been consumed. At the expiration of twenty-four hours the titration of a 10-cc. subsample required 3.60 cc. of 0.1 *N* sodium hydroxide (using methyl red as indicator), equivalent to 1.96 molecular equivalents of formic acid. As previously mentioned, the oxidation of 1-desoxyxylitol should consume three molecular equivalents of sodium periodate and produce two molecular equivalents of formic acid.

Determination of the Acetaldehyde Produced in the Oxidation of 1-Desoxy-D,L-xylitol by Per-iodic Acid.—A 5-cc. aliquot (0.0737 millimole) of a solution of 0.1003 g. of 1-desoxy-D,L-xylitol in 50 cc. of water was oxidized by per-iodic acid and the acetaldehyde produced was determined by the procedures described by Nicolet and Shinn.[6] The consumption of 0.02 *N* iodine (6.68 cc.) corresponded to 0.0668 millimole of acetaldehyde, equivalent to 0.91 mole of acetaldehyde per mole of 1-desoxy-xylitol. As previously indicated, the expected production of acetaldehyde was one molecular equivalent.

Summary

Proof of the structure of the diacetone xylitol of Tipson and Cretcher is presented. Its tosyl derivative reacts with sodium iodide in acetonylacetone solution to form a crystalline iododiacetonexylitol, which is reduced by hydrogen and Raney nickel to a liquid desoxydiacetonexylitol. The latter substance, upon mild acid hydrolysis, yields a sirupy desoxyxylitol, which must be a 1-desoxy derivative because it is oxidized by per-iodic acid or sodium periodate with the consumption of three moles of oxidant and the production of one mole of acetaldehyde. Owing to the meso configuration of xylitol the substances are racemic mixtures. Their structures may now be described by the following names: 2,3,4,5-di-isopropylidene-D,L-xylitol, 1-tosyl-2,3,4,5-di-isopropylidene-D,L-xylitol, 1-iodo-2,3,4,5-di-isopropylidene-D,L-xylitol, 1-desoxy-2,3,4,5-di-isopropylidene-D,L-xylitol, 1-desoxy-D,L-xylitol. The arrangement of the acetal linkages among the 2,3,4,5-positions remains undecided.

The applicability of the Oldham–Rutherford rule to sugar alcohols is discussed.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY. No. 291]

The Formation of Anhydro Derivatives by the Action of Alkali upon Some Mononitrate-acetates of Glucose and Methylglucoside

BY E. K. GLADDING[1] AND C. B. PURVES

The recognition that the organic esters of sulfonic acids not only are cleaved by alkaline reagents in the sense $R_1R_2R_3C{-}O\vdots SO_2R$, but also in the sense $R_1R_2R_3C\vdots O{-}SO_2R$, explains the frequency with which the course of the reaction resembles the hydrolysis of the corresponding alkyl chloride, $R_1R_2R_3C\vdots Cl$.[2] Walden inversions often occur in both cases[3,4] and today are attributed to the formation of a charged, asymmetric carbonium ion, $R_1R_2R_3C^+$, whose rearrangement to an electrically neutral molecule is associated with the expulsion of a proton. The final molecule may contain a double bond, an anhydro ring, or be combined with a negative group, such as alkoxyl, derived from the environment. These ideas have been very successfully used to explain the chemical behavior of sugar sulfonates in alkaline media[5,6,7] and there is evidence that *p*-toluenesulfonic esters of cellulose react in a similar way.[8]

The mechanism underlying the reaction between alkali and the esters of nitric acid has not been studied extensively and most of the published work is restricted to the identification of the products.[9] Guncotton, for example, suffers rapid oxidative degradation when immersed in aqueous caustic soda, and carbon dioxide and sodium nitrite are formed.[9] Degradation in presence of diphenylamine and traces of copper salts produces oxidized and nitrated derivatives of the base.[10,11] Degradation is marked in ammonia at 65°[12] and we have found that such a weak base as pure, dry pyridine causes a vigorous decomposition of dissolved, stabilized guncotton at steam-bath temperature. Nitrogen dioxide is evolved in this decomposition as a volatile pyridine addition complex that readily crystallizes when cooled. Nef,[13] however, has emphasized that simple, aliphatic nitrates, sulfates

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[1] Du Pont Cellulose Fellow, 1942–1943. Present address, Magnolia Petroleum Co., Field Research Department, Dallas, Texas.

[2] Ferns and Lapworth, *J. Chem. Soc.*, 273 (1912).

[3] Phillips, *ibid.*, 44 (1923).

[4] Kenyon, Phillips and Turley, *ibid.*, 399 (1925). See also Day and Ingold, *Trans. Faraday Soc.*, **37**, 686 (1941), who reviewed the hydrolysis of carboxylic esters.

[5] Hirst and Peat, *Ann. Repts. Chem. Soc.*, **31**, 173 (1934); **32**, 280 (1935).

[6] Peat, *ibid.*, **36**, 258 (1939).

[7] Isbell, *Ann. Rev. Biochem.*, **9**, 65 (1940).

[8] Gardner and Purves, THIS JOURNAL, **65**, 444 (1943).

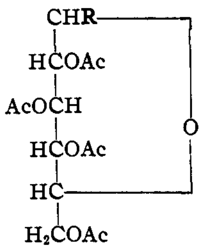
[9] Kenyon and H. LeB. Gray, *ibid.*, **58**, 1422 (1936), referred to many results concerning the decomposition of low-molecular nitrates by alkali.

[10] Maraour, *Bull. soc. chim.*, [5] **3**, 2240 (1936).

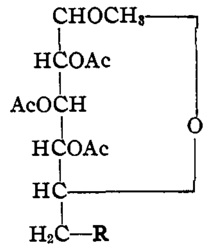
[11] Becker and Hunold, *Z. ges. Schiess- u. Sprengstoffw.*, **33**, 213, 244 (1938). Literature reviews included.

[12] Chernitskaya, Kargin and Gutenmakker, *J. Applied Chem.*, U. S. S. R., **13**, 1159 (1940); *Chem. Abs.*, **35**, 2322 (1941).

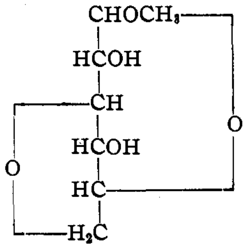
[13] Nef, *Ann.*, **309**, 126 (1899).



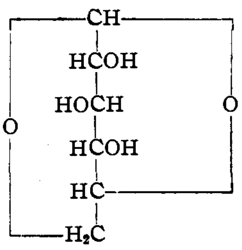
I. R, ONO_2
Ia. R, Cl or Br
Ib. R, $O-SO_2CH_3$
Ic. R, OCH_3



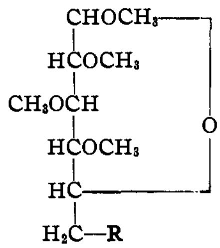
II. R, ONO_2
IIa. R, Cl or Br
IIb. R, $O-SO_2C_7H_7$



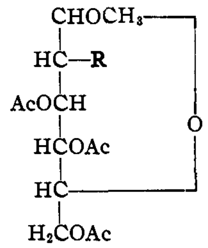
III



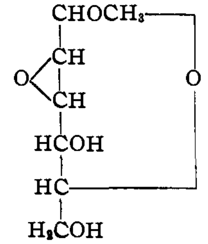
IV



V. R, ONO_2
Va. R, OH
Vb. R, Br



VI. R, ONO_2
VIa. R, $O-SO_2C_7H_7$



VII

and halides are analogous in their behavior toward alcoholic caustic potash, although in the case of the nitrates the formation of unsaturates is suppressed and an oxidation–reduction process often produces potassium nitrite and the corresponding aldehyde or ketone. This process is stated to proceed quantitatively with benzyl nitrate, glycol dinitrate and glycerol trinitrate, but to be completely suppressed with methyl nitrate, which gives large yields of methyl ether. Ethyl and higher nitrates produce ethers mixed with decomposition products derived from carbonyl compounds exposed to excess alkali. A straightforward hydrolysis to the aliphatic alcohol occurs to an extent which, although small, increases with the stability of the nitrate toward alkali. It is also known that the *beta* forms of tetraacetyl glucosyl nitrate (Structure I)[14,15] and chloride (Ia)[15,16] resemble each other in their ready isomerization to the *alpha* configurations and that the latter produce tetraacetyl-β-methylglucoside (Ic) when warmed with methanol and barium carbonate.[17] This reaction apparently involves a Walden inversion. Tetraacetyl glucosyl methylsulfonate (Ib) also gives (Ic) when dissolved in methanol.[18] Another instance of the resemblance between halides, sulfonates and perhaps nitrates is known when these groups are present in the sixth position of methylglucoside (Structures IIa, IIb and II). Aqueous or alcoholic caustic soda produces high yields of 3,6-anhydromethylglucoside (III) from the two former[5,6,7] and the rotatory change undergone by the 6-nitrate (II) suggests that the reaction follows a similar course.[19]

The foregoing illustrations tend to show that the action of alcoholic caustic soda on a carbohydrate nitrate may remove the elements of nitric acid and produce anhydro or alkoxyl derivatives, either with or without Walden inversions. Unsaturated products may possibly be encountered. An ordinary hydrolysis, leading to sodium nitrate and the parent carbohydrate, may also take place and the third possibility is that the nitrate group may be reduced to nitrite and the carbohydrate oxidized to carbonyl derivatives. The latter, of course, would quickly undergo further change in the excess alkali. The present article assesses the practical importance of these possibilities for four simple cases (Structures I, II, V and VI) and demonstrates that the analogy in principle between the behavior of corresponding halogen, *p*-toluenesulfonyl and nitrate derivatives toward alkali is probably of wide application in the carbohydrate field.

Experimental

Materials.—2,3,4,6-Tetraacetyl-α-D-glucopyranosyl nitrate (α-acetonitroglucose, I) was prepared by nitrating 10 g. of dry, commercial *beta*, not *alpha*, glucose pentacetate dissolved in 100 cc. of chloroform with an equal volume of ice-cold, chloroform-soluble nitric acid.[17,20] The observed m. p., 148–49° (cor.), and specific rotation in chloroform, 148°,[21] were each one degree less than the recorded values.

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[14] Skraup and Kremann, *Monatsh.*, **22**, 1037 (1901).

[15] Schlubach, Stadler and Wolf, *Ber.*, **61**, 287 (1928).

[16] Schlubach, *ibid.*, **59**, 840 (1926).

[17] Koenigs and Knorr, *ibid.*, **34**, 957 (1901).

[18] Helferich and Gnüchtel, *Ber.*, **71**, 712 (1938). The methylsulfonate had a specific rotation of 121.4° in chloroform and in consequence was probably of the alpha configuration.

[19] Oldham, *J. Chem. Soc.*, 2841 (1925).

[20] Behrend and Roth, *Ann.*, **331**, 359 (1904).

[21] Unless otherwise stated, all specific rotations were observed at 20° with sodium light, and m. p.'s were corrected for the emergent thermometer stem.

Crude, crystalline D-glucosan<1,5>β<1,6> prepared from starch was methylated[22] and the resulting, crystallized trimethyl derivative on nitration gave crystalline 2,3,4-trimethyl-α-glucosyl-1,6-dinitrate. The latter, when boiled with methanol and barium carbonate, gave 2,3,4-trimethyl-β-methyl-D-glucopyranoside-6-nitrate (V) in an over-all yield of 50%. The product, m. p. 52–54°, had a specific levorotation, observed at 25° in chloroform, of −7° (*c*, 4.35) and analyzed correctly. Oldham[19] found the levorotation to be −5.2° but otherwise the physical constants and yields he recorded were checked throughout the synthesis.

The preparation and properties of 2,3,4-triacetyl-α-methyl-D-glucopyranoside-6-nitrate (II) and 3,4,6-triacetyl-β-methyl-D-glucopyranoside-2-nitrate (VI) have been described elsewhere.[23]

Methods.—A solution made by diluting 30 cc. of 4 *N* aqueous caustic soda to 100 cc. with methanol was used in determining the alkali-lability of the nitrate groups (Fig. 1). Samples weighing 0.10 to 0.14 g. were shaken at room temperature with 5-cc. aliquots of the alkali until solution was complete. Duplicate solutions were titrated at different times with 0.1 *N* hydrochloric acid. Miller's method of estimating nitrite[24] was used because it is valid in presence of a large excess of nitrate. A stock solution contained 30 cc. of water, 50 cc. of concentrated hydrochloric acid and 20 cc. of dimethylaniline that was free from the monomethyl derivative. This solution did not deteriorate noticeably when stored in the dark. A small aliquot, 0.25 to 1.0 cc., of the nitrite solution was made acid to litmus with hydrochloric acid and was diluted to 10 cc. with water. The addition of 0.5 cc. of the stock solution produced intensely yellow *p*-nitrosodimethylaniline and the transmission of light by the solution became constant within two hours. A photoelectric colorimeter, a blue filter and 1-cm. glass cells were used to estimate the transmission, and distilled water in an identical cell was the standard taken for 100% transmission.

The standard nitrite solution contained 0.5050 g. of the c. p. sodium salt in 500 cc. of water, or 14.6 × 10^{-6} mole of nitrite in 1 cc. Dilutions were made to bracket the concentration of nitrite in the unknown. Although Beer's law did not apply exactly, a plot of log % transmission against nitrite concentration was linear up to about 2 × 10^{-6} mole per cc.

Action of Alkali on α-Acetonitroglucose (I) (A).—A suspension of 5.04 g. (0.017 mole) of the acetonitroglucose in 100 cc. of methanol was mixed at room temperature with 50 cc. of absolute 1.75 *N* sodium methylate (0.088 mole). Solution was complete within five minutes and the molecular rotation of the slightly yellow liquid acquired a final constant value of −6,500 within ten minutes. The solution was acidified with glacial acetic acid after one hour and was evaporated to dryness under diminished pressure. The product obtained by acetylating the residue with pyridine, 30 cc., and acetic anhydride, 15 cc., contained constituents, 3.56 g., that were extracted from the aqueous acetylation liquors by chloroform. These constituents partly crystallized when seeded with tetraacetyl-β-methylglucopyranoside and recrystallizations from 6-cc. volumes of methanol left 1.3 g. (28%) of this substance as hexagonal plates or stout prisms with the correct elementary analysis. The m. p., 102.5–104.5° (cor.), and the specific levorotation of −18.0° in chloroform agreed with the accepted constants.[25]

A duplicate experiment gave 3.49 g. of crude, acetylated material which on this occasion crystallized completely, rather than partly, to a hard mass, m. p. 83–90°. Four recrystallizations from methanol and ethanol alternately left the main fraction still melting over the broad range of 85 to 102° and with a specific levorotation of −28.6° in methanol. A brief microscopic examination, kindly carried out by Dr. T. R. P. Gibb, showed all the crystals to be biaxial and probably monoclinic with large optic angles. The optic sign was usually positive but was negative for a few rod-like crystals. The mother liquors yielded prismatic needles, m. p. 80–90°, with a rotation of −34° in methanol.

Since the first experiment proved that at least 1.3 g. of tetraacetyl-β-methylglucoside was present, and since this substance had a specific levorotation of −21.8° in methanol,[25] the remaining constituent, or constituents, of the mixture had a levorotation of at least −40°. Triacetylglucosan occurs as needles and has a levorotation of −45.5° in methanol.[26] *Anal.* Calcd. for tetraacetylmethylglucoside: acetyl, 47.5; OCH_3, 8.56. Calcd. for triacetylglucosan; acetyl, 44.8; OCH_3, 0.0. Found for main fraction prior to powdering and mixing: acetyl, 46.8; OCH_3, 3.1, 8.1.

(B) A solution of 10 g. (0.034 mole) of acetonitroglucose in 50 cc. of peroxide-free 1,4-dioxane was cooled in a water-bath and stirred while 100 cc. of 1.75 *N* aqueous caustic soda was added slowly. The mixture at first became cloudy but subsequently clarified to give a slightly yellow solution whose color quickly darkened. After standing for twenty-four hours, a 1-cc. sample of the very dark brown liquid contained 8.1 × 10^{-6} mole of nitrite, corresponding to 4.5% of the original nitrate groups.

The remainder was acidified with acetic acid and was evaporated under reduced pressure to a dark gum. Methylation[22] of this gum gave a chloroform-soluble product that distilled completely at 112–114° (5 mm.) and crystallized completely when nucleated with 2,3,4-trimethylglucosan <1,5>β<1,6>; yield, 1.8 g. or 33%. Two recrystallizations from ether left the long needles with m. p. 56–58° and a specific levorotation of −61.8° in water. Trimethylglucosan, which is difficult to purify, has m. p. 62–65° and a rotation of −63.5°.[27a] A mixed m. p. with an authentic sample was not depressed and the elementary analyses were satisfactory.

Action of Alkali on Triacetyl-α-methylglucoside-6-nitrate (II).—(A) The sample, 6.08 g. or 0.0167 mole, was wetted with 38 cc. of ethanol and the total volume was made up to 60 cc. with aqueous, 4 *N* caustic soda (about 0.08 mole). After solution was complete (thirty minutes), the liquid was kept at 75–80° for seventy minutes or until its molecular rotation had decreased to 9,180°. A quantitative conversion to the 3,6-anhydro derivative required M_D 9,850°. One cc. of the liquid contained 5.2 × 10^{-6} mole of nitrite, corresponding to 1.9% of the original nitrate.

The remaining 53 cc. was acidified with acetic acid and evaporated under reduced pressure to dryness. Five 25-cc. volumes of boiling acetone extracted the product, which was recovered and dissolved in 20 cc. of hot ethyl acetate. This solution was dried with a little anhydrous sodium sulfate and after filtration was evaporated. The residual, straw colored sirup crystallized solidly when nucleated with 3,6-anhydro-α-methylglucopyranoside (III); yield, 2.0 g. or 77%. After two recrystallizations from ethyl acetate, the m. p. of the product, 105.5–107.5°, and the specific rotation of 56.5° in water agreed with the constants of the 3,6-anhydro derivative.[28] The elementary analysis also checked.

A duplicate experiment was carried out in which the mixture of triacetyl methylglucoside-6-nitrate and alkali was kept at room temperature for two days. Since the molecular rotation decreased to 13,300 in these conditions, instead of to the proper value of 9,850, the reaction was completed by heating at 70° for thirty minutes. An 88% yield of crystalline anhydro-methylglucoside was isolated and 2% of the nitrate groups were reduced to nitrite.

(B) A suspension of 5.03 g. (0.0138 mole) of the triacetyl methylglucoside-6-nitrate in 100 cc. of absolute methanol was mixed at room temperature with 50 cc. of freshly pre-

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(22) West and Holden, THIS JOURNAL, **56**, 930 (1934).

(23) Gladding and Purves, *ibid.*, **66**, 153 (1944).

(24) Miller, *Analyst*, **37**, 345 (1912). See also Snell and Snell, "Colorimetric Methods of Analysis," D. van Nostrand Co., New York, 1937, Vol. I, p. 647.

(25) Hudson and Dale, THIS JOURNAL, **37**, 1264 (1915).

(26) Tanret, *Bull. soc. chim.*, [3] **11**, 949 (1894).

(27) Irvine and Oldham, *J. Chem. Soc.*, (a) 1744 (1921); (b) 2729 (1925).

(28) Haworth, Owen and Smith, *ibid.*, 88 (1941).

pared, 1.3 *N* sodium methylate in methanol. Solution was complete within five minutes but the molecular rotation decreased to the nearly correct value of 9,890 only after forty-eight days. The crude, crystalline product amounted to 1.72 g., or 77%, and an easy purification left it with physical constants in agreement with those already given for 3,6-anhydro-α-methylglucopyranoside.

Action of Alkali on 2,3,4-Trimethyl-β-methylglucoside-6-nitrate (V).—A 5.06 g. (0.018 mole) sample of the 6-nitrate was heated at 60° with 4.0 g. (0.10 mole) of caustic soda dissolved in 150 cc. of 50% aqueous methanol. The container was an Erlenmeyer flask with a wired-in rubber stopper. Solution of the 6-nitrate was complete within two hours but the liquid was too discolored to be observed on the polarimeter. The consumption of alkali, followed by titrating 5-cc. aliquots with standard acid, amounted to 1.17, 1.38 and 1.46 moles per nitrate group after six, twenty and twenty-four hours, respectively, of heating at 60°. These measurements were corrected by means of blank experiments containing none of the methylglucoside nitrate. Aliquots of 0.25 and 0.35 cc., withdrawn at the latter time, contained 11.5 × 10^{-6} and 17 × 10^{-6} mole of nitrite, corresponding to 19 and 20% of the original nitrate.

The remaining 59 cc. of the original solution was extracted while still alkaline with two 50-cc. volumes of chloroform. These extracts, after being combined, dried and evaporated, yielded 2.0 g. of a colorless sirup that quickly crystallized. After recrystallizations from 50 and 30 cc. volumes of warm ligroin, the long white needles melted at 92.5–93.5° and had specific levorotations at 25° of −20.8° in methanol and −21.2° in chloroform. A m. p. of 93–94°, rotations of −22.9°[27] to −25.1° in methanol,[29] and of −20.6° in chloroform,[30] have been observed for 2,3,4-trimethyl-β-methylglucopyranoside. An 0.130-g. sample of this substance would liberate 12.3 cc. of methane, corrected to N. T. P., in a Zerewitinoff estimation of active hydrogen. The value found was 12.7 cc.

The aqueous residue from the chloroform extractions was acidified with hydrochloric acid and then re-extracted with chloroform. A dark sirup, 0.5 g. recovered from the extract crystallized spontaneously and nearly completely. Recrystallization from ligroin gave long needles that were non-acidic, contained no double bonds and melted at 87–93°. Since this product was identified as slightly impure 2,3,4-trimethyl-β-methylglucopyranoside, the total crude yield of the latter was raised to 2.5 g. or to 75%.

Action of Alkali on 3,4,6-Triacetyl-β-methylglucoside-2-nitrate (VI).—A solution of 6.06 g. of the 2-nitrate in 18 cc. of peroxide-free dioxane was shaken at room temperature with 60 cc. of 1.67 *N* aqueous sodium hydroxide and precipitated material redissolved within two hours. Table I gives the subsequent change in the observed and the molecular rotation of the solution, whose volume was 77 cc.

TABLE I

ROTATORY CHANGE OF THE METHYLGLUCOSIDE-2-NITRATE IN ALKALI

Hours	α^a	$[M]_D$	Hours	α^a	$[M]_D$
2.5	−3.25°	−15,000°	5.5	−3.86°	−17,900°
3.5	3.50	16,200	8.7	4.02	18,600
4.0	3.63	16,800	10.4	4.17	19,300
4.5	3.73	17,300	23	4.58	21,200[b]

[a] Observed in a 1-dm. tube. [b] Corresponds to a specific levorotation of −120° if anhydromethylhexoside (mol. wt. 176) was the sole product.

After twenty-three hours, 3-cc. samples contained 14.7 × 10^{-6} mole of nitrite, equivalent to 2.3% of the original nitrate groups.

The remainder of the solution, 72 cc., was examined by the methods already described for the isolation of 3,6-anhydromethylglucoside. A clear, colorless sirup resulted in a yield of 2.30 g. or 84%, and with a specific levorotation of −101° in water at 26°. A negative test for nitrate groups was obtained with ferrous sulfate and concentrated sulfuric acid. In a test for the presence of unsubstituted, adjacent hydroxyl groups, an 0.0545-g. sample reduced 0.7 cc. of 0.1 *N* sodium periodate at *p*H 4.1 in two hours, or in circumstances where 1 mole of methylglucopyranoside reduced the correct amount of 2 mole.[31] The estimation showed that the amount of any methylhexopyranoside present in the sirup did not exceed 5 or 6%. An 0.3-g. sample of the sirup, when acetylated with acetic anhydride and pyridine, gave 0.29 g. of an uncrystallized acetate with a levorotation of −68.8° in chloroform. This acetate required 7.85 cc. of *N* sodium hydroxide per gram in an acetyl estimation. Calcd. for the diacetate of an anhydromethylhexoside, 7.73 cc.; for the tetraacetate of a methylhexoside, 11.5 cc.

The remainder of the unacetylated sirup, 1.9 g., partly crystallized. Cautious dilution of the mass with 10 cc. of ethyl acetate–ethyl ether led to the separation of 0.18 g. of long, feathery needles melting at 127–136° and with a specific levorotation of −111° in water. An 0.0493-g. sample reduced 0.765 cc. of 0.1 *N* sodium periodate or 0.07 mole per mole of crystals, calculated as anhydromethylhexoside. Evaporation of the mother liquors from the crystals gave a residual sirup with a specific levorotation of −106° in water. When a 2.58% solution in 0.01 *N* hydrochloric acid was heated on the steam-bath,[32,33] the rotations observed in a 1-dm. tube were −2.72 (calcd), −1.26, −0.85 and −0.65° after zero, thirty, one hundred and twenty and two hundred minutes, respectively. The solution had developed reducing properties and quickly deposited a yellow precipitate when treated at room temperature with 3 cc. of acetic acid and 2.5 cc. of phenylhydrazine. This precipitate was too small in amount for a detailed examination. The development of reducing power, however, showed that methylglycosidic groups in the sirup had been hydrolyzed.

Anal. Calcd. for an anhydromethylhexoside, $C_7H_{12}O_5$: C, 47.7; H, 6.8, OCH_3, 17.6. Calcd. for a methylhexoside, $C_7H_{14}O_6$: C, 43.3; H, 7.2; OCH_3, 16.0. Found for the crystals: C, 46.4, 45.9, 46.0; H, 6.9, 7.1, 6.9. Found for the residual sirup: C, 46.0, 45.7, 45.4; H, 7.1, 7.3[34]; OCH_3, 16.4. Neither the crystals nor the sirup were obtained in a pure condition. Although the sirup was volatile at 150–165° (3 mm.), an attempt to purify it by vacuum distillation failed owing to rapid decomposition.

Discussion

The quick neutralization of five moles of alkali by tetraacetyl-α-glucosyl nitrate (Structure I, Fig. 1) confirms the fact that the nitrate group in the reducing position of glucose is at least as labile as the four acetyl groups. The yellow gum obtained by dissolving the nitrate in absolute sodium methylate was acetylated prior to examination and the chloroform-soluble portion amounted to 75%. On one occasion, when the crude, acetylated product crystallized spontaneously but incompletely, there was no difficulty in isolating a 28% yield of crystalline tetraacetyl-β-methylglucoside (Ic) and in characterizing it definitely. Crystallization of the crude product was complete on a subsequent occasion and an attempt to isolate the glucoside by fractional recrystallization was unsuccessful. The physical properties of the fractions suggested that the

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[29] Haworth and Wylam, *J. Chem. Soc.*, 3120 (1923).

[30] Fowler, Buckland, Brauns and Hibbert, *Can. J. Research*, **15B**, 486 (1937).

[31] *Cf.* Malaprade, *Bull. soc. chim.*, [5] **1**, 833 (1934).

[32] Haworth, *Ber.*, **65A**, 43 (1932).

[33] Haworth, Porter and Waine, *J. Chem. Soc.*, 2254 (1932).

[34] These microcombustions were carried out by Miss Zelma Weiss, to whom the authors express their thanks.

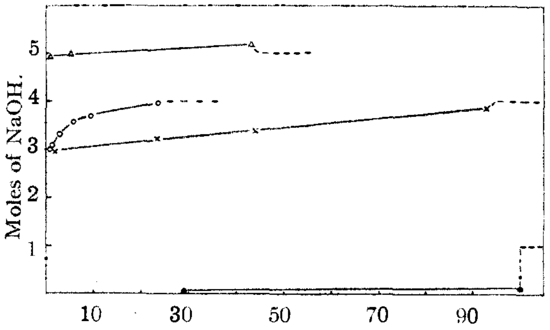

Fig. 1.—Rates of de-acylation by 1.2 *N* aqueous methanolic sodium hydroxide at 25°: 2,3,4,6-tetraacetyl-α-glucosyl-1-nitrate, △; 3,4,6-triacetyl-β-methylglucoside-2-nitrate, ○; 2,3,4-triacetyl-α-methylglucoside-6-nitrate, ×, and 2,3,4-trimethyl-β-methylglucoside-6-nitrate, ●; broken lines show theoretical consumptions of alkali.

original was a mixture of almost equal amounts of tetraacetyl-β-methylglucoside and the more levorotatory triacetylglucosan $<1,5>\beta<1,6>$. This interpretation was confirmed when the formation of methylglucoside was suppressed by replacing the absolute sodium methylate with caustic soda dissolved in aqueous dioxane, glucosan (IV) being isolated in 33% yield as the crystalline, trimethyl derivative. The formation of glucosan in these reactions completes the analogy between the behavior of tetraacetyl glucosyl-α-nitrate and the corresponding α-bromide (Ia), which is known to give glucosan when treated in succession with trimethylamine and aqueous barium hydroxide.[35] The analogy, indeed, suggests that the trimethylamine step in the latter preparation may be unnecessary. It is plausible to assume that alkali forms the same carbonium ion from both the α-nitrate and the α-bromide and that a Walden inversion occurs as this ion combines with solvent methanol to give β-methylglucoside, or with the primary alcoholic group of the glucose residue to give glucosan. The explanation, however, fails to account for the formation of glucosan in similar conditions from beta, but not from alpha, phenylglucoside[36] and must at present be accepted with great reserve.

About one quarter of the tetraacetylglucosyl nitrate used in the experiments with absolute sodium methylate produced a yellow gum that was not examined in detail. A much darker colored gum comprised two-thirds of the product obtained with caustic soda in aqueous dioxane. Since only 4.5% of the nitrate groups was reduced to sodium nitrite in the latter experiment, the oxidation of carbohydrate during denitration was likewise insignificant and the gum did not originate in the action of excess alkali upon oxidized glucose residues. This action was probably exerted upon glucose, or upon a reducing intermediate at the glucose level of oxidation, that was formed during denitration. It is apparent that such substances did not reduce sodium nitrate to nitrite in the experimental conditions.

The nitrate group in 2,3,4-triacetyl-α-methylglucoside-6-nitrate (II) neutralized one mole of alkali more slowly than the three acetyl groups (Fig. 1) and only 2% was identified as sodium nitrite in the resulting, nearly colorless solution. Both aqueous alcoholic caustic soda and absolute sodium methylate caused the molecular rotation of the 6-nitrate to decrease to a value corresponding to a practically quantitative formation of 3,6-anhydro-α-methylglucopyranoside (III)[19] and in both cases 77–88% yields of this substance were isolated in a crystalline condition. The preparation of the anhydroglucoside from the 6-nitrate, therefore, proceeds at least as smoothly as those employing the 6-bromo (IIa),[37] the 6-*p*-toluenesulfonyl (IIb)[28] or the 6-sulfonyl[38] derivative.

The nitrate group in 3,4,6-triacetyl-β-methylglucoside-2-nitrate (VI) was removed by alkali somewhat more rapidly than that in the isomeric 6-nitrate (Fig. 1), and only 2.3% was reduced to sodium nitrite. Sodium hydroxide dissolved in aqueous dioxane gave an 84% yield of a clear, colorless, non-reducing, nitrate-free sirup about one-tenth of which eventually crystallized as needles, m. p. 127–136°. Analytical data and physical properties showed that both the crystals and the residual sirup were impure anhydromethylhexosides. An estimation for unsubstituted, adjacent hydroxyl groups by the periodate method showed that, if methylhexoside was present, its amount did not exceed 6% in either fraction. This denitration, therefore, followed a path fundamentally similar to that observed for the deacylation of 2-*p*-toluenesulfonyl-β-methylglucoside (VIa) to a sirup consisting mainly of 2,3-anhydro-β-methyl mannoside (VII).[39,40] The latter sirup, however, had a levorotation of −25° in water, whereas the rotations of the crystals and the residual sirup isolated from the 2-nitrate were −111 and −106°, respectively. Perhaps the discrepancy is connected with the use of sodium methylate in chloroform at 0° as the alkali in one case and sodium hydroxide in aqueous dioxane at 25° in the other. The first reagent produced an anhydro sirup with a specific levorotation of −80 to −90° from triacetyl-3-*p*-toluenesulfonyl-β-methylglucoside[41] in circumstances where a boiling solution of sodium hydroxide in aqueous acetone yielded a product with the large levorotation of −328°.[42] Ohle and Wilcke[42] are of the opinion that 2,3-anhydro derivatives may

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[35] Karrer and Smirnhoff, *Helv. Chim. Acta*, **4**, 817 (1921).

[36] Montgomery, Richtmyer and Hudson, This Journal, **65**, (1943).

[37] Fischer and Zach, *Ber.*, **45**, 456 (1912).

[38] Duff and Percival, *J. Chem. Soc.*, 830 (1941).

[39] Haworth, Hirst and Panizzon, *ibid.*, 154 (1934).

[40] Lake and Peat, *ibid.*, 1417 (1938).

[41] Peat and Wiggins, *ibid.*, 1088 (1938).

[42] Ohle and Wilcke, *Ber.*, **71**, 2316 (1938).

sometimes rearrange to other anhydro structures, such as the 3,6, either with or without Walden inversions. Although an examination of the mixture from the methylglucoside-2-nitrate along these lines was outside the scope of the present work, it was observed that at least a portion resembled 3,6-anhydromethylhexosides to the extent that the glucosidic group was very readily removed by acid hydrolysis.[28]

The three denitrations already discussed tend to show that the preferred alkaline cleavage of carbohydrate nitrate groups takes place in the sense $R_1R_2CH{\vdots}O{-}NO_2$ and leads to the quick expulsion of the elements of nitric acid in a substantially unreduced condition. The dependence of this method of elimination upon a facile production of methylglucoside or anhydro structures is illustrated in Fig. 1, by the relatively great stability displayed toward alkali by 2,3,4-trimethyl-β-methylglucoside-6-nitrate (V), in which the methyl ether groups block anhydro formation. More drastic conditions promoted a straightforward hydrolysis to crystalline 2,3,4-trimethyl methylglucoside (Va), which was isolated in 75% yield. The alkaline hydrolyses of the "blocked" *p*-toluenesulfonyl radicals in such substances as 2-tosyl-3,4,6-trimethyl-β-methylglucoside[39], 2-methyl-3,4-isopropylidine-6-tosyl-α-methylgalactoside[43] and 2,5-dimethyl-3-tosyl-β-methylxylofuranoside[44] proceed with difficulty but often in high yield along exactly the same lines. No Walden inversions were observed[45] and the hydrolyses were therefore attributed to scission in the sense $R_1R_2CH{-}O{\vdots}SO_2C_7H_7$. It is probably legitimate to assume the similar mechanism, $R_1CH_2{-}O{\vdots}NO_2$, for the scission of the "blocked" nitrate group in the present case.

The most interesting aspect of this denitration was the reduction of no less than 20% of the organic nitrate to sodium nitrite and the decomposition of up to 25% of the methylated carbohydrate to a discolored tar that slowly neutralized some of the excess alkali. These occurrences showed unequivocally that the direct hydrolysis of "blocked" nitrate groups was slow enough to render the still slower side-reaction, $R_1CH_2{-}O{-}NO_2 \rightarrow R_1CHO + HNO_2$, of considerable importance. When it is remembered that a proton is readily expelled from the methylene group in benzyl alcohol and that the oxidative cleavage is quantitative with benzyl nitrate,[13] it appears possible that the mechanism involves the loss of a methylene proton from the scission fragment $R_1CH_2{-}O{-}$ and rearrangement to $R_1CH{=}O$. This mechanism resembles that advanced to explain the formation of *p*-toluenesulfinic acid when certain N-benzyl sulfonamides are heated in strong alkali,[46] although no search seems to have been made for sulfinic acids among the hydrolysis products of "blocked" sulfonyl residues in carbohydrates. The alkaline hydrolysis of 6-bromo-2,3,4-trimethyl-β-methylglucoside (Vb) is reported to yield unsaturated substances[27b]; presumably by the loss of halogen from the sixth carbon atom and of a proton from the adjacent, rather than from the same, position.

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Summary

1. When 2,3,4-triacetyl-α-methylglucopyranoside-6-nitrate was denitrated by aqueous or alcoholic caustic soda, the product consisted almost entirely of 3,6-anhydro-α-methylglucopyranoside. An 84% yield of a semi-crystalline mixture of crude anhydro methylhexosides was recovered after submitting 3,4,6-triacetyl-β-methylglucopyranoside-2-nitrate to a similar denitration. The constitution of the mixture was not examined in detail.

2. 2,3,4,6-Tetraacetyl-α-glucosyl nitrate and absolute sodium methylate produced a 75% yield of β-methylglucopyranoside mixed with a second substance, which was supposed to be glucosan <1,5>β<1,6>. The latter was isolated in 33% yield when aqueous alcoholic sodium hydroxide was substituted for the absolute sodium methylate.

3. Aqueous alcoholic sodium hydroxide slowly hydrolyzed 2,3,4-trimethyl-β-methylglucopyranoside-6-nitrate to the 2,3,4-trimethylglucoside in 75% yield. The remainder was recovered as a discolored gum and 20% of the nitrate groups was reduced to sodium nitrite. Only 2 to 4.5% of nitrite resulted in (1) and (2) where an easy formation of methylglucoside or of anhydro derivatives was possible.

4. The very close analogy between the behavior toward alkali of these nitrates and the corresponding *p*-toluenesulfonyl, sulfonyl and halide derivatives was emphasized.

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(43) Bell and Williamson, *J. Chem. Soc.*, 1196 (1938).

(44) Robertson and Gall, *ibid.*, 1600 (1937).

(45) Cutler and Peat, *ibid.*, 782 (1939), cite other literature references.

(46) Holmes and Ingold, *ibid.*, 1305 (1926). See also review on mechanism and kinetics of elimination reactions by Hughes and Ingold, *Trans. Faraday Soc.*, **37**, 657 (1941).