene-D-glucose 3-nitrate. (i) The 3-nitrate (3.85 g., 0.01 mole) in methanolic sodium methoxide (50 ml.; sodium, 0.26 g., 0.011 mole) was boiled under reflux for 8 hr. The coloured mixture was evaporated and the residue extracted with water. The precipitate was ground, extracted again with water, collected, and dried in a desiccator. This solid (3.42 g.), m. p. 107—109°, recrystallised twice from *n*-heptane, was 1 : 2.5 : 6-di-O-cyclohexylidene-D-glucose (2.0 g., 59%),  $[\alpha]_D^{24} +1.85^\circ$  (*c* 1.7), m. p. 131.5—132.5°. Starting compound (0.74 g., 19%) was isolated from the mother-liquor.

(ii) A solution of the nitrate (7.697 g., 1 mole) in anhydrous methanol (100 ml.) containing sodium (0.7074 g., 1.5 mole) was boiled under reflux for 13 hr. The evaporated mixture, after extraction with chloroform, was dissolved in water. An aqueous extract of the chloroform solutions was combined with this solution and the volume was made up to 250 ml. Titration of aliquot parts against hydrochloric acid showed that 1.49 equivalents of sodium had been consumed during the reaction. 10% Aqueous potassium iodide (5 ml.) was added to each neutralised aliquot part, and carbon dioxide was bubbled through the whole. 2*N*-Hydrochloric acid (10 ml.) was introduced below the liquid surface; the liberated iodine, titrated with sodium thiosulphate, was equivalent to 34% of nitrite ion. When a portion of the original solution was first boiled with ammonium chloride (0.5 g.) for 10 min. to decompose nitrite, no iodine was liberated on addition of potassium iodide and hydrochloric acid, showing the absence of oxidising agents other than sodium nitrite.

The chloroform extracts of the original reaction mixture were evaporated to a syrup which, crystallised from light petroleum (b. p. 80—100°), was 1 : 2.5 : 6-di-O-cyclohexylidene-D-glucose (4.463 g., 69% of nitrate consumed), m. p. 132°. The concentrated mother-liquor crystallised from methanol, to give starting compound (0.365 g.).

(iii) A solution of the nitrate (3.863 g.) was treated with sodium (0.355 g.) in methanol (50 ml.) as in the preceding experiment. The dark brown mixture was filtered through sintered glass, and its volume was made up to 100 ml. with anhydrous methanol. This solution did not decolorise bromine in carbon tetrachloride or permanganate in aqueous acetone. A portion (50 ml.) of the solution was evaporated and the residue was extracted several times with water. The volume of the extract was made up to 100 ml. After it had been neutralised with 2*N*-sulphuric acid, mixed with ammonium sulphamate (0.4 g.) and 2*N*-sulphuric acid (6 ml.), and kept overnight, the solution was halved and raised nearly to the b. p. Then to each half was added nitron (0.5 g.) in 5% acetic acid (5 ml.). The solutions were cooled in ice-water for 2 hr., and the precipitates of nitron nitrate were collected, washed, and dried to constant weight (0.3902 g., 0.3893 g., equiv. to 42% of nitrate ion).

(b) 1 : 2-5 : 6-*Di-O-cyclohexylidene-D-glucose 3-toluene-p-sulphonate*. (i) Methanol (50 ml.) containing sodium (0.6 g.) and the 3-toluene-*p*-sulphonate (5.6 g.) was boiled under reflux for 23 hr. Acetic acid (0.3 ml.) was added, and methanol was evaporated. The solid residue was shaken with warm benzene; evaporation of the benzene extract yielded a white solid, which, recrystallised from *n*-heptane, was 1 : 2-5 : 6-*di-O-cyclohexylidene-D-glucose* (3.7 g., 94%).

(ii) When the quantity of sodium used was 0.02 g., unchanged starting compound (96%) was recovered.

(iii) When the toluene-*p*-sulphonate was treated as in (i) but at room temperature for 21 days, starting compound (91%) was recovered.

(c) 1 : 2-3 : 4-*Di-O-isopropylidene-D-galactose 6-toluene-p-sulphonate*. A solution of sodium (0.33 g.) and the 6-toluene-*p*-sulphonate (2.0 g.) in methanol (25 ml.) was boiled under reflux for 25 hr. Acetic acid (0.1 ml.) was added, and the evaporated mixture was extracted twice with chloroform. Evaporation of the combined extracts gave a colourless oil which did not decolorise bromine in carbon tetrachloride or potassium permanganate in aqueous acetone. The oil, chromatographed in benzene solution, yielded, on elution with benzene, starting compound (0.1 g., 5%) and, on elution with chloroform, 1 : 2-3 : 4-*di-O-isopropylidene-D-galactose* (1.12 g., 90%), identified by conversion into the corresponding 6-nitrate.

When a similar reaction was stopped after 2 hr. starting compound (84%) was recovered.

(d) 1 : 2-3 : 4-*Di-O-isopropylidene-D-galactose 6-nitrate*. A solution of this nitrate (3.06 g., 1 mol.) in methanol (50 ml.) containing sodium (0.69 g.) was boiled under reflux for 5 hr. Excess of sodium methoxide was neutralised with acetic acid, the solvent was evaporated, and the residue was extracted with chloroform. Evaporation of the extract gave a syrup which did not decolorise bromine or permanganate. Chromatography, as described in the preceding experiment, gave unchanged compound (1.15 g., 37%) and 1 : 2-3 : 4-*di-O-isopropylidene-D-galactose* (0.97 g., 37%), identified as its toluene-*p*-sulphonate.

The reaction mixture, boiled under reflux for 1 hr. only, yielded the same products (54 and 25% respectively).

*Reaction of Nitrates and Sulphonates with Sodium Iodide*.—In these experiments each reaction mixture was evaporated to dryness; the residue was extracted twice with chloroform, and the chloroform solution was washed successively with sodium thiosulphate solution and water. The chloroform was evaporated and the resulting product was crystallised.

(a) 1 : 2-5 : 6-*Di-O-cyclohexylidene-D-glucose 3-nitrate*. Acetone (20 ml.) containing sodium iodide (4.2 g.) and 1 : 2-5 : 6-*di-O-cyclohexylidene-D-glucose 3-nitrate* (3.5 g.) was heated in a sealed tube at 100° for 48 hr. The product, recrystallised from *n*-heptane, was 1 : 2-5 : 6-*di-O-cyclohexylidene-D-glucose* (1.83 g., 59%), m. p. 129—130°. Unchanged 3-nitrate (0.21 g., 6%) was isolated from the mother-liquor.

(b) 1 : 2-3 : 4-*Di-O-isopropylidene-D-galactose 6-nitrate*. *iso*Butyl methyl ketone (50 ml.) containing sodium iodide (1.8 g.) and 1 : 2-3 : 4-*di-O-isopropylidene-D-galactose 6-nitrate* (3.06 g.) was boiled under reflux for 47 hr. The syrup, crystallised from aqueous ethanol, was 6-deoxy-6-iodo-1 : 2-3 : 4-*di-O-isopropylidene-D-galactose* (2.04 g., 55%), m. p. 71°,  $[\alpha]_D^{21} -52.5^\circ$  (c 1.0).

A sealed tube containing the 6-nitrate (1.50 g.), sodium iodide (0.9 g.), and acetone (20 ml.) was heated at 100° for 47 hr. The product was 6-deoxy-6-iodo-1 : 2-3 : 4-*di-O-isopropylidene-galactose* (1.01 g., 55%), m. p. 71°.

(c) Treatment of methyl  $\beta$ -*L*-arabinoside 2 : 3 : 4-tritoluene-*p*-sulphonate and 1 : 2-5 : 6-*di-O-cyclohexylidene-D-glucose 3-toluene-p-sulphonate* with sodium iodide in acetone at 100° for 45 hr. gave unchanged compounds in yields of 73% and 78% respectively.

(d) When methyl 4 : 6-*O*-benzylidene-3-deoxy-3-iodo- $\alpha$ -D-glucoside<sup>24</sup> (0.2 g.) was heated with sodium iodide (0.4 g.) in anhydrous acetone (5 ml.) at 100° for 4 days in a sealed tube, very little discolouring occurred. Evaporation of the solvent followed by recrystallisation from methanol yielded unchanged starting compound (75%), m. p. 193°,  $[\alpha]_D^{20} -9.3^\circ$  (*c* 0.5).

*Reduction of 1 : 2-3 : 4-Di-O-isopropylidene-D-galactose 6-Nitrate with Lithium Aluminium Hydride.*—A solution of the 6-nitrate (3.06 g.) in anhydrous ether (30 ml.) was added dropwise during 1 hr. to a stirred suspension of lithium aluminium hydride (0.6 g.) in boiling anhydrous ether (40 ml.). After another 48 hours' boiling, water (40 ml.) was added cautiously to the mixture. The aqueous layer was separated and extracted with more ether (50 ml.). The combined ethereal solutions, washed with dilute sulphuric acid and with water, were dried ( $K_2CO_3$ - $Na_2SO_4$ ). Evaporation of the solvent yielded a syrup which was chromatographed in benzene. Elution with benzene, followed by crystallisation of the solid from aqueous ethanol, gave unchanged starting compound (0.24 g., 8%), m. p. 61°. Elution with chloroform yielded a colourless syrup (1.54 g.) which, distilled at 0.1 mm., was 1 : 2-3 : 4-di-*O*-isopropylidene-D-galactose (57%). This was identified as the 6-nitrate (1.43 g., 83%), m. p. 61°.

A similar reaction, stopped after 17 hr., gave unchanged compound (39%) and 1 : 2-3 : 4-di-*O*-isopropylidene-D-galactose (33%).

*Reaction of Nitrates, Sulphonates, and Acetates with Sodium Nitrite.*—(a) *Methyl 4 : 6-O-benzylidene- $\alpha$ -D-glucoside 3-nitrate.* A solution of the 3-nitrate (4.62 g.) and sodium nitrite (2.92 g.) in 80% ethanol (50 ml.) was boiled under reflux for 7 days. On cooling, the solution deposited crystals which were collected, dried, and recrystallised from alcohol, to give starting compound (52%), m. p. 168—169°. Evaporation of the reaction mother-liquor gave a syrup which crystallised from benzene, to yield methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside (0.53 g., 15%), m. p. 160°.

(b) *Methyl 4 : 6-O-benzylidene- $\alpha$ -D-glucoside 2 : 3-dinitrate.* The dinitrate (3 g.) and sodium nitrite (1.86 g.) were boiled under reflux (moisture excluded) in ethanol (50 ml.) for 21 hr. The evaporated mixture was dissolved in benzene, filtered, and chromatographed. Elution with benzene, followed by chloroform, yielded fractions which were recrystallised, to give starting compound (0.95 g., 32%), m. p. 122.5—123°, and methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 3-nitrate (0.89 g., 34%), m. p. 169—170°.

When methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 2 : 3-dinitrate (2 g.) was boiled under reflux in 80% ethanol alone for 4 days, starting compound (75%) only was recovered.

(c) *Methyl 4 : 6-O-benzylidene- $\alpha$ -D-glucoside 2-methanesulphonate 3-nitrate.* A solution of this ester (3.2 g.) and sodium nitrite (1.66 g.) in 80% ethanol (40 ml.) was boiled under reflux for 21 hr. The products, isolated by chromatography as in the preceding experiment, were starting compound (1.3 g., 41%), m. p. 129—130°, and methyl 4 : 6-*O*-benzylidene- $\alpha$ -D-glucoside 2-methanesulphonate (1.2 g., 42%), m. p. 132°.

(d) *Methyl 4 : 6-O-benzylidene-2-O-methyl- $\alpha$ -D-glucoside 3-nitrate.* This compound (2.5 g.) was boiled with sodium nitrite (1.54 g.) as described in the previous experiment. Starting compound (2.2 g., 88%) was recovered.

(e) *1 : 2-5 : 6-Di-O-cyclohexylidene-D-glucose 3-nitrate.* A solution of this nitrate (3.85 g.) and sodium nitrite (2.07 g.) in 80% ethanol (50 ml.) was boiled under reflux for 3 days. The evaporated mixture was extracted twice with chloroform. Evaporation of the combined extracts yielded a syrup which, dissolved in the minimum amount of hot methanol and refrigerated, gave starting compound (1.84 g., 48%), m. p. 82°. The concentrated mother-liquor was dissolved in warm *n*-heptane, and the white solid (1.04 g.) which was precipitated on cooling was 1 : 2-5 : 6-di-*O*-cyclohexylidene-D-glucose (31%), m. p. 129—130°.

(f) *Methyl 2 : 3 : 4-tri-O-acetyl- $\alpha$ -D-glucoside 6-nitrate.* A solution of this nitrate (1 g.) and sodium nitrite (0.29 g.) in 80% ethanol (38 ml.) was boiled under reflux for 2 hr. When cooled, the solution yielded unchanged starting compound (0.83 g., 83%), m. p. 113.5—114.5°. This was redissolved in the mother-liquor, which was then boiled for 16 hr. When the solution was cooled starting compound (0.4 g.) separated. The mother-liquor was then evaporated to dryness and extracted twice with chloroform. Evaporation of the extracts yielded a white solid (0.35 g.) which, after recrystallisation from methanol, was starting compound (0.22 g., total yield 62%), m. p. 113—114°.

(g) *3 : 5-O-Benzylidene-1 : 2-O-isopropylidene-D-glucose 6-nitrate.* Sodium nitrite (0.29 g.) and 3 : 5-*O*-benzylidene-1 : 2-*O*-isopropylidene-D-glucose 6-nitrate (0.5 g.) were boiled under

<sup>24</sup> Newth, Richards, and Wiggins, *J.*, 1950, 2356.



reflux in 80% ethanol for 14 hr. The crystals which separated on cooling were collected, dried, and shown to be starting compound (0.26 g., 52%), m. p. 85°. The mother-liquor was evaporated to a syrup which was dissolved in warm benzene (2 ml.). Petroleum (2 ml.) was added, and after cooling, the white solid which was precipitated was collected, dried, and shown to be 3 : 5-*O*-benzylidene-1 : 2-*O*-isopropylidene-*D*-glucose (0.15 g., 34%), m. p. 142°.

(h) 1 : 2-3 : 4-*Di-O*-isopropylidene-*D*-galactose 6-nitrate. Sodium nitrite (3.39 g.) and 1 : 2-3 : 4-*di-O*-isopropylidene-*D*-galactose 6-nitrate (5.0 g.) were boiled under reflux in 80% ethanol (50 ml.) for 7 days. The mixture was evaporated, and the residue extracted with chloroform. Evaporation of the chloroform extract yielded a syrup, which was chromatographed in benzene (20 ml.). Elution with benzene yielded a solid which, recrystallised from aqueous ethanol, was starting compound (3.9 g., 78%), m. p. 61°. Elution with chloroform (500 ml.) yielded a clear syrup (0.17 g., 4%), shown to be 1 : 2-3 : 4-*di-O*-isopropylidene-*D*-galactose by conversion into its 6-nitrate in high yield.

(i) *Methyl* 4 : 6-*O*-benzylidene- $\alpha$ -*D*-glucoside 2 : 3-diacetate. ( $\alpha$ ) This compound (1.43 g.) and sodium nitrite (0.8 g.) were boiled under reflux in 80% ethanol (25 ml.) for 21 hr. On cooling of the alkaline mixture, starting compound (0.86 g., 60%), m. p. 106°, crystallised. Concentration of the mother-liquor left a residue which was extracted with chloroform. Evaporation of the chloroform yielded a white solid which, recrystallised from water, was methyl 4 : 6-*O*-benzylidene- $\alpha$ -*D*-glucoside (0.14 g., 5%), m. p. 159°.

( $\beta$ ) The above experiment was repeated, but boiling was continued for 7 days. The alkaline reaction mixture, which smelled of benzaldehyde, was evaporated, and the residue was extracted with chloroform. Concentration of the solution yielded a solid which, recrystallised from hot water, gave methyl 4 : 6-*O*-benzylidene- $\alpha$ -*D*-glucoside (4.35 g., 79%), m. p. 162—162.5°.

( $\gamma$ ) When the diacetate (2.33 g.) was boiled in solvent (50 ml.) alone for 6 days, starting compound (1.45 g., 62%) only was obtained.

(j) *Toluene-p*-sulphonates and *methanesulphonates*. *Methyl* 4 : 6-*O*-benzylidene- $\alpha$ -*D*-glucoside 2 : 3-dimethanesulphonate (4.62 g.) was boiled under reflux in ethanol (80 ml.) containing chloroform (35 ml.), water (10 ml.), and sodium nitrite (2 g.) for 21 hr. Starting compound (4.4 g., 95%), m. p. 185°, was recovered.

The corresponding 2 : 3-ditoluene-*p*-sulphonate (5.9 g.) was boiled for 5 days with the mixture described in the previous experiment. Unchanged starting compound (5.2 g., 88%), m. p. 146°,  $[\alpha]_D^{17} + 12.2^\circ$  (*c* 1.6), was recovered.

A solution of 1 : 2-3 : 4-*di-O*-isopropylidene-*D*-galactose 6-toluene-*p*-sulphonate (1.0 g.) and sodium nitrite (0.86 g.) in 80% ethanol (10 ml.) was boiled under reflux for 48 hr. Starting compound (91%) was recovered.

*Action of Sodium Acetate and of Sodium Nitrate in 80% Ethanol on Methyl* 4 : 6-*O*-Benzylidene- $\alpha$ -*D*-glucoside 2 : 3-Dinitrate.—The dinitrate (6.0 g.) in 80% ethanol (120 ml.) containing sodium acetate (6.6 g.) was boiled under reflux for 7 days. Evaporation of the solvent yielded a white solid which was shaken with chloroform (100 ml.) and water (100 ml.). The aqueous layer was extracted with chloroform, the combined chloroform extracts were evaporated, and the residue was chromatographed in benzene. Elution with benzene (400 ml.) and chloroform (400 ml.) in turn yielded starting compound (2.5 g., 42%), m. p. 122°, and methyl 4 : 6-*O*-benzylidene- $\alpha$ -*D*-glucoside 3-nitrate (1.4 g., 37%), m. p. 171—172°.

In a similar experiment, the dinitrate (3.72 g.) and sodium nitrate (2.55 g.) in 80% ethanol (60 ml.) were boiled under reflux for 20 hr. Water (20 ml.) was added, and, on cooling, starting compound (3.60 g., 97%), m. p. 122—123°, was obtained.

*Action of Sodium Acetate in 80% Ethanol on 1 : 2-5 : 6-Di-O-cyclohexylidene-D-glucose 3-Nitrate*.—Sodium acetate (4.08 g.) and 1 : 2-5 : 6-*di-O*-cyclohexylidene-*D*-glucose 3-nitrate (3.85 g.) were boiled in 80% ethanol (48 ml.) for 5 days. The residue obtained by evaporating the solution was shaken with chloroform (50 ml.) and water (50 ml.), and the aqueous layer was shaken with further chloroform (50 ml.). The combined chloroform extracts were evaporated, and the residue was dissolved in hot methanol. On cooling, starting compound (3.33 g., 87%), m. p. 82.5—83°, separated. The mother-liquor was evaporated, and the residue was dissolved in a small quantity of warm *n*-heptane. This solution, on cooling, yielded 1 : 2-5 : 6-*di-O*-cyclohexylidene-*D*-glucose (0.1 g., 3%), m. p. 131°.

*Preparation of Methyl* 4-*O*-Methyl- $\beta$ -*D*-glucoside.—A solution of methyl  $\beta$ -*D*-glucoside 2 : 3 : 4 : 6-tetranitrate<sup>1</sup> (3.74 g., 0.01 mole) and sodium nitrite (3.45 g., 0.05 mole) in 80% ethanol (20 ml.) was boiled under reflux for 5.5 hr. The evaporated mixture was dried in a

vacuum-desiccator, then extracted twice with boiling chloroform. Evaporation of the combined extracts gave a syrup which was chromatographed in benzene. Elution with benzene yielded a trace of syrup, which was discarded. Further elution with chloroform gave a colourless syrup (1.6 g., 49%) which was substantially methyl  $\beta$ -D-glucoside 2 : 3 : 6-trinitrate,  $[\alpha]_D^{15} -10.8^\circ$  (*c* 1.1). Finally, washing the column with ethanol gave unidentified syrup (0.38 g.).

Silver oxide (6 g.) was added in portions (0.5 g.) during 5 hr. to a boiling solution of the trinitrate (1.24 g.) in methyl iodide (25 ml.). After a further 19 hours' boiling the solution was filtered and evaporated to a syrup which was chromatographed in benzene. Evaporation of the benzene eluent left a syrup (0.3 g.) of which was dissolved in glacial acetic acid (2 ml.). Zinc dust and iron filings were added gradually to the solution, and the mixture was warmed gently until no more gas was evolved. Water (20 ml.) was added and the acid was neutralised with sodium carbonate. The solution was filtered and evaporated and the residue was dried in a desiccator. This solid was extracted thrice with boiling ethyl acetate (20 ml.), and the combined extracts were evaporated to 2 ml. On cooling, crystals of methyl 4-O-methyl- $\beta$ -D-glucoside (0.12 g., 60%) were formed, which after recrystallisation twice from ethyl acetate, had m. p. 101—102°. Hayward and Purves<sup>18</sup> record m. p. 101°.

*Methyl  $\beta$ -D-Glucoside 4-Acetate 2 : 3 : 6-Trinitrate.*—Ice-cold acetic anhydride (2 ml.) was added to a solution of methyl  $\beta$ -D-glucoside 2 : 3 : 6-trinitrate (0.4 g.) in pyridine (2 ml.), and the solution was left at room temperature for 6 days. The solid product, which separated when the solution was poured into ice-water, after recrystallisation from ethanol-light petroleum, was *methyl  $\beta$ -D-glucoside 4-acetate 2 : 3 : 6-trinitrate*, m. p. 91° (Found: C, 29.8; H, 3.6.  $C_9H_{13}O_{13}N_3$  requires C, 29.4; H, 3.5%).

The authors are indebted to Courtaulds Scientific and Educational Trust Fund for a Postgraduate Research Scholarship (to T. C. S.).

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[Received, August 9th, 1957.]