525. *Sugar Nitrates. Part I. Removal of Nitrate and Toluene-p-sulphonyl Groups from Esters of Substituted Methyl-D-glucosides.*

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The major products obtained by the alkaline hydrolysis of 2 : 3-dinitrates and 3-nitrates of 4 : 6-acetals of α-methyl-D-glucosides are found to be the glucose derivatives, although small amounts of the acetals of methyl-2 : 3-anhydro-α-D-alloside have also been isolated. This is in contrast to the corresponding toluene-*p*-sulphonates which give the 2 : 3-anhydro-alloside, usually as the sole product. In the case of a 3-nitrate 2-toluene-*p*-sulphonate, however, the anhydro-alloside is obtained in high yield. 4 : 6-Ethylidene β-methyl-D-glucoside 2 : 3-dinitrate is more difficult to hydrolyse than is its anomer : the only product obtained is the 3-nitrate. This in turn is extremely stable, but when it is hydrolysed 4 : 6-ethylidene 2 : 3-anhydro-β-methyl-D-alloside only is detected. The reductive fission of such nitrates by lithium aluminium hydride gives the 4 : 6-acetal of the glucoside. The nitrates are converted into the corresponding acetates by heating them with sodium iodide in acetic anhydride.

The main purpose of this investigation was to compare the course of alkaline hydrolysis of sugar nitrates with that of sulphonates. Since complications arise when 4 : 6-benzylidene α-methyl-D-glucoside is nitrated (Oldham, *J. Soc. Chem. Ind.*, 1934, **53**, 236T) the preparation of derivatives of α- and β-methyl-D-glucosides substituted at positions 4 and 6 by aliphatic groups was studied. The direct reaction of α-methyl-D-glucoside with paraldehyde in the presence of sulphuric acid or with acetaldehyde and zinc chloride leads to the production of 4 : 6-ethylidene 2 : 3-oxydiethylidene α-methyl-D-glucoside,* which is recovered unchanged after treatment with dinitrogen pentoxide in chloroform. It is of interest that although in the formation of this compound three new asymmetric carbon atoms are introduced only one isomer has been obtained and that is the one previously prepared by Appel and Haworth (*J.*, 1938, 793). Attempts to obtain 4 : 6-ethylidene α-methyl-D-glucoside by partial hydrolysis of the " oxy "-compound indicated that the yields were too low for preparative purposes, and so indirect methods starting from 4 : 6-benzylidene α-methyl-D-glucoside were investigated. The liquid product obtained by the hydrolysis of 4 : 6-benzylidene α-methyl-D-glucoside 2 : 3-diacetate was condensed with

* The name 2 : 3-oxidodiethylidene was used by Appel and Haworth (*loc. cit.*) for the radical –CHMe·O·CHMe–.

paraldehyde but no solid product was obtained even after deacetylation. This was possibly due to acetyl migration, resulting in a mixture of α-methyl-D-glucoside diacetates. A similar sequence from the 2 : 3-dibenzoate gave crystalline 4 : 6-ethylidene α-methyl-D-glucoside identical with Appel and Haworth's compound (*loc. cit.*). In contrast to the behaviour of β-methyl-L-arabinoside (Oldham and Honeyman, *J.*, 1946, 986), only one of the two possible 4 : 6-ethylidene α-methyl-D-glucosides has so far been isolated. The same selectivity was evident in the preparation of 4 : 6-ethylidene α-methyl-D-glucoside 2 : 3-ditoluene-*p*-sulphonate directly from 4 : 6-ethylidene α-methyl-D-glucoside or indirectly from the 4 : 6-benzylidene compound. The most practical method for preparation of 4 : 6-ethylidene α-methyl-D-glucoside was an adaptation of that described by Mellies, Mehltretter, and Rist (*J. Amer. Chem. Soc.*, 1951, **73**, 294) for other acetals. On treatment of α-methyl-D-glucoside with paraldehyde and concentrated hydrochloric acid for a short period the desired compound became the major product and was readily separated from the "oxy"-compound and unchanged α-methyl-D-glucoside. In order to study the effect of the substituent at positions 4 and 6 on the stability of ester groups at positions 2 and 3, 4 : 6-propylidene α-methyl-D-glucoside was prepared by a method similar to that used for the ethylidene compound. Dewar and Fort's method (*J.*, 1944, 492) was used for preparing 4 : 6-ethylidene β-methyl-D-glucoside, shown to be a single individual by quantitative conversion into the crystalline diacetate and then quantitative deacetylation to the original compound. Although the reactions have been less fully investigated it has been established that β-methyl-D-glucoside readily forms crystalline 2 : 3-oxydipropylidene 4 : 6-propylidene β-methyl-D-glucoside with propaldehyde and the corresponding oxydi-*n*-butylidene compound with *n*-butaldehyde. The structures of these two products have been assumed by analogy; again, only one of the possible isomers has been isolated.

Many sugar nitrates have been prepared by Oldham's method (*J.*, 1925, **127**, 2840) which uses fuming nitric acid in chloroform but has the disadvantage that it removes acid-labile groups. Thus, Dewar, Fort, and McArthur (*J.*, 1944, 499) found that 4 : 6-ethylidene β-methyl-D-glucoside is converted by this method into β-methyl-D-glucoside 2 : 3 : 4 : 6-tetranitrate. Gladding and Purves (*J. Amer. Chem. Soc.*, 1944, **66**, 153) found fuming nitric acid containing phosphoric oxide to be convenient. The method used in the present work is Oldham's modified one (see, *e.g.*, Bell and Synge, *J.*, 1937, 1711; 1938, 833), using dinitrogen pentoxide in chloroform. The reactions are extremely rapid, usually occupying five minutes at 0°, and the products, isolated in high yield, are easily purified, well-defined crystalline substances. The reaction has been found useful as a rapid and simple way of detecting unsubstituted alcoholic hydroxyl groups.

Reductive methods have generally been used for removing nitrate groups, *e.g.*, iron dust in acetic acid (Oldham, *loc. cit.*, 1925), a mixture of zinc and iron dusts in acetic acid (Dewar and Fort, *J.*, 1944, 492, 497), and catalytic hydrogenation (Kuhn, *J. Amer. Chem. Soc.*, 1946, **68**, 1761). Zinc in acetic anhydride converts the nitrate into the corresponding acetate (Hoffman, Bower, and Wolfrom, *ibid.*, 1947, **69**, 249). In none of these methods is any complication such as anhydro-ring formation or inversion of configuration likely, nor, indeed, has any been detected. In one notable case Dewar and Fort (*loc. cit.*) obtained 2 : 4-dimethyl β-methyl-D-glucoside from its 3 : 6-dinitrate. During the present investigation removal of nitrate groups by lithium aluminium hydride in boiling ether has been found to proceed normally but slowly, so that even after two days unchanged nitrate was recovered. By this method 4 : 6-propylidene α-methyl-D-glucoside 2 : 3-dinitrate has been converted into 4 : 6-propylidene α-methyl-D-glucoside together with some of its 3-nitrate; a similar result was obtained with 4 : 6-ethylidene β-methyl-D-glucoside 2 : 3-dinitrate. Thus, reductive fission with lithium aluminium hydride resembles that of other reagents in that reaction proceeds at (*a*) and not at (*b*).

These processes are termed nitryl–oxy-fission and alkyl–oxy-fission, respectively, by analogy with the expressions commonly used for hydrolysis of simple carboxylic esters. It is of interest that Schmid and Karrer (*Helv. Chim. Acta*, 1949, **32**, 1371) have found that toluene-*p*-sulphonyloxy-groups attached to a primary carbon atom may be removed by reduction with lithium aluminium hydride either by sulphonyl–oxy-fission, as when 1-tosyl "β"-di*iso*propylidene D-fructose is reduced to "β"-di*iso*propylidene D-fructose, or by alkyl–oxy-fission, as in the conversion of di*iso*propylidene 6-tosyl D-galactose into di*iso*-propylidene D-fucose.

Sodium iodide in acetone has also proved of value for removal of nitrate groups, and is of particular interest because of its selectivity. The nitrate group attached to $C_{(6)}$ of aldohexosides is replaced by an iodine atom. Nitrate groups on secondary carbon atoms are, in some cases, replaced by hydroxyl groups, presumably *via* an unstable iodo-compound which is hydrolysed during purifications involving aqueous solutions. In this way Dewar and Fort (*loc. cit.*, p. 492) converted 4 : 6-ethylidene β-methyl-D-glucoside 2 : 3-dinitrate into the 3-nitrate, and 2 : 3-dimethyl β-methyl-D-glucoside 4 : 6-dinitrate into 2 : 3-dimethyl 6-deoxy-6-iodo-β-methyl-D-glucoside. This reaction converted β-methyl-D-glucoside 2 : 3 : 4 : 6-tetranitrate chiefly into 6-deoxy-6-iodo-β-methyl-D-glucoside 2-nitrate, with the 3-nitrate as a by-product (Dewar, Fort, and McArthur, *loc. cit.*). The method has now been found to be useful for converting 4 : 6-propylidene α-methyl-D-glucoside 2 : 3-dinitrate in high yield into the 3-nitrate, whose structure has been proved by methylation and hydrolysis to 2-methyl α-methyl-D-glucoside (Haworth, Hirst, and Teece, *J.*, 1931, 2858).

The action of sodium iodide in acetic anhydride on toluene-*p*-sulphonates has been found by Hann, Wolfe, and Hudson (*J. Amer. Chem. Soc.*, 1944, **66**, 1898) to be the same as when acetone is used. Barker and Goodrich (*J.*, 1949, S 233) extended the use of sodium iodide in acetic anhydride to cases where the tosyloxy-group is on a primary carbon atom attached to a secondary carbon atom with a free hydroxyl group, thus avoiding production of an unsaturated compound. This reagent has been found to react with 4 : 6-ethylidene β-methyl-D-glucoside 2 : 3-dinitrate to give, after three hours at 100°, 4 : 6-ethylidene β-methyl-D-glucoside 2-acetate 3-nitrate or, after three hours' boiling, the 2 : 3-diacetate.

A good illustration of the resistance of nitrates to alkali is the ready conversion of β-methyl-D-glucoside 2 : 4-diacetate 3 : 6-dinitrate into β-methyl-D-glucoside 3 : 6-dinitrate (Dewar and Fort, *loc. cit.*, p. 492). The alkaline hydrolysis, even of simple alkyl nitrates, has not been thoroughly investigated. Nef (*Annalen*, 1899, **309**, 126) has shown that their reaction with alcoholic potassium hydroxide is in many ways analogous to that of the corresponding sulphates and halides. With nitrates, however, the reaction leading to unsaturated compounds is of minor importance, but a slow oxidation–reduction process appears which may become dominant, as when benzyl nitrate is converted quantitively into benzaldehyde and potassium nitrite. Some direct hydrolysis to alcohol also occurs, but usually to a small extent only, although this increases with the stability of the nitrate. With methyl and ethyl nitrates the chief product with alcoholic alkali is an ether, together with decomposition products arising from carbonyl by-products. The hydrolysis of glycerol trinitrate has been studied by Nef (*loc. cit.*) and by Klason and Carlson (*Ber.*, 1906, **39**, 2752), but it is uncertain whether glycerol is formed. The resistance of cellulose nitrate to alkali has been demonstrated by Kenyon and Gray (*J. Amer. Chem. Soc.*, 1946, **58**, 1422), who showed that a large proportion of nitrite is produced. When attached to $C_{(1)}$ of an aldose the methanesulphonyloxy- and the nitrate group react in the same way as a halogen atom (Helferich and Gnüchtel, *Ber.*, 1938, **71**, 712; Koenigs and Knorr, *Ber.*, 1901, **34**, 957). Reaction of nitrate on $C_{(1)}$ has been shown by Gladding and Purves (*J. Amer. Chem. Soc.*, 1944, **66**, 76) to be as rapid as that of acetoxyl groups, and, to complete the analogy of nitrate with halogens, the product obtained is 1 : 6-anhydro-β-D-glucopyranose.

A nitrate group on $C_{(6)}$ of glucose is also similar in reaction to sulphonate or halogen (Fischer and Zach, *Ber.*, 1912, **45**, 456; Haworth, Owen, and Smith, *J.*, 1941, 88; Gladding and Purves, *loc. cit.*, p. 76). The alkaline hydrolysis of sugar sulphonates has been thoroughly investigated and the principles and mechanism were reviewed by Peat (*Ann. Reports*, 1939, **36**, 258; *Adv. Carbohydrate Chem.*, 1946, **2**, 37) and by Isbell (*Ann. Rev. Biochem.*, 1940, **9**, 65). The product obtained in this way by Haworth, Hirst, and Panizzon

(*J.*, 1934, 154) from 2-tosyl β-methyl-D-glucoside is 2 : 3-anhydro-β-methyl-D-mannoside, *i.e.*, hydrolysis at position 2 has resulted in alkyl–oxy-fission. Hydrolysis of 4 : 6-benzylidene α-methyl-D-glucoside 2 : 3-ditoluene-*p*-sulphonate gives a practically quantitative yield of 4 : 6-benzylidene 2 : 3-anhydro-α-methyl-D-alloside (Robertson and Griffith, *J.*, 1935, 1193; Robertson and Whitehead, *J.*, 1940, 319; Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1727). Here, the tosyl group is removed from position 2 (sulphonyl–oxy-fission), whereas on position 3 the tosyloxy-group is removed (alkyl–oxy-fission). The same is true of 4 : 6-benzylidene α-methyl-D-altroside 2 : 3-ditoluene-*p*-sulphonate which, as shown by Robertson and Whitehead (*loc. cit.*), is hydrolysed quantitatively to 4 : 6-benzylidene 2 : 3-anhydro-α-methyl-D-mannoside. Further evidence for this difference in the mode of removal of the two tosyl groups in 2 : 3-ditoluene-*p*-sulphonates arises from the present work. Alkaline hydrolyses of the 2 : 3-ditoluene-*p*-sulphonates of 4 : 6-ethylidene and 4 : 6-propylidene α-methyl-D-glucoside proceed readily to give, in each case, a high yield of a single crystalline methyl-2 : 3-anhydro-D-hexoside derivative : that from the ethylidene compound is 4 : 6-ethylidene 2 : 3-anhydro-α-methyl-D-alloside; that from the propylidene compound is also considered to be an alloside because of its formation, described below, from 4 : 6-propylidene α-methyl-D-glucoside 3-nitrate. Alkaline hydrolysis of 4 : 6-ethylidene β-methyl-D-glucoside 2 : 3-ditoluene-*p*-sulphonate was more difficult and less straightforward. Some unchanged ester was recovered, together with an unidentified by-product, but the chief product (40%) was a 4 : 6-ethylidene 2 : 3-anhydro-β-methyl-D-hexoside, which was identical with that obtained, as described below, from 4 : 6-ethylidene β-methyl-D-glucoside 3-nitrate, and is considered, therefore, to be the alloside.

Only one example has previously been investigated of the alkaline hydrolysis of a sugar nitrate in which the nitrate group is *trans* to an adjacent free hydroxyl group. Gladding and Purves (*loc. cit.*, p. 76) treated β-methyl-D-glucoside 3 : 4 : 6-triacetate 2-nitrate in this way and obtained in good yield a syrup with the elementary analysis, free hydroxyl group content, and behaviour towards periodate of a methylanhydrohexoside. This syrup deposited crude crystals of the same analysis, but neither the syrup nor the solid was completely characterised. However, it was concluded that the analogy between nitrates and sulphonates applied in such cases. In the examples studied during this work, this has not been found. The substances hydrolysed and the products obtained, with approximate yields, are set out in the Table.

Substance	Reagent and conditions	Products
4 : 6-Ethylidene α-methylglucoside 2 : 3-dinitrate	0·5% of Na in boiling MeOH, 1 day	4 : 6-Ethylidene α-methylglucoside (55%), its 3-nitrate (44%)
4 : 6-Propylidene α-methylglucoside 2 : 3-dinitrate	,, ,,	4 : 6-Propylidene α-methylglucoside (32%); 4 : 6-propylidene 2 : 3-anhydro-α-methylalloside (13%)
4 : 6-Propylidene α-methylglucoside 3-nitrate	0·6% of Na in boiling MeOH, 40 hrs.	4 : 6-Propylidene α-methylglucoside (52%); 4 : 6-propylidene 2 : 3-anhydro-α-methylalloside (19%)
4 : 6-Propylidene 2-tosyl α-methylglucoside 3-nitrate	0·5% of Na in boiling MeOH, 1 day	4 : 6-Propylidene 2 : 3-anhydro-α-methylalloside (78%); 4 : 6-propylidene α-methylglucoside (18%)
4 : 6-Ethylidene β-methylglucoside 2 : 3-dinitrate	0·3% of Na in MeOH, 28 days room temp.	Unchanged
	0·15% of Na in boiling MeOH, 1 day	Unchanged (40%); 4 : 6-ethylidene β-methylglucoside 3-nitrate (40%)
	0·8% of KOH in boiling aq. ethanol, 1 day	4 : 6-Ethylidene β-methylglucoside 3-nitrate (77%); unchanged (16%)
4 : 6-Ethylidene β-methylglucoside 3-nitrate	,, ,,	Unchanged (80%); 4 : 6-ethylidene 2 : 3-anhydro-β-methylalloside (7%)

Although the evidence obtained does not suffice to explain the course of hydrolysis of sugar nitrates, certain features are apparent. In all cases, hydrolysis of a 2 : 3-dinitrate or a 3-nitrate of the 4 : 6-acetals of α-methyl-D-glucoside gives chiefly the glucoside, with minor amounts in some cases of a 2 : 3-anhydro-α-methyl-D-alloside. It is not possible for the glucoside to be a secondary product resulting from the production and subsequent opening of an ethylene oxide ring, because sodium methoxide was used and a methyl group

would necessarily have been introduced at position 2 or 3. Thus, the only mode detected for the removal of the nitrate group from $C_{(2)}$ is by nitryl–oxy-fission, which is also the chief course in the removal from $C_{(3)}$. The small quantities of anhydrohexoside derivatives resulted from hydrolysis of 3-nitrates and it is assumed that they are anhydro-D-allosides formed by alkyl–oxy-fission of a small proportion. The case of 2-tosyl 4 : 6-propylidene α-methyl-D-glucoside 3-nitrate is noteworthy, for here the chief product is the 2 : 3-anhydro-α-methyl-D-alloside. The tosyloxy-group on $C_{(2)}$ is apparently hydrolysed quantitatively by sulphonyl–oxy-fission, just as for the 2 : 3-ditoluene-*p*-sulphonates already mentioned. The effect of the tosyl group on $C_{(2)}$ has been to reverse the reaction of the nitrate on $C_{(3)}$: alkyl–oxy-fission predominates, although some rupture of the nitryl–oxy-bond occurs.

4 : 6-Ethylidene β-methyl-D-glucoside 2 : 3-dinitrate is more stable to alkali, and the only product detected is the 3-nitrate, *i.e.*, the nitryl–oxy-bond is broken when the nitrate on $C_{(2)}$ is removed. The 3-nitrate is also extremely stable. The small amount of hydrolysis which took place led to 4 : 6-ethylidene 2 : 3-anhydro-β-methyl-D-alloside, *i.e.*, the nitrate group on $C_{(3)}$ is removed only by alkyl–oxy-fission.

The mode of hydrolysis of these 2 : 3-dinitrates apparently is intermediate between those of sulphonates and carboxylates. In a preliminary account of this work (Ansell, Honeyman, and Williams, *Chem. and Ind.*, 1952, 149) a possible explanation for this was suggested. That interpretation, however, is tentative only, and further work is in progress to clarify, among other influences, the effect on the course of alkaline hydrolysis of groups at positions 1, 4, and 6.

Experimental

Unless otherwise stated, the light petroleum used had b. p. 60—80°; solutions in ether, chloroform, or benzene were dried over sodium sulphate, and solvents were evaporated at reduced pressure.

Dinitrogen Pentoxide.—The method used was a simplified version of that of Gold, Hughes, Ingold, and Williams (*J.*, 1950, 2452). The product is less pure than that of these workers, but the presence of dinitrogen tetroxide does not interfere with the preparation of sugar nitrates. The dinitrogen pentoxide was dissolved in dried, redistilled chloroform, and sodium fluoride (2% w/w) was added to remove nitric acid (cf. Caesar and Goldfrank, *J. Amer. Chem. Soc.*, 1946, **68**, 372).

4 : 6-*Ethylidene* 2 : 3-*Oxydiethylene* α-*Methyl*-D-*glucoside.*—Appel and Haworth's method (*J.*, 1938, 793) gave a product of m. p. 182—183°, $[\alpha]_D^{18}$ +82·0° (*c*, 0·22 in chloroform). Appel and Haworth record m. p. 183—183·5°, $[\alpha]_D^{20}$ +83·5° (in chloroform).

Dewar and Fort's method (*loc. cit.*, p. 492) for preparing 4 : 6-ethylidene β-methyl-D-glucoside yielded 4 : 6-ethylidene 2 : 3-oxydiethylidene α-methyl-D-glucoside (3·5 g., 49%), m. p. and mixed m. p. 183°, $[\alpha]_D^{20}$ +83° (*c*, 0·2 in chloroform).

Acetaldehyde (50 ml.), α-methyl-D-glucoside (5 g.), and anhydrous zinc chloride (5 g.) were shaken for 24 hours at room temperature and then poured into ice-water. The white crystalline precipitate of 4 : 6-ethylidene 2 : 3-oxydiethylidene α-methyl-D-glucoside (3·5 g., 50%) had m. p. 183° (from alcohol).

Attempted Nitration of 4 : 6-*Ethylidene* 2 : 3-*Oxydiethylidene* α-*Methyl*-D-*glucoside.*—The compound (2 g.) was dissolved in dry chloroform (25 ml.) and dinitrogen pentoxide (2·9 g.) in dry chloroform (18 ml.) was added. After 5 minutes at 0° the solution was poured into ice-water containing a small amount of sodium hydrogen carbonate. The chloroform layer was separated, washed, dried, and evaporated, giving, after recrystallisation, 4 : 6-ethylidene 2 : 3-oxydiethylidene α-methyl-D-glucoside.

Attempted Preparation of 4 : 6-*Ethylidene* α-*Methyl*-D-*glucoside from* 4 : 6-*Ethylidene* 2 : 3-*Oxydiethylidene* α-*Methyl*-D-*glucoside.*—(*a*) (cf. Haworth and Appel, *loc. cit.*). 2 : 3-Oxydiethylidene 4 : 6-ethylidene α-methyl-D-glucoside (2 g.) gave unchanged starting material (1 g.), m. p. 182—183°, α-methyl-D-glucoside (0·4 g.), m. p. and mixed m. p. 162—163°, and 4 : 6-ethylidene α-methyl-D-glucoside (0·2 g.), m. p. 76—77°.

(*b*) After a solution of 4 : 6-ethylidene 2 : 3-oxydiethylidene α-methyl-D-glucoside (1·5 g.) in acetone (100 ml.) containing water (1 ml.) and concentrated hydrochloric acid (0·4 ml.) had been kept for 15 minutes the rotation was constant and the solution was neutralised with silver carbonate. After concentration the first crystals which separated were starting material (0·5 g.), m. p. and mixed m. p. 182—183°. Further concentration led to the deposition of large

needles (0·5 g.), m. p. 160—161°, which after recrystallisation from alcohol had m. p. 163—164°, undepressed after admixture with α-methyl-D-glucoside.

Indirect Preparation of 4 : 6-*Ethylidene* α-*Methyl-*D-*glucoside.*—A solution of 4 : 6-benzylidene α-methyl-D-glucoside (5 g.; Hibbert, *Canad. J. Res.*, 1942, **20**, *B*, 175) in acetic anhydride (15 ml.) containing sodium acetate (1·5 g.) was heated at 100° for 1 hour and then poured into ice-water. The product, recrystallised from alcohol, gave 4 : 6-benzylidene α-methylglucoside 2 : 3-diacetate (5 g., 75%) as needles, m. p. 108°, $[\alpha]_D^{18}$ +75·5° (*c*, 1·9 in chloroform). Freudenberg, Toepffer, and Anderson (*Ber.*, 1928, **61**, 1758), who prepared this compound by a different method, record m. p. 108°, $[\alpha]_D^{20}$ +76° (*c*, 2·0 in chloroform).

A solution of the 2 : 3-diacetate (10 g.) in acetone (95 ml.) and water (5 ml.) was hydrolysed with 0·025N-hydrochloric acid. After 6 days at room temperature the optical rotation became constant. The solution was neutralised with solid potassium carbonate and concentrated, and the residue washed with sodium hydrogen sulphite solution. The aqueous filtrate was extracted with chloroform, and the chloroform solution dried and concentrated. The residual syrup was shaken with paraldehyde (50 ml.) and concentrated sulphuric acid (0·06 ml.) for 48 hours. Evaporation of excess of paraldehyde left a syrup which has not crystallised after prolonged storage in a vacuum-desiccator.

A cold solution of freshly distilled benzoyl chloride (15 ml.) in pyridine (30 ml.) was added to a cooled solution of 4 : 6-benzylidene α-methyl-D-glucoside (16 g.) in pyridine (30 ml.). After 24 hours at room temperature the reaction mixture was diluted with chloroform and extracted successively with water, dilute sulphuric acid, sodium hydrogen carbonate solution, and water. The chloroform solution was dried and concentrated to a syrup which crystallised on addition of ethanol. Recrystallisation from alcohol gave 4 : 6-benzylidene α-methyl-D-glucoside 2 : 3-dibenzoate (16 g., 57%), needles, m. p. 149—150°, $[\alpha]_D^{20}$ +98° (*c*, 1·1 in chloroform). Ohle and Spencker (*Ber.*, 1928, **61**, 2392) give m. p. 148°, $[\alpha]_D^{20}$ +96·9° (in chloroform).

A solution of the 2 : 3-dibenzoate (16 g.) in acetone (300 ml.) containing concentrated hydrochloric acid (0·6 ml.) was boiled under reflux for 6½ hours. Barium carbonate (1 g.) was added and the solution left overnight. After steam-distillation the solution was extracted with chloroform, and the extracts were dried and concentrated, to give crude α-methyl-D-glucoside 2 : 3-dibenzoate (12 g., 92%) as a glass. A solution of this (10 g.) in paraldehyde (80 ml.) containing concentrated sulphuric acid (0·1 ml.) was shaken for 48 hours. After neutralisation with sodium hydrogen carbonate the filtered solution was evaporated and 4 : 6-ethylidene α-methyl-D-glucoside 2 : 3-dibenzoate (6 g., 56%) was obtained as a syrup. This, dissolved in methanol (50 ml.), containing sodium (0·01 g.), was kept for 24 hours at room temperature. Evaporation left a syrup which crystallised on addition of ether. Recrystallisation from ether–light petroleum gave 4 : 6-ethylidene α-methyl-D-glucoside (2 g., 65%), m. p. 76—77°, $[\alpha]_D^{19}$ +109·1° (*c*, 0·48 in water).

Direct Preparation of 4 : 6-*Ethylidene* α-*Methyl-*D-*glucoside.*—α-Methylglucoside (8 g.) was stirred at room temperature with paraldehyde (18 ml.) and concentrated hydrochloric acid (1·6 ml.) for 2 hours. Water (100 ml.) was then added and the solid which separated was filtered off. The filtrate was neutralised with sodium hydrogen carbonate and evaporated. After extraction of the residue with hot carbon tetrachloride, α-methylglucoside (5 g., 63%) was isolated from the residue. The carbon tetrachloride extracts were dried (K_2CO_3) and evaporated. Recrystallisation of the solid residue from ether–light petroleum gave 4 : 6-ethylidene α-methyl-D-glucoside (1·5 g., 17%), m. p. 75·5—76·5°.

2 : 3-*Oxydipropylidene* 4 : 6-*Propylidene* α-*Methyl-*D-*glucoside.*—α-Methylglucoside (11 g.), propaldehyde (40 ml.), and concentrated sulphuric acid (0·1 ml.) were shaken for 3 days at room temperature and the solid which separated (7 g., 37%) was filtered off and recrystallised twice from ethanol, giving 2 : 3-oxydipropylidene 4 : 6-propylidene α-methyl-D-glucoside, m. p. 140·5—141°, $[\alpha]_D^{20}$ +75·8° (*c*, 0·58 in chloroform) (Found: C, 57·7; H, 8·6. Calc. for $C_{16}H_{28}O_7$: C, 57·8; H, 8·4%). Mellies, Mehltretter, and Rist (*loc. cit.*) record m. p. 142·5—143·5°, $[\alpha]_D^{25}$ +73·2° (*c*, 2·5 in chloroform).

By the method of Mellies *et al.*, the same compound, m. p. 140—141°, was obtained.

4 : 6-*Propylidene* α-*Methyl-*D-*glucoside.*—Propaldehyde (20 ml.), α-methylglucoside (16 g.), and concentrated hydrochloric acid (2 ml.) were stirred at room temperature until all the solid had dissolved (40 minutes) and stirring continued for another 30 minutes. Water was added and the precipitate of crude 2 : 3-oxydipropylidene 4 : 6-propylidene α-methyl-D-glucoside (3 g., 11%) was collected. The solution was neutralised with aqueous sodium hydrogen carbonate and evaporated. Extraction of the residue with benzene left α-methylglucoside (approx. 8 g.). The benzene solution was dried and concentrated to a syrup, which crystallised on addition of

ether. Recrystallisation from light petroleum–benzene gave 4 : 6-propylidene α-methyl-D-glucoside (7 g., 38%), m. p. 102°, $[\alpha]_D^{18}$ +122° (*c*, 0·6 in chloroform). Mellies *et al.* (*loc. cit.*) record m. p. 102—103°, $[\alpha]_D^{25}$ +122·1° (*c*, 1·8 in chloroform).

4 : 6-*Ethylidene α-Methyl-D-glucoside* 2 : 3-*Ditoluene*-p-*sulphonate*.—(*a*) A solution of 4 : 6-benzylidene α-methyl-D-glucoside (12 g.) in pyridine (20 ml.) was mixed with a solution of toluene-*p*-sulphonyl chloride (30 g.) in pyridine (60 ml.), while the temperature was kept below 10°. After 6 days at room temperature the reaction mixture was poured into water, the product crystallising. Recrystallisation from alcohol gave 4 : 6-benzylidene 2 : 3-ditosyl α-methyl-D-glucoside (25 g., 99%), needles, m. p. 152—154°, $[\alpha]_D^{20}$ +15·2° (*c*, 1·4 in chloroform).

A solution of this (4 g.) in acetone (45 ml.) and water (5 ml.) containing hydrochloric acid (0·05N) was left for 8 days at room temperature (optical rotation then constant). After the solution had been neutralised with solid potassium carbonate, acetone was evaporated and the residue extracted with chloroform. After being shaken with sodium hydrogen sulphite solution the extract was dried and evaporated. The residual glass was shaken for 48 hours with paraldehyde (20 ml.), containing concentrated sulphuric acid (0·04 ml.). After neutralisation of the clear solution and evaporation, a syrup was obtained which later crystallised. Recrystallisation from ethanol yielded plates of 4 : 6-*ethylidene α-methyl-D-glucoside* 2 : 3-*ditoluene*-p-*sulphonate* (2·4 g., 77%), m. p. 154—155°, $[\alpha]_D^{20}$ +57·2° (*c*, 0·6 in chloroform) (Found : C, 52·3; H, 5·4; S, 12·2. $C_{23}H_{28}O_{10}S_2$ requires C, 52·2; H, 5·3; S, 12·1%).

(*b*) 4 : 6-Ethylidene α-methyl-D-glucoside (2 g.) in pyridine (10 ml.) was cautiously mixed with toluene-*p*-sulphonyl chloride (10 g.) in pyridine (50 ml.). After 4 days at room temperature the solution was poured into ice-water and the precipitate was recrystallised from ethanol and identified as the foregoing 2 : 3-ditoluene-*p*-sulphonate by its m. p. 153—154°, undepressed on admixture.

Alkaline Hydrolysis of 4 : 6-*Ethylidene α-Methyl-D-glucoside* 2 : 3-*Ditoluene*-p-*sulphonate*.—(*a*) A chloroform solution (10 ml.) of this ester (0·9 g.) was mixed with sodium (0·15 g.) in methanol (4·2 ml.) and kept for 3 days at room temperature. The solution was filtered and concentrated, and the solid residue (0·4 g.), crystallised from ether, was unchanged starting substance, m. p. 155°, unchanged on admixture with the authentic compound. No other product was isolated.

(*b*) A solution of the ester (8 g.) in methanol (200 ml.) containing sodium (1 g.) was boiled under reflux until the solid had dissolved (18 hours). Next morning the solution was filtered and diluted with water (250 ml.). It was then extracted with chloroform and the chloroform solution evaporated, leaving a white crystalline solid. This was purified by chromatography in ether on alumina, elution with ether, and recrystallisation of the main fraction from ether–light petroleum, to give 4 : 6-ethylidene 2 : 3-anhydro-α-methyl-D-alloside as long needles (3 g., 90%), $[\alpha]_D^{20}$ +114° (*c*, 1·3 in chloroform), m. p. 125—126°, mixed m. p. with an authentic specimen 126—127°). Peat and Wiggins (*J.*, 1938, 1088) record m. p. 128°, $[\alpha]_D^{20}$ +100° (in chloroform).

4 : 6-*Propylidene α-Methyl-D-glucoside* 2 : 3-*Ditoluene*-p-*sulphonate*.—A solution of 4 : 6-propylidene α-methyl-D-glucoside (2 g.) in dry pyridine (15 ml.) was treated with a cold solution of toluene-*p*-sulphonyl chloride (5 g.) in pyridine (10 ml.), and the mixture left for 4 days at room temperature. When the reaction mixture was poured into ice-water (100 ml.) the product crystallised. Recrystallisation from ethanol yielded 4 : 6-*propylidene α-methyl-D-glucoside* 2 : 3-*ditoluene*-p-*sulphonate* (4 g., 86%), needles, m. p. 127·5—128°, $[\alpha]_D^{20}$ +46·1° (*c*, 4·1 in chloroform) (Found : C, 53·3; H, 5·6. $C_{24}H_{30}O_{10}S_2$ requires C, 52·9; H, 5·5%).

Alkaline hydrolysis. A solution of the foregoing ester (5 g.) and sodium (0·6 g.) in methanol (50 ml.) was boiled under reflux for 24 hours, cooled, neutralised with acetic acid (0·2 ml.), and then concentrated. The residue was extracted with carbon tetrachloride, and the solution concentrated to a solid. Recrystallisation from ether–light petroleum gave long needles (2 g., 92%), m. p. 125—128°, and a further recrystallisation from light petroleum (b. p. 80—100°)–ethanol gave pure 4 : 6-*propylidene* 2 : 3-*anhydro-α-methyl-D-alloside*, m. p. 131—132°, $[\alpha]_D^{20}$ +120·9° (*c*, 0·8 in chloroform) (Found : C, 55·9; H, 7·7. $C_{10}H_{16}O_5$ requires C, 55·6; H, 7·4%).

4 : 6-*Ethylidene α-Methyl-D-glucoside* 2 : 3-*Dinitrate*.—Five minutes after a solution of 4 : 6-ethylidene α-methyl-D-glucoside (2·7 g., 1 mol.) in chloroform (50 ml.) was mixed with a solution of dinitrogen pentoxide (4·8 g., 3·5 mols.) in chloroform (50 ml.) at 0°, it was poured into ice-water. The product was extracted with chloroform and the extracts were washed with ice-water and then with cold saturated sodium hydrogen carbonate solution. After drying, the solvent was evaporated. Recrystallisation of the residue from light petroleum gave 4 : 6-*ethylidene α-methyl-D-glucoside* 2 : 3-*dinitrate* (2·2 g., 58%), stout needles, m. p. 96—97°, $[\alpha]_D^{20}$

+139·5° (*c*, 2·96 in chloroform) (Found: C, 35·4; H, 4·9; N, 8·7. $C_9H_{14}O_{10}N_2$ requires C, 34·9; H, 4·5; N, 9·0%).

Alkaline hydrolysis. A solution of 4 : 6-ethylidene α-methyl-D-glucoside 2 : 3-dinitrate (1·4 g.) in methanol (40 ml.) was boiled under reflux with sodium (0·2 g.) for 25 hours. The cooled solution was neutralised with glacial acetic acid (0·1 ml.), light petroleum (60 ml.) was added, and the solvents were evaporated. The residue was extracted, first with ether, then with chloroform, and the two extracts separately chromatographed on alumina. Fractions (50 ml.) were collected, with ether–chloroform (4 vol. : 1 vol.) as eluant in each case. After examination the appropriate fractions were combined. The first fractions gave a solid (0·52 g., 44%), which crystallised from light petroleum (b. p. 40—60°)–ether as long needles of 4 : 6-*ethylidene α-methyl-D-glucoside* 3-*nitrate*, m. p. 172—173°, $[\alpha]_D^{20}$ +150·3° (*c*, 0·45 in chloroform) (Found: C, 41·1; H, 5·7. $C_9H_{15}O_8N$ requires C, 40·8; H, 5·7%). Later fractions gave a solid (0·53 g., 55%), which crystallised from ether–light petroleum as needles, being 4 : 6-ethylidene α-methyl-D-glucoside, m. p. 76°, unchanged when mixed with authentic substance.

Characterisation of 4 : 6-*Ethylidene* α-*Methyl-D-glucoside* 3-*Nitrate.*—Methylation of 4 : 6-ethylidene α-methyl-D-glucoside 3-nitrate (0·35 g.) with methyl iodide (4 ml.) and silver oxide (0·3 g.) gave a crystalline product (0·24 g., 64%) which, recrystallised from light petroleum, yielded 4 : 6-*ethylidene* 2-*methyl* α-*methyl-D-glucoside* 3-*nitrate*, stout needles, m. p. 82·5—83·5°, $[\alpha]_D^{20}$ +111·4° (*c*, 0·3 in chloroform) (Found: 43·3; H, 6·4. $C_{10}H_{17}O_8N$ requires C, 43·0; H, 6·1%).

A solution containing 4 : 6-ethylidene 2-methyl α-methyl-D-glucoside 3-nitrate (0·22 g.) and sodium sulphide (0·4 g.) in alcohol (25 ml.) was left for 1 day at room temperature. The solution was filtered, diluted with water, and concentrated. The residue was extracted with chloroform, and the dried chloroform solution evaporated to a solid which crystallised from dry ether as long needles. It was 4 : 6-*ethylidene* 2-*methyl* α-*methyl-D-glucoside* (0·1 g., 54%), m. p. 125—126°, $[\alpha]_D^{20}$ +95·1° (*c*, 1·03 in chloroform).

A solution of 4 : 6-ethylidene 2-methyl α-methyl-D-glucoside (0·08 g.) in acetone (10 ml.), containing hydrochloric acid (0·05 ml.), was boiled under reflux for 18 hours. The cooled solution was neutralised with barium carbonate, and filtered. Evaporation of the filtrate left a syrup which crystallised from ethyl acetate as short needles, being 2-methyl α-methyl-D-glucoside (0·04 g., 56%), m. p. 145—146°. Haworth, Hirst, and Teece record m. p. 145—147° (*J.*, 1931, 2858): the m. p. of a sample of their material was not depressed by that made during this work.

4 : 6-*Propylidene* α-*Methyl-D-glucoside* 2 : 3-*Dinitrate and* 3-*Nitrate.*—(*a*) Dinitrogen pentoxide (7 g., 4 mols.) in chloroform (100 ml.) was mixed with a solution of 4 : 6-propylidene α-methyl-D-glucoside (4 g., 1 mol.) in chloroform (100 ml.), and left at 0° for 5 minutes. The solution was poured into ice-water, and the chloroform layer washed successively with ice-water, cold saturated sodium hydrogen carbonate solution, and water. The dried solution was concentrated to a syrup which partly crystallised. The crystalline portion was dissolved in the minimum quantity of methanol–light petroleum from which there separated slowly 4 : 6-*propylidene* α-*methyl-D-glucoside* 3-*nitrate* (0·3 g., 7%), needles, m. p. 156—157°, $[\alpha]_D^{18}$ +154·2° (*c*, 0·72 in chloroform) (Found: C, 43·4; H, 5·9; N, 5·0. $C_{10}H_{17}O_8N$ requires C, 43·1; H, 6·1; N, 5·0%).

(*b*) The reaction was repeated with 4 : 6-propylidene α-methyl-D-glucoside (8 g., 1 mol.) and dinitrogen pentoxide (17 g., 5 mols.) in chloroform (280 ml.), and a reaction time of 15 minutes at 0°. The product, separated as in (*a*), was a syrup which did not crystallise.

The combined non-crystalline products from the two reactions were chromatographed in anhydrous ether on alumina. Elution was by anhydrous ether, ether–chloroform, and chloroform, successively. Fractions of 120 ml. were collected, the first of which contained a syrup (9·6 g.) which crystallised as large prisms. Recrystallisation from light petroleum gave 4 : 6-*propylidene* α-*methyl-D-glucoside* 2 : 3-*dinitrate* (9·3 g., 56%), m. p. 55·5—56°, $[\alpha]_D^{18}$ +142·4° (*c*, 1·4 in chloroform) (Found: C, 37·3; H, 5·1; N, 8·5. $C_{10}H_{16}O_{10}N_2$ requires C, 37·1; H, 4·9; N, 8·6%). Later fractions, which crystallised at once, were combined and recrystallised from alcohol–light petroleum (b. p. 80—100°), to give 4 : 6-propylidene α-methyl-D-glucoside 3-nitrate (1·7 g., 12%) as long needles, m. p. 157—158°.

Conversion of 4 : 6-*Propylidene* α-*Methyl-D-glucoside* 2 : 3-*Dinitrate into the* 3-*Nitrate.*—A solution of 4 : 6-propylidene α-methyl-D-glucoside 2 : 3-dinitrate (2·2 g.) and sodium iodide (4·5 g.) in acetone (20 ml.) was heated for 16 hours at 100°. Evaporation led to 4 : 6-propylidene α-methyl-D-glucoside 3-nitrate (1·61 g., 87%) as long needles, m. p. 157°.

Characterisation of 4 : 6-*Propylidene* α-*Methyl-D-glucoside* 3-*Nitrate.*—4 : 6-Propylidene α-methyl-D-glucoside 3-nitrate (0·5 g.) with methyl iodide (10 ml.) and silver oxide (0·8 g.) at 45°

gave a product (0·45 g., 88%) which was recrystallised from light petroleum (b. p. 40—60°), giving *2-methyl* 4 : 6-*propylidene* α-*methyl*-D-*glucoside* 3-*nitrate* as needles, m. p. 53·5—54°, $[\alpha]_D^{20}$ +138·2° (*c*, 0·7 in chloroform) (Found : C, 45·5; H, 6·4. $C_{11}H_{19}O_8N$ requires C, 45·1; H, 6·5%).

A solution of this (0·4 g.) in alcohol (30 ml.) was treated with sodium sulphide (0·6 g.) at room temperature for 24 hours. The solution was then filtered, and water (5 ml.) added to the filtrate which was then distilled. The residue was extracted with chloroform, the extracts were dried and evaporated, and the crystals (0·26 g., 78%) which separated were found, after recrystallisation from ether–light petroleum, to be *2-methyl* 4 : 6-*propylidene* α-*methyl*-D-*glucoside*, m. p. 114—115°, $[\alpha]_D^{18}$ +113·8° (*c*, 0·8 in chloroform) (Found : C, 53·4; H, 7·9. $C_{11}H_{20}O_6$ requires C, 53·2; H, 8·1%).

After a solution of this (0·16 g.) in acetone (30 ml.), containing concentrated hydrochloric acid (0·1 ml.), had been kept at room temperature for 28 days, excess of solid potassium carbonate was added. Filtration, and evaporation of the filtrate, afforded crystals (0·05 g., 35%), which after recrystallisation from ethyl acetate were found to be 2-methyl α-methyl-D-glucoside, m. p. 144—146°, mixed m. p. with an authentic specimen 143—145°.

Alkaline Hydrolysis of 4 : 6-*Propylidene* α-*Methyl*-D-*glucoside* 2 : 3-*Dinitrate*.—The dinitrate (3·8 g.) in methanol (100 ml.), containing sodium (0·5 g.), was heated under reflux for 24 hours. The cooled solution was filtered and the filtrate was concentrated. The solvent-free residue was chromatographed in ether on alumina. Successive elution with ether, ether–chloroform, and chloroform–ethanol gave, from early fractions, 4 : 6-propylidene 2 : 3-anhydro-α-methyl-D-alloside (0·32 g., 13%), m. p. and mixed m. p. 132—133°. The later fractions gave 4 : 6-propylidene α-methyl-D-glucoside (0·72 g., 32%), m. p. alone or mixed with an authentic specimen, 101—102°, $[\alpha]_D^{18}$ +124·6° (*c*, 0·8 in chloroform).

Alkaline Hydrolysis of 4 : 6-*Propylidene* α-*Methyl*-D-*glucoside* 3-*Nitrate*.—A solution of the 3-nitrate (1 g.) in methanol (40 ml.) containing sodium (0·25 g.) was boiled under reflux for 40 hours. The solution was cooled, neutralised with acetic acid (0·1 ml.), and concentrated. Water (30 ml.) was added and the solution extracted with chloroform. Evaporation of the dried extract gave a residue which was chromatographed in anhydrous ether on alumina, elution being by anhydrous ether. The first fractions (80 ml.) gave 4 : 6-propylidene 2 : 3-anhydro-α-methyl-D-alloside (0·15 g., 19%), needles, m. p. 128—130° (unchanged when mixed with the product prepared from 4 : 6-propylidene 2 : 3-ditosyl α-methyl-D-glucoside). The remaining fractions (300 ml.) gave 4 : 6-propylidene α-methyl-D-glucoside (0·43 g., 52%), m. p. and mixed m. p. 102°.

4 : 6-*Propylidene* α-*Methyl*-D-*glucoside* 3-*Nitrate* 2-*Toluene*-p-*sulphonate*.—A solution of 4 : 6-propylidene α-methyl-D-glucoside 3-nitrate (1·25 g.) in pyridine (20 ml.) was mixed with a cold solution of toluene-*p*-sulphonyl chloride (2·5 g.) in pyridine (15 ml.). After 6 days at room temperature the mixture was poured into ice-water and the product extracted with chloroform. The extracts were dried and concentrated, and the residue was recrystallised from ethanol–light petroleum, to give 4 : 6-*propylidene* 2-*tosyl* α-*methyl*-D-*glucoside* 3-*nitrate* (1 g., 53%), needles, m. p. 98—99°, $[\alpha]_D^{20}$ +104·4° (*c*, 0·6 in chloroform) (Found : C, 47·6; H, 5·6; N, 3·1. $C_{17}H_{23}O_{10}NS$ requires C, 47·6; H, 5·3; N, 3·2%).

Alkaline hydrolysis. A solution of the foregoing ester (0·82 g.) and sodium (0·1 g.) in methanol (50 ml.) was boiled under reflux for 24 hours. The solution was concentrated and excess of water (30 ml.) was added. The whole was then extracted with chloroform (total volume, 500 ml.). Evaporation of the dried extracts left a residue which was chromatographed in ether on alumina. On elution with ether–chloroform the first fractions (200 ml.) contained 4 : 6-propylidene 2 : 3-anhydro-α-methyl-D-alloside (0·32 g., 78%), m. p. and mixed m. p. 129—130°, $[\alpha]_D^{18}$ +113° (*c*, 0·2 in chloroform). The last fractions (150 ml.) gave 4 : 6-propylidene α-methyl-D-glucoside (0·08 g., 18%), needles, m. p. and mixed m. p. 101—102°.

Reduction of 4 : 6-*Propylidene* α-*Methyl*-D-*glucoside* 2 : 3-*Dinitrate with Lithium Aluminium Hydride*.—After boiling under reflux for 36 hours, a solution of 4 : 6-propylidene α-methyl-D-glucoside 2 : 3-dinitrate (2·5 g.) and lithium aluminium hydride (0·5 g.) in anhydrous ether (50 ml.) was treated with water (50 ml.), then neutralised with dilute sulphuric acid. After filtration, the ethereal layer was dried (Na_2SO_4) and evaporated. Recrystallisation of the residue from light petroleum gave 4 : 6-propylidene α-methyl-D-glucoside 3-nitrate (0·4 g., 19%), m. p. 157°. The syrup obtained by evaporation of the mother-liquor crystallised from light petroleum (b. p. 40—60°), giving 4 : 6-propylidene α-methyl-D-glucoside 2 : 3-dinitrate (0·8 g., 31%) as needles, m. p. 56°. Extraction of the aqueous layer with ether gave 4 : 6-propylidene α-methyl-D-glucoside (0·8 g., 45%), m. p. and mixed m. p. 101°.

β-*Methylglucoside*.—A solution of acetobromoglucose (130 g.; prepared by Barczai-Martos and Korosy's method, *Nature*, 1950, **165**, 369) in methanol (250 ml.) was boiled under reflux with silver carbonate (40 g.) for an hour. After filtration of the hot solution, sodium (0·02 g.) was added and the whole left overnight at room temperature. Concentration, followed by seeding, gave β-methyl-D-glucoside (44 g., 74%), m. p. 107—108° (from alcohol).

2 : 3-*Oxydipropylidene* 4 : 6-*Propylidene* β-*Methyl-D-glucoside*.—Propaldehyde (24 ml.), β-methyl-D-glucoside (10 g.), and concentrated hydrochloric acid (1 ml.) were kept at room temperature for 7 hours. After dilution with chloroform and filtration from methylglucoside (5 g.) the solution was neutralised with potassium carbonate, filtered again, and concentrated. The crystals (2 g.) which separated recrystallised from alcohol, giving 2 : 3-*oxydipropylidene* 4 : 6-*propylidene* β-*methyl-D-glucoside* as needles, m. p. 117—118°, $[\alpha]_D^{18}$ −61·7° (*c*, 0·74 in chloroform) (Found : C, 57·9; H, 8·4. $C_{16}H_{28}O_7$ requires C, 57·8; H, 8·4%).

4 : 6-*Butylidene* 2 : 3-*Oxydibutylidene* β-*Methyl-D-glucoside*.—After β-methyl-D-glucoside (15 g.), *n*-butaldehyde (60 ml.), and concentrated sulphuric acid (0·15 ml.) had been shaken for 48 hours at room temperature, the solid (12 g., 43%) was collected and recrystallised from absolute alcohol, to give 4 : 6-*butylidene* 2 : 3-*oxydibutylidene* β-*methyl-D-glucoside*, m. p. 84—85°, $[\alpha]_D^{20}$ −52·5° (*c*, 0·47 in chloroform) (Found : C, 61·3; H, 9·2. $C_{18}H_{34}O_7$ requires C, 61·0; H, 9·1%).

Attempted acetylation of this compound with acetic anhydride and sodium acetate gave unchanged material, confirming the absence of free hydroxyl groups.

Acetylation of 4 : 6-*Ethylidene* β-*Methyl-D-glucoside*.—Acetic anhydride (16 ml.), 4 : 6-ethylidene β-methyl-D-glucoside (6 g.) and fused sodium acetate (2 g.) were heated for 1 hour at 100°. The crystalline product obtained on pouring the solution into water was recrystallised from alcohol, to give 4 : 6-ethylidene β-methyl-D-glucoside 2 : 3-diacetate (6·5 g., 94%), m. p. 179—180°, $[\alpha]_D^{17}$ −51·5° (*c*, 0·14 in chloroform) (Found : C, 51·7; H, 6·6. Calc. for $C_{13}H_{20}O_8$: C, 51·3; H, 6·6%). Helferich and Appel (*Ber.*, 1931, **64**, 1845) give m. p. 180·5—182°, $[\alpha]_D^{20}$ −65·9° (in chloroform).

Deacetylation of 4 : 6-*Ethylidene* β-*Methyl-D-glucoside* 2 : 3-*Diacetate*.—After a solution of sodium (0·01 g.) and 4 : 6-ethylidene β-methyl-D-glucoside 2 : 3-diacetate (0·5 g.) in methanol (20 ml.) had been kept for 2 hours at room temperature the solvent was evaporated, leaving 4 : 6-ethylidene β-methyl-D-glucoside (100%), m. p. and mixed m. p. 183—184°.

4 : 6-*Ethylidene* β-*Methyl-D-glucoside* 2 : 3-*Ditoluene*-p-*sulphonate*.—A solution of 4 : 6-ethylidene β-methyl-D-glucoside (6 g.) in pyridine (20 ml.) was mixed with a cold solution of toluene-*p*-sulphonyl chloride (15·6 g., 3 mols.) in pyridine (30 ml.). After 4 days at room temperature the mixture was poured into ice-water (400 ml.). Recrystallisation of the precipitate from methanol gave 4 : 6-*ethylidene* β-*methyl-D-glucoside* 2 : 3-*ditoluene*-p-*sulphonate* (8·4 g., 58%), needles, m. p. 162—162·5°, $[\alpha]_D^{20}$ −33·6° (*c*, 0·64 in chloroform) (Found : C, 52·4; H, 5·2; S, 12·4. $C_{23}H_{28}O_{10}S_2$ requires C, 52·3; H, 5·3; S, 12·1%).

Alkaline hydrolysis. (*a*) An ice-cold solution of sodium (1·8 g.) in methanol (28 ml.) was added to the ditoluene-*p*-sulphonate (9 g.) in chloroform (75 ml.). After 3 days at 0° and 1 day at room temperature the solution was diluted with water and the chloroform layer washed with water. After being dried ($CaCl_2$) the chloroform was evaporated, leaving unchanged compound (6 g., 67%), m. p. 161—162°. The aqueous mother-liquor and washings, which were optically inactive, were not examined.

(*b*) A solution of the ester (24 g., 1 mol.) in methanol (140 ml.) was boiled under reflux with sodium (2 g., 2 mols.) for 17 hours. The solution was cooled and filtered, and the filtrate was diluted with water (100 ml.) and then extracted with chloroform (total volume 3 l.). The residue obtained by evaporation of the dried extract was chromatographed in anhydrous ether on alumina and eluted with light petroleum (b. p. 40—60°) and then with ethanol. The early fractions contained a trace (0·03 g.) of an unidentified syrup. There followed crystals (3·56 g., 39%), m. p. 77—78°, which, after recrystallisation from light petroleum, were identified as 4 : 6-*ethylidene* 2 : 3-*anhydro*-β-*methyl-D-alloside*, m. p. 79°, $[\alpha]_D^{18}$ −43·6° (*c*, 0·8 in chloroform) (Found : C, 53·7; H, 7·2. $C_9H_{14}O_5$ requires C, 53·5; H, 6·9%). The next fractions gave needles (0·59 g.), m. p. 131°, $[\alpha]_D^{18}$ −50·0° (*c*, 0·25 in chloroform) (Found : C, 55·0; H, 7·3%). This unidentified *substance* sublimed at 80° under reduced pressure. The final fractions gave starting compound (4·5 g., 19%), m. p. and mixed m. p. 160—161°.

Preparation of 4 : 6-*Ethylidene* β-*Methyl-D-glucoside* 3-*Nitrate*.—A solution of 4 : 6-ethylidene methyl-β-D-glucoside 2 : 3-dinitrate (3·5 g.) in acetone (28 ml.) was heated with sodium iodide (7 g.) for 24 hours at 120°. The residue left after evaporation was extracted with chloroform and washed successively with sodium thiosulphate and sodium hydrogen carbonate solutions.

Evaporation of the dried solution left a syrup, which crystallised from alcohol–light petroleum, giving 4 : 6-ethylidene β-methyl-D-glucoside 3-nitrate as needles (2 g., 67%), m. p. 146—147°. Dewar and Fort record m. p. 147°.

Alkaline Hydrolysis of 4 : 6-*Ethylidene* β-*Methyl-*D-*glucoside* 2 : 3-*Dinitrate.*—(*a*) A solution of this dinitrate in methanol containing sodium, kept for 28 days at room temperature, gave unchanged starting compound.

(*b*) A solution of the dinitrate (2 g.) and sodium (0·01 g.) in methanol (50 ml.) was boiled under reflux for 6 hours. The reaction mixture was concentrated and the residue dissolved in light petroleum. Chromatography on silica gel and elution with light petroleum gave unchanged starting material (1·4 g., 70%), m. p. 88—89°. Further elution with acetone–alcohol gave a solid (0·4 g.), which on recrystallisation from light petroleum (b. p. 80—100°) yielded 4 : 6-ethylidene β-methyl-D-glucoside 3-nitrate (0·1 g., 6%), m. p. and mixed m. p. 146°. More unchanged dinitrate (0·25 g., 13%) was recovered from the mother-liquor.

(*c*) When the dinitrate (1·5 g.) was boiled with sodium (0·15 g.) in methanol (100 ml.) for 1 day the products obtained were starting compound (0·6 g., 40%) and 4 : 6-ethylidene β-methyl-D-glucoside 3-nitrate (0·5 g., 40%), m. p. and mixed m. p. 145°.

(*d*) A solution of the dinitrate (2·5 g.) and potassium hydroxide (0·5 g.) in ethanol (45 ml.) and water (15 ml.) was boiled under reflux for 24 hours, then neutralised with acetic acid (0·5 ml.) and concentrated. The residue was dissolved in ether–light petroleum (b. p. 40—60°), and the solution dried and chromatographed on alumina, elution being by ether–light petroleum (b. p. 40—60°). The first fractions gave unchanged dinitrate (0·4 g., 15%), m. p. 88—89°. The other fractions, together with the product obtained by finally washing the column with alcohol, gave 4 : 6-ethylidene β-methyl-D-glucoside 3-nitrate (1·6 g., 77%), m. p. 145—146°, $[\alpha]_D^{20}$ −31·7° (*c*, 0·4 in chloroform).

Alkaline Hydrolysis of 4 : 6-*Ethylidene* β-*Methyl-*D-*glucoside* 3-*Nitrate.*—Sodium (0·1 g.) in methanol (10 ml.) was added to 4 : 6-ethylidene β-methyl-D-glucoside 3-nitrate (1 g.) in chloroform (50 ml.). After 4 days at room temperature the filtered solution was concentrated and the residue purified by chromatography of its acetone solution on alumina, with acetone and then acetone–methanol as eluants. Only unchanged nitrate (0·8 g., 80%), m. p. 143—144°, $[\alpha]_D^{18}$ −31° (*c*, 0·33 in chloroform), was obtained.

A solution of the 3-nitrate (0·4 g.) and potassium hydroxide (0·2 g.) in aqueous alcohol (30 ml.) was boiled under reflux for 24 hours. The solution was concentrated, leaving a residue which was chromatographed on alumina, with ether as eluant. The first fractions (60 ml.) gave 4 : 6-ethylidene 2 : 3-anhydro-β-methyl-D-alloside (0·02 g., 7%), m. p. and mixed m. p. with that obtained from the ditoluene-*p*-sulphonate, 76—78°. Further elution with ether–acetone (200 ml.) gave unchanged nitrate (0·32 g., 80%), m. p. 147°.

Reduction of 4 : 6-*Ethylidene* β-*Methyl-*D-*glucoside* 2 : 3-*Dinitrate with Lithium Aluminium Hydride.*—A solution of the 2 : 3-dinitrate (2 g.) in ether (50 ml.) was boiled under reflux for 54 hours with lithium aluminium hydride (0·8 g.) in ether (50 ml.). Excess of water was added, followed by dilute sulphuric acid. The aqueous layer was extracted with ether and then dried, and the combined ethereal solutions were evaporated. The solid obtained (0·7 g.) was dissolved in ether–light petroleum and from this solution separated 4 : 6-ethylidene β-methyl-D-glucoside 3-nitrate (0·02 g.), m. p. 143—145°, $[\alpha]_D^{21}$ −34° (*c*, 0·2 in chloroform). The mother-liquor was chromatographed on alumina. Elution with anhydrous ether (200 ml.) gave unchanged dinitrate (0·52 g., 26%), m. p. 88—89°. Elution with ether–chloroform (150 ml.) yielded more 4 : 6-ethylidene β-methyl-D-glucoside 3-nitrate (0·03 g.), m. p. 145°. Further elution with chloroform–ethanol (150 ml.) gave needles (0·06 g.), m. p. 180—182°. The aqueous mother-liquor from the neutralised mixture was concentrated somewhat and extracted exhaustively with chloroform and then with ether, to give needles (0·58 g.), m. p. 182—183°. The last two crops were combined and identified as 4 : 6-ethylidene β-methyl-D-glucoside (0·64 g., 45%).

Reaction of 4 : 6-*Ethylidene* β-*Methyl-*D-*glucoside* 2 : 3-*Dinitrate with Sodium Iodide in Acetic Anhydride.*—Acetic anhydride (25 ml.), 4 : 6-ethylidene β-methyl-D-glucoside 2 : 3-dinitrate (2 g.), and sodium iodide (4 g.) were heated for 3 hours at 100°. The solution was poured into ice-water and left for 1 day. A chloroform extract therefrom was washed with sodium thiosulphate and sodium hydrogen carbonate solutions. Distillation of the dried solution left a syrup (1·5 g., 76%) which, crystallised from light petroleum (b. p. 80—100°), gave 4 : 6-ethylidene β-methyl-D-glucoside 2-acetate 3-nitrate, m. p. 124—125°, $[\alpha]_D^{18}$ −38·0° (*c*, 0·24 in chloroform) (Found : C, 42·5; H, 5·3; N, 4·6. Calc. for $C_{11}H_{17}O_9N$: C, 43·0; H, 5·3; N, 4·6%). Dewar and Fort (*loc. cit.*) record m. p. 128—129°, $[\alpha]_D^{20}$ −44° (in chloroform). An authentic specimen, m. p. 126—127°, had mixed m. p. with that prepared above, 125—126°.

Acetic anhydride (25 ml.), sodium iodide (8 g.), and 2 : 3-dinitrate (4 g.) were boiled under reflux for 3 hours. The product isolated as in the previous experiment was 4 : 6-ethylidene β-methyl-D-glucoside 2 : 3-diacetate (2·5 g., 64%), m. p. 170—172°, mixed m. p. with an authentic specimen, 172—173°.

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