524. *Sugar Nitrates. Part V.* Removal of Nitrate Groups.*

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Sugar nitrates are completely converted into the alcohols by excess of hydrazine hydrate in boiling ethanol. In this way a nitrate group is removed selectively from a compound also containing toluene-*p*-sulphonate, methanesulphonate, methyl, or benzyl groups. Treatment of D-glucose 2 : 3-dinitrates with one mol. of hydrazine hydrate gives equal amounts of the two mononitrates, making D-glucose 2-nitrates more readily available.

*cyclo*Hexyl nitrate with sodium iodide in methanol gives sodium nitrate and *cyclo*hexene. *trans-cyclo*Hexane-1 : 2-diol dinitrate and 1 : 3-*O*-benzylideneglycerol 2-nitrate are resistant to reaction with sodium iodide, but small amounts of the alcohols are produced. Sodium iodide in acetone with 1 : 3-2 : 4-di-*O*-ethylidenesorbitol 5 : 6-dinitrate gives 5 : 6-didehydro-5 : 6-dideoxy-1 : 3-2 : 4-di-*O*-ethylidenesorbitol (mainly) and 1 : 3-2 : 4-di-*O*-ethylidenesorbitol 6-nitrate, the latter also being obtained by reaction of the 5 : 6-dinitrate with sodium nitrite in aqueous ethanol.

cis- and *trans-cyclo*Hexane-1 : 2-diol dinitrates with cold concentrated sulphuric acid yield the corresponding di(hydrogen sulphates).

HYDRAZINE HYDRATE is an excellent reagent for reducing sugar nitrates.[1] In contrast to the complex reaction of the nitrates of primary aliphatic alcohols,[2] sugar nitrates are reduced by hydrazine, even in aqueous ethanol, with formation of the alcohol only. The procedure is similar to that for the reduction of aromatic nitro-compounds with hydrazine

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* Part IV, *J.*, 1958, 537.

[1] Ennor, Honeyman, and Stening, *Chem. and Ind.*, 1956, 1308.

[2] Merrow and Van Dolah, *J. Amer. Chem. Soc.*, 1954, **76**, 4522.

hydrate in the presence of Raney nickel,[3] palladium–charcoal,[4] or copper or iron powder,[5] but for sugar nitrates a catalyst is generally unnecessary. The method enables a nitrate group to be removed selectively from a compound also containing toluene-*p*-sulphonate, methanesulphonate, methyl, or benzyl groups.

The 2 : 3-dinitrates of methyl 4 : 6-*O*-ethylidene-α-D-glucoside and its anomer, and of methyl 4 : 6-*O*-benzylidene-α-D-glucoside are partially reduced when boiled in ethanol for 3·5 hours with 1·2 moles of hydrazine hydrate per mole of dinitrate. From each dinitrate, equal amounts of the two mononitrates and a little starting compound were obtained. Thus the reaction proceeds equally readily for each nitrate group and is independent of the nature of the 4 : 6-acetal grouping and of the configuration of the methyl group. This method makes such 2-nitrates available for the first time, although a low yield of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2-nitrate has been obtained through migration of the nitrate group from $C_{(3)}$ to $C_{(2)}$.[6] Proof that migration of nitrate does not occur during the reactions with hydrazine was obtained by boiling methyl 4 : 6-*O*-ethylidene-α-D-glucoside 3-nitrate with an equimolecular proportion of hydrazine hydrate in ethanol for 3 hours: unchanged starting compound (31%) and methyl 4 : 6-*O*-ethylidene-α-D-glucoside (43%) (but no 2-nitrate) were isolated. The reaction of methyl 4 : 6-*O*-ethylidene-α-D-glucoside 2-nitrate was similar.

Sugar acetates, benzoates, and benzenesulphinates, esterified on primary or secondary alcoholic groups, are converted into the alcohols on being boiled with hydrazine hydrate in ethanol for 90 minutes. Methyl 4 : 6-*O*-benzylidene-α-D-glucoside was obtained from its 2 : 3-diacetate, and acetamide and 1 : 2-3 : 5-di-*O*-methylene-D-glucose from the 6-acetate. This shows that fission of the oxygen–carbon bond takes place during deacetylation. Benzoyl groups are removed more slowly; for example, after 90 minutes' boiling, 1 : 2-5 : 6-di-*O*-*cyclo*hexylidene-D-glucose 3-benzoate was recovered (52%) together with 1 : 2-5 : 6-di-*O*-*cyclo*hexylidene-D-glucose (31%) and benzamide (14%). After 14 hours' boiling, the products were starting compound (1%), 1 : 2-5 : 6-di-*O*-*cyclo*hexylidene-D-glucose (90%), benzamide (7%), and benzhydrazide (33%). The benzhydrazide may have been formed by reaction of benzamide with excess of hydrazine, a reaction which is known to occur in aqueous solution.[7] Analogous products were obtained from 1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucose 3-benzoate, and methyl 4 : 6-*O*-benzylidene-α-D-glucoside was obtained from its 2 : 3-dibenzoate and from its 2 : 3-dibenzenesulphinate. This is another example of sulphinates' reacting in the manner of carboxylic esters and unlike sulphonates.[6]

Kuhn [8] achieved quantitative reduction of sugar nitrates at room temperature by catalytic hydrogenation under pressure with palladium–charcoal. These reactions have now been found to proceed smoothly at atmospheric pressure.

In Part II [6] a possible mechanism was suggested to explain the replacement by hydroxyl of a nitrate group on a secondary carbon atom in a sugar on reaction with sodium iodide in methanol. However, a fully substantiated reaction sequence was not presented. To try to rectify this, it was considered desirable to study a simple compound having a nitrate group on a secondary carbon atom which, when treated with sodium iodide in methanol, would give the corresponding alcohol. *cyclo*Hexyl nitrate is the simplest compound having a nitrate group on a secondary carbon atom which forms part of a six-membered ring. This nitrate with sodium iodide in methanol at 100° during 66 hours gave *cyclo*hexene, sodium nitrate (in nearly quantitative yield), and a little iodine, but no inorganic nitrite. This reaction is therefore not analogous to those of secondary sugar nitrates, which invariably yield the alcohol, free iodine, and inorganic nitrite. It is noteworthy that *cyclo*hexyl

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[3] Balcom and Furst, *J. Amer. Chem. Soc.*, 1953, **75**, 4334; Furst and Moore, *ibid.*, 1957, **79**, 5492.

[4] Dewar and Mole, *J.*, 1956, 2556.

[5] Kubota, Nara, and Onishi, *J. Pharm. Soc. Japan*, 1956, **76**, 801.

[6] Honeyman and Morgan. *J.*, 1955, 3660.

[7] Curtius and Struve, *J. prakt. Chem.*, 1894, **50**, 295.

[8] Kuhn, *J. Amer. Chem. Soc.*, 1946, **68**, 1761.

nitrate decomposes on distillation into *cyclo*hexene and nitric acid.[9] The structure of 1 : 3-*O*-benzylideneglycerol 2-nitrate is more like those of pyranose sugar nitrates. This compound reacted very slowly with sodium iodide in methanol at 100° and after 44 hours was unchanged apart from formation of a little 1 : 3-*O*-benzylideneglycerol, sodium nitrite, and iodine. *trans-cyclo*Hexane-1 : 2-diol dinitrate has been found to be very resistant to reaction with sodium iodide: after its solution in *n*-propyl alcohol had been boiled for 5 days, unchanged starting compound was recovered, together with only a small quantity of the diol. Thus these reactions, although analogous to those of secondary sugar nitrates, are too slow to permit detailed kinetic studies.

Bladon and Owen[10] found that 1 : 3-2 : 4-di-*O*-ethylidenesorbitol 5 : 6-ditoluene-*p*-sulphonate reacted readily with sodium iodide in acetone at 100°, to yield 5 : 6-didehydro-5 : 6-dideoxy-1 : 3-2 : 4-di-*O*-ethylidenesorbitol. The corresponding 5 : 6-dinitrate has now been heated with sodium iodide in acetone at 100° for 2 hours, 5 : 6-didehydro-5 : 6-dideoxy-1 : 3-2 : 4-di-*O*-ethylidenesorbitol (14%), 1 : 3-2 : 4-di-*O*-ethylidenesorbitol 6-nitrate (12%), and unchanged starting compound being obtained; after 21 hours' reaction, the products were the dehydro-compound (51%) and the 6-nitrate (8%). This is the first instance of the formation of an ethylenic compound from a sugar nitrate. The first stage in the formation of the unsaturated compound is probably the replacement, by iodine, of the nitrate group on the primary carbon atom. Although chromatography was used for separating the products, no 6-deoxy-6-iodo-1 : 3-2 : 4-di-*O*-ethylidenesorbitol 5-nitrate was isolated, suggesting that if formed it was rapidly converted into the unsaturated compound. Bladon and Owen[10] postulated intermediate formation of an unstable vicinal di-iodide in the reaction of ditoluene-*p*-sulphonates of 1 : 2-glycols with sodium iodide, leading to unsaturated products. However, a similar mechanism is unlikely to hold for the reaction of the nitrates because in all known examples nitrate groups on secondary carbon atoms are replaced by hydroxyl and not by iodine. Probably, 6-deoxy-6-iodo-1 : 3-2 : 4-di-*O*-ethylidenesorbitol 5-nitrate yields the unsaturated compound directly by a mechanism analogous to that proposed by Foster and Overend[11] for terminal vicinal ditoluene-*p*-sulphonates.

Sodium nitrite in aqueous ethanol reacted slowly with the dinitrate of *trans-cyclo*hexane-1 : 2-diol; after 6 days' boiling the dinitrate was mainly unchanged, apart from a little which had been converted into the *trans*-diol. The 5-nitrate group of 1 : 3-2 : 4-di-*O*-ethylidenesorbitol 5 : 6-dinitrate was removed slowly but selectively by this reagent. As with 1 : 2-3 : 4-di-*O*-*iso*propylidene-D-galactose 6-nitrate,[1] the nitrate group on the primary carbon atom resists attack, confirming the view that the reaction of sodium nitrite is fundamentally different from that of sodium iodide.

Qualitative tests show that when a compound containing a nitrate group is stirred with cold concentrated sulphuric acid nitric acid is liberated. This is detectable with diphenylamine[12] or *NN'*-diphenylbenzidine,[13] each of which gives an intense blue colour. The possible use of concentrated sulphuric acid for removing nitrate groups was investigated in the cases of *cis*- and *trans-cyclo*hexane-1 : 2-diol dinitrate. After treatment of these esters with cold concentrated sulphuric acid during 10 minutes the di(hydrogen sulphates) of the diols were isolated as their barium and bisphenylhydrazine salts. The assigned configurations were confirmed by hydrolysing the di(hydrogen sulphates) to the respective diols. The same esters were obtained directly by treating the diols with concentrated sulphuric acid. Esters which display complex ionisation in sulphuric acid are not regenerated when the solution is poured into water.[14] Thus *cis*- and *trans-cyclo*hexane-1 : 2-diol dinitrate probably undergo complex ionisation in sulphuric acid, similar to that suggested by Kuhn[15]

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[9] Fichter and Petrovitch, *Helv. Chim. Acta*, 1941, **24**, 253.
[10] Bladon and Owen, *J.*, 1950, 598.
[11] Foster and Overend, *J.*, 1951, 3452.
[12] Oldham, *J.*, 1925, 2840.
[13] Dewar and Fort, *J.*, 1944, 492.
[14] Hammett and Treffers, *J. Amer. Chem. Soc.*, 1937, **59**, 1708.
[15] Kuhn, *ibid.*, 1947, **69**, 1974.

for ethyl nitrate on the basis of cryoscopic and spectroscopic evidence. Hydrolysis did not occur when the sulphuric acid solution was poured into water, for the *trans*-dinitrate is not decomposed by aqueous sulphuric acid.

EXPERIMENTAL

Unless stated, solutions in benzene or chloroform were dried over anhydrous sodium sulphate, evaporations were conducted under reduced pressure, specific rotations were determined in dry chloroform, and the light petroleum used had b. p. 60—80°.

Chromatographic separations were carried out with columns of activated alumina, Type H, 100/200 S mesh, supplied by Messrs. Peter Spence & Sons, Ltd.

100% Hydrazine hydrate was used.

At the end of the time specified for the preparation of esters in pyridine a little water was added to decompose excess of acid chloride, and the solution was left for 30 min. before it was poured into water.

Where appropriate, identity was established by mixed m. p. and infrared spectra.

Analytical Procedures.—The presence of nitrite ion was established by the appearance of a red colour after the addition of a solution of sulphanilic acid in acetic acid, followed by a solution of α-naphthylamine.

Sodium nitrate in the absence of nitrite was detected by fusion of the solid to give nitrite which liberated iodine from acidified aqueous potassium iodide. Nitrate was determined quantitatively by reduction to ammonia with Devarda's alloy.

Preparation of Nitrates.—Fuming nitric acid (*d* 1·50; 4·8 ml.) in acetic anhydride (12 ml.) was added slowly to methyl 4 : 6-*O*-benzylidene-α-D-mannoside [16] (6·0 g.) suspended in acetic anhydride (12 ml.) at 0°. After 10 min. at room temperature, the resulting solution was poured into iced aqueous potassium carbonate. After being washed with dilute aqueous potassium carbonate and then with water and dried, the crystalline product (7·0 g., 88%) was recrystallised from methanol, to yield *methyl* 4 : 6-O-*benzylidene*-α-D-*mannoside* 2 : 3-*dinitrate* (5·46 g., 69%), m. p. 142°, $[\alpha]_D^{20}$ $-3{\cdot}1°$ (*c* 2·4) (Found: C, 45·4; H, 4·5; N, 7·4. $C_{14}H_{16}O_{10}N_2$ requires C, 45·2; H, 4·3; N, 7·5%).

Unless otherwise stated, this procedure was employed in the succeeding experiments. The product obtained from 1 : 3-2 : 4-di-*O*-ethylidenesorbitol was recrystallised from ethanol–light petroleum or aqueous ethanol, to yield cubes of 1 : 3-2 : 4-*di*-O-*ethylidenesorbitol* 5 : 6-*dinitrate* (70%), m. p. 80—80·5°, $[\alpha]_D^{26}$ $+8{\cdot}7°$ (*c* 3·4) (Found: C, 37·4; H, 4·9; N, 8·3. $C_{10}H_{16}O_{10}N_2$ requires C, 37·0; H, 4·9; N, 8·6%).

The crude precipitate obtained from 1 : 3-*O*-benzylideneglycerol was recrystallised from methanol to give needles of 1 : 3-O-*benzylideneglycerol* 2-*nitrate* (27%), m. p. 93—93·5° (Found: C, 53·5; H, 5·1; N, 6·1. $C_{10}H_{11}O_5N$ requires C, 53·3; H, 4·9; N, 6·2%).

A solution of the viscous product obtained from *trans-cyclo*hexane-1 : 2-diol was dissolved in ether and washed with aqueous sodium hydrogen carbonate and then with water near 0°. Evaporation of the dried ether solution yielded a liquid which was chromatographed. Elution by light petroleum afforded *trans-cyclo*hexane-1 : 2-diol dinitrate (67%), n_D^{20} 1·4754, m. p. 17·5—18°. Christian and Purves [17] record m. p. 18·5—19°.

The same procedure was followed with the *cis*-isomer except that elution with benzene yielded *cis-cyclo*hexane-1 : 2-diol dinitrate (64%), m. p. 22—23°, which, after one recrystallistion from light petroleum, had m. p. 24°, n_D^{20} 1·4772. Christian and Purves [17] record m. p. 24·5—25°, n_D^{21} 1·4790.

In the case of *cyclo*hexanol, the reaction solution was left at 0° overnight. The oily product, dissolved in light petroleum, was repeatedly washed with aqueous sodium hydrogen carbonate and then with water until the aqueous extract was neutral. The dried petroleum solution was evaporated and the residue was distilled to yield *cyclo*hexyl nitrate (74%), b. p. 56—58°/7 mm., middle fraction, b. p. 56°/7 mm., n_D^{20} 1·4546, d_{16}^{16} 1·104 (Found: N, 9·6. Calc. for $C_6H_{11}O_3N$: N, 9·65%). Kornblum and Teitelbaum [18] record n_D^{20} 1·4562, d_4^{20} 1·1043.

Reduction of Sugar Nitrates with Hydrazine Hydrate.—A solution of methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate (1·49 g., 1 mol.) and hydrazine hydrate (1·20 g., 6 mol.) in

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[16] Schwarz, unpublished results.

[17] Christian and Purves, *Canad. J. Chem.*, 1951, **29**, 926.

[18] Kornblum and Teitelbaum, *J. Amer. Chem. Soc.*, 1952, **74**, 3078.

ethanol (15 ml.) was boiled under reflux for 90 min. Excess of hydrazine was then decomposed by boiling the solution with Raney nickel for 15 min. The solution, after being filtered, was evaporated to a solid which, recrystallised from chloroform–light petroleum, was methyl 4 : 6-*O*-benzylidene-α-D-glucoside (0·90 g., 80%), m. p. 164—165°.

In succeeding experiments, unless otherwise stated, this procedure was used, except that chloroform was added when the compound was insufficiently soluble in boiling ethanol.

Repetition of the above experiment but without addition of nickel led to the same product (74%).

The results are summarised in the annexed Table.

Compound reduced	Yield (%) of alcohol	M. p.	$[\alpha]_D^{20}$
1 : 2-5 : 6-Di-*O*-*cyclo*hexylidene-D-glucose 3-nitrate	90	133—134°	+1·1°
1 : 2-3 : 4-Di-*O*-*iso*propylidene-D-galactose 6-nitrate	100	Liquid *	−57·3
Methyl 4 : 6-*O*-benzylidene-α-D-mannoside 2 : 3-dinitrate	84	142—143	+63·5
Methyl 4 : 6-*O*-benzylidene-α-D-altroside 2 : 3-dinitrate	74	170	+116
Methyl 4 : 6-*O*-benzylidene-α-D-altroside 3-nitrate	98	169—170	+115
1 : 3-2 : 4-Di-*O*-ethylidenesorbitol 5 : 6-dinitrate	75	212—213	−11·5 (H_2O)

* Identified as the 6-toluene-*p*-sulphonate, m. p. 90—91°.

Partial Reduction of 2 : 3-*Dinitrates with Hydrazine*.—A solution of methyl 4 : 6-*O*-ethylidene-α-D-glucoside 2 : 3-dinitrate (6·20 g., 1 mol.) and hydrazine hydrate (1·2 g., 1·2 mol.) in ethanol (30 ml.) was boiled under reflux for 3·5 hr., then evaporated, and the residue was chromatographed in benzene. Elution with this solvent and recrystallisation from light petroleum yielded unchanged starting compound (0·28 g., 4·5%), m. p. 100—101°. Elution with ether removed, in the early fractions, a solid which recrystallised from ethanol–light petroleum in long needles of *methyl* 4 : 6-O-*ethylidene*-α-D-*glucoside* 2-*nitrate* (1·81 g., 34%), m. p. 133°, $[\alpha]_D^{17\cdot5}$ +147° (*c* 1·1) (Found: C, 40·8; H, 5·6; N, 4·9%). Further elution with ether and finally with chloroform yielded a solid which, recrystallised from ethanol–light petroleum, was the 3-nitrate (1·82 g., 34%), m. p. 173—174°. No product was eluted by ethanol.

By similar reactions, methyl 4 : 6-*O*-ethylidene-β-D-glucoside 2 : 3-dinitrate gave the 2-*nitrate* (22%), m. p. 144°, $[\alpha]_D^{20}$ −43·8° (*c* 1·0) (Found: C, 40·9; H, 5·7; N, 5·0. $C_9H_{15}O_8N$ requires C, 40·8; H, 5·7; N, 5·3%), the 3-nitrate (24%), and unchanged starting compound (3%), whereas methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate yielded starting compound (8%), the 2-nitrate (30%), and the 3-nitrate (28%).

Characterisation of the 2-*Nitrates*.—Silver oxide (2 g.) was added in portions to a suspension of methyl 4 : 6-*O*-ethylidene-α-D-glucoside 2-nitrate (0·70 g.) in boiling methyl iodide (6 ml.). The mixture was boiled for 8 hr. before the silver residue was filtered off and washed with chloroform, and the combined filtrate and washings were evaporated. The crystalline residue (0·71 g., 96%), m. p. 86—87°, recrystallised from methanol, gave prisms of *methyl* 4 : 6-O-*ethylidene*-3-O-*methyl*-α-D-*glucoside* 2-*nitrate*, m. p. 87—87·5°, $[\alpha]_D^{20}$ +147° (*c* 0·8) (Found: C, 42·8; H, 6·1. $C_{10}H_{17}O_8N$ requires C, 43·0; H, 6·1%). A solution of this compound (0·70 g.) and hydrazine hydrate (0·37 g.) in ethanol (7 ml.) was boiled under reflux for 1·5 hr. The product, recrystallised from chloroform–light petroleum, was methyl 4 : 6-*O*-ethylidene-3-*O*-methyl-α-D-glucoside (0·45 g., 76%), m. p. 106°, $[\alpha]_D^{21}$ +146° (*c* 1·3) (Found: C, 51·2; H, 7·7. Calc. for $C_{10}H_{18}O_6$: C, 51·3; H, 7·7%). Jeanloz and Gut [19] record m. p. 106—107°, $[\alpha]_D^{21}$ +150° ± 5°. A solution of this compound (0·14 g.) in aqueous N-sulphuric acid (10 ml.) was heated at 100° for 6 hr. The solution was neutralised with barium carbonate and filtered, and the filtrate was evaporated to a syrup which solidified after repeated evaporation of its solutions in ethanol. Recrystallisation from ethanol yielded 3-*O*-methyl-α-D-glucose [20] (0·06 g., 51%), m. p. 158—160°.

Methylation of methyl 4 : 6-*O*-ethylidene-β-D-glucoside 2-nitrate yielded a solid (95%), m. p. 81·5—82·5°, which recrystallised from light petroleum in prisms of *methyl* 4 : 6-O-*ethylidene*-3-O-*methyl*-β-D-*glucoside* 2-*nitrate*, m. p. 83—84°, $[\alpha]_D^{20}$ −22° (*c* 0·5) (Found: C, 42·7; H, 6·0%). Reaction of this compound with hydrazine hydrate yielded a solid which, recrystallised from chloroform–light petroleum, was methyl 4 : 6-*O*-ethylidene-3-*O*-methyl-β-D-glucoside (75%) m. p. 133—134°. Dewar and Fort [13] record m. p. 134°.

Methylation of methyl 4 : 6-*O*-benzylidene-α-glucoside 2-nitrate yielded a solid (98%),

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[19] Jeanloz and Gut, *J. Amer. Chem. Soc.*, 1954, **76**, 5793.
[20] Glen, Myers, and Grant, *J.*, 1951, 2568.

m. p. 149—150°, which recrystallised from methanol in needles of *methyl* 4 : 6-O-*benzylidene*-3-O-*methyl*-α-D-*glucoside* 2-*nitrate*, m. p. 149—150°, $[\alpha]_D^{20}$ +102° (*c* 1·1) (Found: C, 53·1; H, 5·6. $C_{15}H_{19}O_8N$ requires C, 52·8; H, 5·6%). Reduction of this with hydrazine hydrate yielded a solid which, recrystallised from ethanol, was methyl 4 : 6-*O*-benzylidene-3-*O*-methyl-α-D-glucoside (70%), $[\alpha]_D^{20}$ +118° (*c* 1·1 in $CHCl_2{\cdot}CHCl_2$), m. p. 146°, undepressed on admixture with a sample prepared in the following experiment. Bolliger and Prins [21] record m. p. 150—151°, $[\alpha]_D^{14}$ +119·5° (in $CHCl_2{\cdot}CHCl_2$) for this compound.

Methanol (2 ml.) containing sodium (50 mg.) and methyl 4 : 6-*O*-benzylidene-3-*O*-methyl-α-D-glucoside 2-toluene-*p*-sulphonate (70 mg.) was boiled under reflux for 8 hr. The cooled solution was neutralised with acetic acid and then evaporated. The residual solid was shaken with warm benzene, and this extract was chromatographed. Elution with benzene removed impurities but washing the column with chloroform afforded a solid which, recrystallised from ethanol–light petroleum, was methyl 4 : 6-*O*-benzylidene-3-*O*-methyl-α-D-glucoside (29 mg., 63%), m. p. 146—147°, $[\alpha]_D^{18}$ +117° (*c* 1·0 in $CHCl_2{\cdot}CHCl_2$).

Reduction of Methyl 4 : 6-O-*Ethylidene*-α-D-*glucoside* 3-*Nitrate and* 2-*Nitrate*.—A solution of the 3-nitrate (0·795 g., 1 mol.) and hydrazine hydrate (0·15 g., 1 mol.) in ethanol (7 ml.) was boiled under reflux for 3 hr. Evaporation yielded a solid which was chromatographed in chloroform solution. Elution with chloroform yielded starting compound (0·25 g., 31%) which after being recrystallised from ethanol–light petroleum had m. p. 175—176°. Ethanol eluted a solid which, recrystallised from ether, was methyl 4 : 6-*O*-ethylidene-α-D-glucoside (0·28 g., 43%), m. p. 75—76°.

Similar reaction with the 2-nitrate yielded unchanged starting compound (25%) and methyl 4 : 6-*O*-ethylidene-α-D-glucoside (47%).

Preparation of Methyl 4 : 6-O-*Ethylidene*-α-D-*glucoside Mononitrate Monotoluene*-p-*sulphonates*.—Toluene-*p*-sulphonyl chloride (0·46 g.) in pyridine (0·5 ml.) was added to a solution of the 3-nitrate (0·53 g.) in pyridine (0·7 ml.) at 0°. After 23 hr. at room temperature, the mixture was poured into ice-water, and the resulting solid was recrystallised from ethanol giving needles of *methyl* 4 : 6-O-*ethylidene*-α-D-*glucoside* 3-*nitrate* 2-*toluene*-p-*sulphonate* (0·66 g., 79%), m. p. 134—134·5°, $[\alpha]_D^{22}$ +104° (*c* 1·0) (Found: C, 46·1; H, 4·8. $C_{16}H_{21}O_{10}NS$ requires C, 45·8; H, 5·0%).

Similarly the 2-nitrate was converted into cubes of *methyl* 4 : 6-O-*ethylidene*-α-D-*glucoside* 2-*nitrate* 3-*toluene*-p-*sulphonate* (55%), m. p. 152—153°, $[\alpha]_D^{20}$ +96·3° (*c* 1·2) (Found: C, 45·9; H, 5·0%).

Selective Removal of Nitrate Groups with Hydrazine Hydrate.—The compounds which were recovered unchanged after being boiled with hydrazine hydrate in ethanol during 1·5 hr. in the presence or absence of Raney nickel included methyl 4 : 6-*O*-benzylidene-α-D-glucoside ditoluene-*p*-sulphonate (88%), dimethanesulphonate (86%), dimethyl ether (88%), and dibenzyl ether (94%), 1 : 2-3 : 4-di-*O*-*iso*propylidene-D-galactose 6-toluene-*p*-sulphonate (81%), and methyl 2 : 3-anhydro-4 : 6-*O*-benzylidene-α-D-alloside (89%).

Selective removal of the nitrate group from the mononitrate of each of the following compounds was achieved under the standard conditions described above: methyl 4 : 6-*O*-benzylidene-α-D-glucoside 3-toluene-*p*-sulphonate (71%), m. p. 159—160°, 2-toluene-*p*-sulphonate (74%), m. p. 153·5—154°, $[\alpha]_D^{21}$ +62·9° (*c* 1·3), 2-methanesulphonate (70%), m. p. 131·5—132°, $[\alpha]_D^{22}$ +72° (*c* 1·1), 3-methanesulphonate (87%), m. p. 142—143°, $[\alpha]_D^{24}$ +88° (*c* 1·0), clustered needles (from chloroform–light petroleum) of *methyl* 4 : 6-O-*ethylidene*-α-D-*glucoside* 2-*toluene*-p-*sulphonate* (88%), m. p. 150°, $[\alpha]_D^{22}$ +82·1° (*c* 1·2) (Found: C, 51·6; H, 5·9; S, 8·3. $C_{16}H_{22}O_8S$ requires C, 51·3; H, 5·9; S, 8·6%), and the 3-*toluene*-p-*sulphonate* (69%), m. p. 145—145·5°, $[\alpha]_D^{22}$ +68·4° (*c* 0·7) (Found: C, 51·0; H, 6·1; S, 8·4%).

Reactions of Hydrazine Hydrate with Esters of Carboxylic Acids.—Unless stated, the reactions were carried out with hydrazine hydrate in ethanol solution, as described above.

Methyl 4 : 6-*O*-benzylidene-α-D-glucoside was obtained from the 2 : 3-diacetate (in 78% yield), from the 2 : 3-dibenzenesulphinate (53%), and from the 2 : 3-dibenzoate (71%, after 14 hours' reaction). The solution resulting from treatment of 1 : 2-3 : 5-di-*O*-methylene-D-glucose 6-acetate was evaporated to a syrup which was chromatographed in benzene–chloroform. Benzene eluted no product, but chloroform removed a colourless syrup. Long needles of acetamide (44%), m. p. 80—81°, were removed from the syrup by sublimation at 100°/13

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[21] Bolliger and Prins, *Helv. Chim. Acta*, 1945, **28**, 465.

mm. The residual syrup crystallised with difficulty from ethanol–light petroleum to 1 : 2-3 : 5-di-*O*-methylene-D-glucose (59%), m. p. 62—63°, $[\alpha]_D^{22}$ +42·5° (*c* 0·8 in EtOH). Schmidt, Distelmaier, and Reinhard [22] record m. p. 63°, $[\alpha]_D^{20}$ + 43·8° (EtOH).

After reaction of 1 : 2-5 : 6-di-*O*-*cyclo*hexylidene-D-glucose 3-benzoate the solution was evaporated to a syrup which was chromatographed in benzene. Elution with this solvent yielded a solid which, recrystallised from methanol, was unchanged starting compound (52%), m. p. 110—111°. Washing the column with chloroform afforded a solid which, recrystallised from *n*-heptane, was 1 : 2-5 : 6-di-*O*-*cyclo*hexylidene-D-glucose (31%), m. p. 132—133°. Final elution with ethanol yielded benzamide (14%), m. p. 125—126°.

On repetition of the experiment with Raney nickel present throughout the heating with hydrazine hydrate, unchanged starting compound (84%), 1 : 2-5 : 6-di-*O*-*cyclo*hexylidene-D-glucose (7%), and benzamide (3%) were obtained.

14 Hours' boiling without catalyst gave unchanged starting compound (1%) and 1 : 2-5 : 6-di-*O*-*cyclo*hexylidene-D-glucose (90%). On elution of the chromatographic column with chloroform–ethanol (10 : 1) the early fractions, recrystallised from chloroform–light petroleum, yielded benzamide (7%). Final elution with ethanol gave, after recrystallisation from ethanol–light petroleum, benzhydrazide (33%), m. p. 111—112°.

Reaction of 1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucose 3-benzoate for 5·5 hr. afforded unchanged starting compound (4%), 1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucose (74%), benzamide (4%), and benzhydrazide (36%).

Catalytic Hydrogenation of Sugar Nitrates.—A solution of the nitrate (0·5 g.) in methanol (20 ml.) was shaken with palladium–charcoal (0·25 g.) in hydrogen at room temperature and atmospheric pressure, filtered, and evaporated. The results are summarised in the annexed Table.

Compound reduced	Yield (%) of alcohol	M. p.	Reaction time (hr.)
1 : 2-5 : 6-Di-*O*-*cyclo*hexylidene-D-glucose 3-nitrate	99	133—134°	1·5
Methyl 4 : 6-*O*-benzylidene-α-D-glucoside 2 : 3-dinitrate	98	163—164	2·5
1 : 3-2 : 4-Di-*O*-ethylidenesorbitol 5 : 6-dinitrate	100	210—212	3·5
Methyl α-D-glucoside 2 : 3 : 4 : 6-tetranitrate	96	165—166	4·5

Reaction of cyclo*Hexyl Nitrate with Sodium Iodide.*—A sealed tube containing sodium iodide (15 g., 0·1 mole) and *cyclo*hexyl nitrate (5·80 g., 0·04 mole) dissolved in anhydrous methanol (40 ml.) was heated at 100° for 44 hr. The mixture was then distilled and the residue was found to contain sodium nitrate (88%) and free iodine (3·3%), but no nitrite. The distillate, b. p. 48—77°, containing *cyclo*hexene (69%),[23] was made up to 100 ml. with carbon tetrachloride. A solution of bromine (1·8 g.) in carbon tetrachloride (20 ml.) was added during 20 min. to half of the solution at 0° with stirring. Solvents and excess of *cyclo*hexene were evaporated and the residue, after being distilled under reduced pressure, was 1 : 2-dibromo*cyclo*hexane (1·90 g.), b. p. 100—102°/12 mm.

Reaction for 66 hr. yielded *cyclo*hexene (75%), free iodine (2·2%), and sodium nitrate (95%).

Reaction of 1 : 3-O-*Benzylideneglycerol* 2-*Nitrate with Sodium Iodide.*—A sealed tube containing the 2-nitrate (4·50 g.) and sodium iodide (9·0 g.) dissolved in anhydrous methanol (40 ml.) was kept at 100° for 44 hr. The mixture was evaporated and chloroform and water were added to the residue which contained free iodine (3·3%) and sodium nitrite (2·6%). The chloroform solution was evaporated and the residue was chromatographed in benzene. Elution with this solvent yielded unchanged starting compound (3·73 g., 83%), m. p. 93—93·5° (from methanol). Further elution with chloroform afforded a solid which, recrystallised from *iso*propyl alcohol–light petroleum (1 : 1), was 1 : 3-*O*-benzylideneglycerol [24] (0·06 g., 2%), m. p. 82—83°.

When the experiment was repeated but with a reaction time of 90 hr. unchanged compound (71%) and the corresponding alcohol (5%) were obtained.

Reaction of trans-cyclo*Hexane*-1 : 2-*diol Dinitrate with Sodium Iodide.*—A solution of the dinitrate (4·12 g.) and sodium iodide (18 g.) in *n*-propyl alcohol (150 ml.) was boiled under reflux for 5 days. The residue obtained on evaporation was extracted with chloroform, and the combined extracts were washed with aqueous sodium thiosulphate. The chloroform solution was evaporated and the residue was chromatographed in benzene. Elution with

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[22] Schmidt, Distelmaier, and Reinhard, *Chem. Ber.*, 1953, **86**, 741.

[23] Wild, " Estimation of Organic Compounds," Univ. Press, Cambridge, 1953, p. 14.

[24] Verkade and van Roon, *Rec. Trav. chim.*, 1942, **61**, 831.

benzene–light petroleum (1 : 4) yielded unchanged starting compound (2·40 g., 58%). On washing the column with chloroform, a dark liquid was obtained which, on distillation under reduced pressure, yielded an unidentified colourless liquid (0·05 g.), b. p. 126—130°/14 mm. Ethanol removed *trans*-diol (0·08 g., 4%).

Reaction of 1 : 3-2 : 4-*Di*-O-*ethylidenesorbitol* 5 : 6-*Dinitrate with Sodium Iodide*.—A sealed tube containing the dinitrate (3·24 g., 0·01 mol.) and sodium iodide (4·5 g., 0·03 mol.) dissolved in acetone (50 ml.) was kept at 100° for 2 hr. The mixture was treated as in the previous experiment. Elution of the column with benzene–light petroleum (1 : 1) yielded, in the early fractions, a syrup which, crystallised from light petroleum, was unchanged starting compound (1·14 g., 35%), m. p. 80—80·5°. Next, benzene–light petroleum followed by benzene removed a solid which recrystallised from ethyl acetate in needles of 5 : 6-didehydro-5 : 6-dideoxy-1 : 3-2 : 4-di-*O*-ethylidenesorbitol (0·28 g., 14%), m. p. 122—123°, $[\alpha]_D^{20}$ $-24·3°$ (*c* 1·8). Bladon and Owen [10] record m. p. 122—123°, $[\alpha]_D^{21}$ $-23·8°$. Washing the column with chloroform gave a syrup which crystallised from ethanol–light petroleum in prisms of 1 : 3-2 : 4-*di*-O-*ethylidenesorbitol* 6-*nitrate* (0·34 g., 12%), m. p. 129·5—130°, $[\alpha]_D^{23}$ $+12·9°$ (*c* 7·0) (Found: C, 43·3; H, 5·9; N, 4·6. $C_{10}H_{17}O_8N$ requires C, 43·0; H, 6·1; N, 5·0%).

After reaction for 21 hr. the products were 5 : 6-didehydro-5 : 6-dideoxy-1 : 3-2 : 4-di-*O*-ethylidenesorbitol (51%) and the 6-nitrate (8%).

Characterisation of 1 : 3-2 : 4-*Di*-O-*ethylidenesorbitol* 6-*Nitrate*.—Toluene-*p*-sulphonyl chloride (0·83 g.) in pyridine (2 ml.) was added to a solution of the 6-nitrate (1·12 g.) in pyridine (2 ml.) at 0°. After 3 days at room temperature the mixture was poured into ice-water. The resulting solid, recrystallised from methanol, yielded prisms of 1 : 3-2 : 4-*di*-O-*ethylidenesorbitol* 6-*nitrate* 5-*toluene*-p-*sulphonate* (1·28 g., 74%), m. p. 111—112°, $[\alpha]_D^{21}$ $+6·3°$ (*c* 3·9) (Found: C, 47·5; H, 5·2; S, 7·1. $C_{17}H_{23}O_{10}NS$ requires C, 47·1; H, 5·3; S, 7·4%).

A solution of this ester (0·87 g.) and hydrazine hydrate (0·30 g.) in ethanol (9 ml.) was boiled under reflux with a little Raney nickel for 1·5 hr. Excess of hydrazine was decomposed by boiling the solution with more nickel and the solution, after being filtered, was evaporated. The resulting solid (0·75 g., 96%), m. p. 127—128°, recrystallised from methanol in needles of 1 : 3-2 : 4-*di*-O-*ethylidenesorbitol* 5-*toluene*-p-*sulphonate*, m. p. 128°, $[\alpha]_D^{25}$ $-29·1°$ (*c* 2·8) (Found: C, 52·7; H, 5·9; S, 7·9. $C_{17}H_{24}O_8S$ requires C, 52·6; H, 6·2; S, 8·3%).

A solution of this ester (0·26 g.) and benzoyl chloride (0·12 g.) in pyridine (1·5 ml.) was left at room temperature for 22 hr., then poured into ice-water and the precipitate was chromatographed. Elution with ether yielded a solid which, recrystallised from light petroleum, gave soft needles of 1 : 3-2 : 4-di-*O*-ethylidenesorbitol 6-benzoate 5-toluene-*p*-sulphonate (0·18 g., 55%), m. p. 122—123°, $[\alpha]_D^{24}$ $+9·3°$ (*c* 2·4) (Found: C, 58·5; H, 6·0. Calc. for $C_{24}H_{28}O_9S$: C, 58·5; H, 5·7%). Matheson and Angyal [25] record m. p. 121°, $[\alpha]_D^{23}$ $+5·5°$.

Reactions of Nitrates with Sodium Nitrite in Aqueous Ethanol.—*trans*-*cyclo*Hexane-1 : 2-diol dinitrate (6·18 g., 0·03 mol.) and sodium nitrite (12·4 g., 0·18 mol.) were boiled under reflux in 70% ethanol (60 ml.) for 6 days. Water (30 ml.) was then added and the solution was continuously extracted with chloroform. Evaporation of the chloroform solution yielded a dark liquid which was chromatographed in benzene. Elution with light petroleum yielded unchanged compound (4·58 g., 74%). Chloroform removed a crude unidentified liquid (0·06 g.), and ethanol eluted the *trans*-diol (0·09 g., 3%), characterised as its dibenzoate.

A solution of 1 : 3-2 : 4-di-*O*-ethylidenesorbitol 5 : 6-dinitrate (5·84 g.) and sodium nitrite (3·7 g.) in 80% ethanol (50 ml.) was boiled under reflux for 101 hr. The brown solution was evaporated and the residue was extracted twice with chloroform. Evaporation of the combined chloroform solutions yielded a syrup which was chromatographed in benzene. Elution with this solvent yielded a syrup which, crystallised from ethanol–light petroleum, was unchanged starting compound (0·71 g., 12%). Elution with chloroform yielded a partly crystalline substance which, recrystallised from ethanol–light petroleum, was 1 : 3-2 : 4-di-*O*-ethylidenesorbitol 6-nitrate (1·25 g., 25%). Final elution with ethanol yielded a solid which, recrystallised from ethanol, was 1 : 3-2 : 4-di-*O*-ethylidenesorbitol (0·48 g., 11%).

After reaction for 23 hr., there was negligible discoloration and the products were unchanged starting compound (50%) and the 6-nitrate (15%).

Reaction of trans-cyclo*Hexane*-1 : 2-*diol Dinitrate with Concentrated Sulphuric Acid*.—The dinitrate (4·1 g., 0·02 mol.) was added with shaking during 10 min. to cold concentrated sulphuric acid (12 ml.). The resulting solution was poured into water and the clear aqueous solution was

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[25] Matheson and Angyal, *J.*, 1952, 1133.

neutralised with barium carbonate. The filtrate was evaporated and the resulting solid residue (7·2 g.) was extracted with boiling 80% ethanol (400 ml.). The insoluble portion and the first crop of crystals which separated from the aqueous ethanol were barium nitrate (1·6 g.). The second crop of clustered needles, *barium* trans-cyclo*hexane*-1 : 2-*diol di*(*hydrogen sulphate*) (3·75 g., 46%), was recrystallised twice from 80% ethanol (Found: Ba, 33·39, 33·41. $C_6H_{10}O_8S_2Ba$ requires Ba, 33·37%).

When the reaction solution was left at room temperature for 1 hr., 13 hr., or 30 hr. the same yield of the same product was obtained.

Just enough N-sulphuric acid was added to saturated aqueous barium *trans-cyclo*hexane-1 : 2-diol di(hydrogen sulphate) (8·22 g.) to precipitate all the barium as sulphate. This was removed by centrifugation, and phenylhydrazine (4·10 g.) dissolved in ethanol (10 drops) was added to the solution. Concentration of the solution yielded white crystals of trans-cyclo*hexane*-1 : 2-*diol di*(*hydrogen sulphate*) *bisphenylhydrazine salt* (7·18 g., 73%), m. p. 181—181·5° (decomp.), which after one recrystallisation from *n*-propyl alcohol had m. p. 182·5—183° (decomp.) [Found: equiv., 246·6; C, 43·8; H, 5·8; S, 12·6%. $C_6H_{12}O_8S_2,(C_6H_5\cdot NH\cdot NH_2)_2$ requires equiv., 246·3; C, 43·9; H, 5·7; S, 13·0%]. The salt decomposed after two or more recrystallisations from boiling *n*-propyl alcohol and had m. p. ~177° (decomp.), varying considerably with the rate of heating. After prolonged storage at room temperature in a securely stoppered tube the salt also decomposed.

Reaction of trans-cyclo*Hexane*-1 : 2-*diol with Concentrated Sulphuric Acid*.—Powdered *trans-cyclo*hexane-1 : 2-diol (5·8 g., 0·05 mol.) was stirred into cold concentrated sulphuric acid (20 ml.) during 10 min. The resulting solution was immediately poured into water, and the clear aqueous solution was neutralised with barium carbonate. Evaporation of the filtered solution yielded a white solid (16·7 g., 75%) which recrystallised from 75% ethanol in fine needles of the *dihydrate* of barium *trans-cyclo*hexane-1 : 2-diol di(hydrogen sulphate) (Found: Ba, 30·5, 30·7; loss in wt. at 75°/0·02 mm., 8·50. $C_6H_{10}O_8S_2Ba,2H_2O$ requires Ba, 30·7; H_2O, 8·0%. Found for the anhyd. *salt*: Ba, 33·3, 33·4%).

The bisphenylhydrazine salt had m. p. 182·5—183° (decomp.), undepressed on admixture with a sample prepared from the dinitrate (Found: equiv., 245·1).

A saturated aqueous solution of the di(hydrogen sulphate) was kept at 93° for 17 hr. Continuous extraction of the resulting solution with chloroform yielded *trans-cyclo*hexane-1 : 2-diol (52%) which, recrystallised from acetone, had m. p. 103·5—104°.

Reaction of cis-cyclo*Hexane*-1 : 2-*diol Dinitrate with Concentrated Sulphuric Acid*.—The *cis*-dinitrate (5·15 g.) was treated in a similar manner to the *trans*-isomer except that the mixture of barium salts was extracted with cold dimethylformamide (30 ml.), leaving undissolved barium nitrate (2·3 g.). The solvent was evaporated and the residue was crystallised from 70% ethanol (300 ml.), giving large needles of *barium* cis-cyclo*hexane*-1 : 2-*diol di*(*hydrogen sulphate*) *dihydrate* (4·5 g., 40%) which was recrystallised twice from 70% ethanol (Found: Ba, 30·4, 30·5%). The *anhydrous salt* was obtained on heating the dihydrate at 85°/0·03 mm. (Found: Ba, 33·2, 33·2%).

The procedure used for the *trans*-isomer was employed to make cis-cyclo*hexane*-1 : 2-*diol di*(*hydrogen sulphate*) *bisphenylhydrazine salt* (74%), m. p. 160—161° (decomp.) (Found: equiv., 246·6; C, 44·0; H, 5·6%). This compound decomposed on being kept in a securely stoppered tube at room temperature for several weeks.

Reaction of cis-cyclo*Hexane*-1 : 2-*diol with Concentrated Sulphuric Acid*.—The procedure used for the *trans*-isomer gave barium *cis-cyclo*hexane-1 : 2-diol di(hydrogen sulphate) dihydrate (70%) which was recrystallised from 62% ethanol (Found: Ba, 30·45, 30·4%).

The bisphenylhydrazine salt had m. p. 160—161° (decomp.), undepressed on admixture with a sample prepared from *cis-cyclo*hexane-1 : 2-diol dinitrate (Found: equiv., 246·6).

The *cis*-diol (72%) was obtained after a saturated aqueous solution of the di(hydrogen sulphate) had been heated at 92° for 24 hr.

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